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Spectrophotometric Determination of Lercanidipine Hydrochloride in Pharmaceutical Formulations

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ABSTRACT;Three simple, precise, accurate and economical UV spectrophotometric methods have been developed and validated for the routine estimation of lercanidipine hydrochloride in bulk drug and pharmaceutical preparations. Standard stock solution was prepared in methanol and further dilutions were carried out with same solvent. The resulting solutions were then scanned in the UV range (200-400nm) in a 10 mm matched quartz cells in a double beam UV-Visible spectrophotometer. The drug shows maximum absorption at 236nm. The same spectrum was derivatised into first order, second order, third order and fourth order derivative, but it shows good derivatised spectrum in D_2 and D_3. The amplitude of the crest at 238nm for D_2 and amplitude of crest at 234nm for D_3 were measured. In these methods the drug obeyed Beer-Lambert's law in the concentration range of 2.5-60µg/ml. The linear regression equations were calculated to be y = 0.0484x-0.0213(R^2=0.9991) for D_0, y = -0.0062x+0.0011(R^2=0.9993) for D_2, and y= -0.0081x+0.0007(R^2=0.9997) for D_3 respectively. The results of estimation of marketed tablet formulations were found to be 99.05±0.002 with their %RSD less than 2. Recovery studies were carried out by addition of known amount of standard drug (80,100 and 120% of labeled claim of a tablet) to the preanalysed tablet solution. The % recovery was found to be 97.218±0.175-100.018±0.373, which indicates accuracy and reliability of the validated methods as well as non-interference from excipients to the developed methods. The intraday and inter day assay was within 2%. The methods were then validated statistically as per the ICH guidelines which yielded good results concerning range, precision, accuracy, specificity, robustness and ruggedness.
Keywords: Lercanidipine Hydrochloride, Spectrophotometry, Validation.

INTRODUCTION

Lercanidipine hydrochloride is chemically described as 3-O-[1-[3, 3-diphenylpropyl (methyl) amino]-2-methylpropan-2-yl] 5-O-methyl 2, 6-dimethyl-4-(3-nitrophenyl)-1, 4-dihydropyridine-3, 5-dicarboxylate hydrochloride. It is a new third generation Ca-antagonist used in the treatment of hypertension [1]. The drug is official in Merck index [2] and Martindale [3]. The literature survey reveals that only few methods have been reported for the determination of Lercanidipine hydrochloride including UV spectrophotometric [4-5], LC–ESI–MS/MS [6], HPLC [7-8], Voltammetric method [9] etc. However no suitable derivative spectrophotometric method is reported till date for the estimation of Lercanidipine hydrochloride. In the present study simple, accurate and precise spectrophotometric methods have been developed for the estimation of Lercanidipine hydrochloride in bulk as well as in pharmaceutical formulations.

MATERIALS AND METHODS

Instrument

Absorbance measurements were made on THERMO UV_1 UV/Visible double beam spectrophotometer with spectral bandwidth 2 nm and 10mm matched quartz cuvettes.

Reagents and solutions

Pharmaceutical grade of Lercanidipine Hydrochloride was gifted by Alembic Limited, Vadodara, India and certified to contain 99.7% of lercanidipine hydrochloride.It was used without further purification. The methanol used was of analytical grade produced by Merck Pvt. Ltd, India.

Preparation of calibration curve

Standard stock solution of Lercanidipine hydrochloride was prepared in methanol. Working standard solutions of Lercanidipine hydrochloride was prepared by taking suitable aliquots of standard drug solution (1000 µg/ml) and volume was made up to 10 ml with methanol. The resulting solutions were then scanned in the UV range (200-400nm) in a 10 mm matched quartz cells in a UV-Visible double beam spectrophotometer. The drug shows maximum absorption at 236nm (fig-1). The same spectrum was derivatised into first order, second order, third order and fourth order derivative, but it shows good derivatised spectrum in D_2 and D_3. The amplitude of the crest at 238nm for D_2 (fig-2) and amplitude of crest at 234nm for D_3 (fig-3) were measured. In these methods the drug obeyed Beer-Lambert's law in the concentration range of 2.5-60µg/ml. The linear regression equations were calculated to be $y=0.0484x-0.0213$($R^2=0.9991$) for D_0 (fig-4), $y=-0.0062x+0.0011$($R^2=0.9993$) for D_2 (fig-5), and $y= -0.0081x+0.0007$($R^2=0.9997$) for D_3 (fig-6) respectively.

Analysis of tablet

Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 10mg of Lercanidipine hydrochloride and 5-7ml of methanol were taken in a 10ml volumetric flask , sonicated for about 30mins, and the volume was made up to 10ml with methanol and filtered by using Whattmann filter paper. From the filtrate an appropriate aliquot was taken in such a way that the final concentration in 10ml lies within the range tested and scanned in the UV range (200-400nm). The same spectrum was derivatised into second order and third order derivative, the amplitude of the crest at 238nm for D_2 and amplitude of crest at 234nm for D_3 were measured. The amount of drug present in the tablet was calculated from the standard graphs. (Table-3)

Method Validation

The developed methods were validated for its accuracy, precision, reproducibility and selectivity. The accuracy of the methods was determined by performing recovery studies on tablet formulation and for prepared solutions containing known amount of drug by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels (80,100 and 120%.) The results are shown in table 4. Also, the experiment was repeated three times in a day to determine intra-day precision and on three different days to determine inter-day precision. The percent relative standard deviations (%RSD) were calculated at each concentration level and the result is given in table 2 .The reproducibility was confirmed by repeating the methods by three different analysts and the % RSD were calculated. The selectivity of the methods was checked by monitoring a standard solution of Lercanidipine hydrochloride in presence of excipients at the same concentration levels as used in tablet using the methods described in the procedure for calibration curves in pharmaceutical tablets.

RESULTS AND DISCUSSION

The proposed methods are simple, rapid and precise and do not suffer from any interference due to excipients of tablet. Various optical characteristics are shown in the table1.The proposed spectrophotometric methods were found to be linear in the range of 2.5-60µg/ml with correlation coefficients (R^2) of 0.9991, 0.9993, and 0.9997 for Do, D_2, D_3 respectively. The regression equations are shown in the table 2. The methods were validated in terms of accuracy, precision, reproducibility and the results are recorded in table 2and 4. The accuracy of the methods was determined by performing recovery studies by standard addition of method in which preanalyzed samples were taken and standard drug was added at three different levels. Values of recovery±SD greater than 97.0% indicate that proposed methods are accurate for the analysis of the drug. The precision of the proposed methods was estimated in terms of inter-day precision and intra-day precision wherein the methods were repeated on three different days and repeated for three different time periods in the same day respectively. The results shown in table 4 indicating %RSD of less than 2% at each level clearly indicate that the proposed methods are precise enough for the analysis of the drug. The reproducibility of the methods was confirmed by performing the proposed methods by three different analysts. The values of %RSD less than 2% indicate that the proposed methods are reproducible for the analysis of Lercanidipine hydrochloride. The selectivity of the methods was checked by monitoring a standard solution of Lercanidipine hydrochloride in presence of excipients at the same concentration level as used in tablet using the methods described in the procedure for calibration curve in pharmaceutical tablets. The excipients too did not show any effect on the estimation of Lercanidipine hydrochloride. Hence, the determination of Lercanidipine hydrochloride in the tablet is considered to be free from interference due to the excipients. Rigorous analysis of the results indicates that the presence of excipients in tablet formulation did not interfere with the final determination of the active component. This reveals that the potential utility of these methods for the routine analysis of Lercanidipine hydrochloride in pharmaceutical preparations.

Table 1 Optical characteristics for Lercanidipine Hydrochloride

Parameters	Obtained Values		
	Do	D_2	D_3
λ_{max}	236nm	238nm	234nm
Beer's Law limit(µg/ml)	2.5-60	2.5-60	2.5-60
Sandell's sensitivity (µg/cm²/0.001 AU)	0.021739	-0.166666	-0.125
Molar extinction Coefficient($L.mole^{-1}.cm^{-1}$)	2.9×10^4	-3.8×10^3	-5.18×10^3
%RSD	1.630737	-1.73238	-1.85062
Regression equation(Y)*	0.0484x-0.0213	-0.0062x+0.0011	-0.0081x+0.0007
%Range of error 0.05 confidence limits 0.01 confidence limits	 ±0.5155 ±0.6786	 ±0.0717 ±0.0944	 ±0.1043 ±0.1373
Correlation co-efficient	0.9991	0.9993	0.9997

Y*=aX+b, where 'a' is slope,'b' is intercept,'X' is concentration in µg/ml and'y' is absorbance unit.

Table 2 Validation Parameters

Sl No.	Parameters		D_0 (At 236nm)	D_2 (at 238nm)	D_3 (at 234nm)
1	Linearity	µg/ml	0.5-60	0.5-60	0.5-60
		Regression eq^n	0.0484x-0.0213	-0.0062x+0.0011	-0.0081x+0.0007
		R^2	0.9991	0.9993	0.9997
2	Precision	Mean	0.45625	-0.05975	-0.08138
		S.D	0.00744	0.001035	0.001506
		%RSD	1.630737	-1.73238	-1.85062
3	Intraday	Mean	0.45	-0.06315	-0.0816
		S.D	0.008165	0.001162	0.001175
		%RSD	1.814437	-1.8399	-1.43963
4	Interday	Mean	0.44	- 0.06253	-0.08185
		S.D	0.008165	0.001097	0.001313
		%RSD	1.855674	-1.75384	-1.60386

Table-3 Determination of Lercanidipine hydrochloride in commercial tablets

Formulation	Label claim	Observed amount* ± S.D	%Recovery of pure drug	%R.S.D
LERKA Tablet (Nicholas Piramal India Limited)	10mg	9.905445 ± 0.002082	99.05	0.454182

*Average of three determinations

Table-4 Accuracy

Sample ID	Pure drug conc. (µg/ml) A	Formulation (µg/ml) B	Total concentration (µg/ml) A+B			%Recovery of pure drug			Statistical analysis (Mean,S.D,%RSD)		
			D_0	D_2	D_3	D_0	D_2	D_3	D_0	D_2	D_3
80%	8	10	17.464	17.596	17.987	97.027	97.759	99.931	97.218	97.909	99.817
80%	8	10	17.526	17.516	18.049	97.371	97.311	100.274	0.175	0.6843	0.5238
80%	8	10	17.506	17.758	17.864	97.256	98.655	99.245	0.180	0.6989	0.5248
100%	10	10	19.737	19.693	19.839	98.688	98.467	99.197	98.894	98.736	99.609
100%	10	10	19.778	20.016	20.024	98.894	100.08	100.123	0.206	1.2318	0.4714
100%	10	10	19.82	19.532	19.901	99.101	97.661	99.506	0.208	1.2476	0.4733
120%	12	10	22.134	21.629	22.074	100.61	98.313	100.336	99.045	98.558	100.018
120%	12	10	21.721	21.79	22.024	98.732	99.046	100.112	1.434	0.4232	0.3736
120%	12	10	21.514	21.629	21.913	97.793	98.313	99.607	1.448	0.4294	0.3735

Figure-1: Spectrum of Lercanidipine Hydrochloride in methanol (D_0)

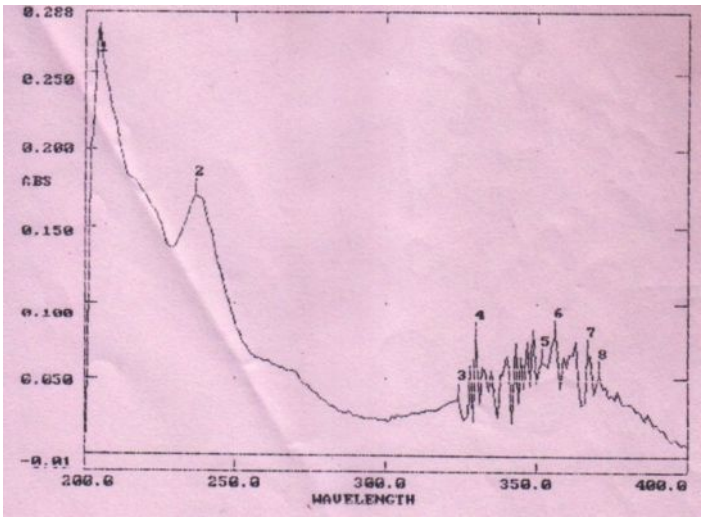


Figure-2: Second Derivative (D_2) Spectrum of Lercanidipine Hydrochloride

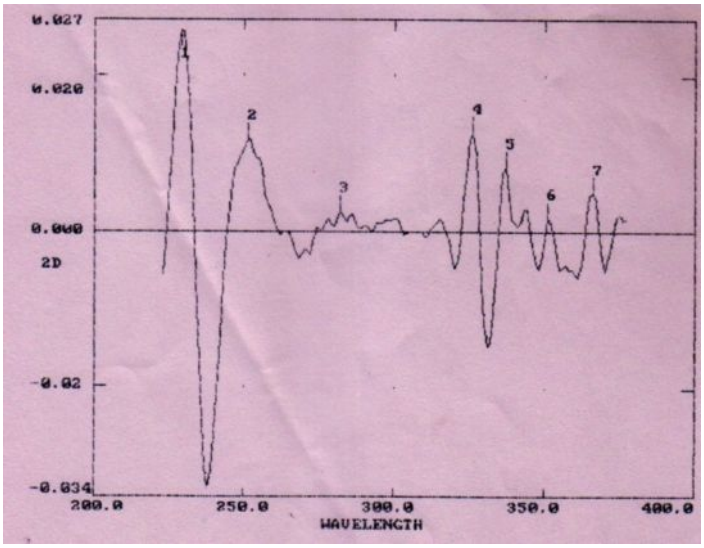


Figure-3: Third Derivative (D_3) Spectrum of Lercanidipine Hydrochloride

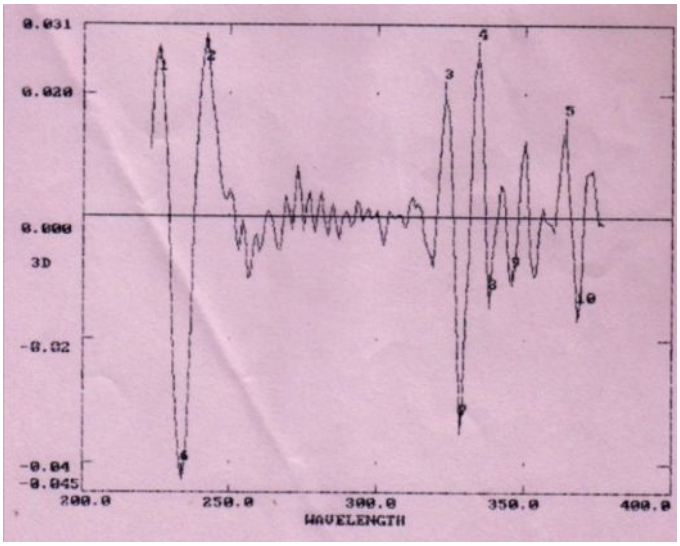


Figure-4: Linearity graph at 236nm (D_0)

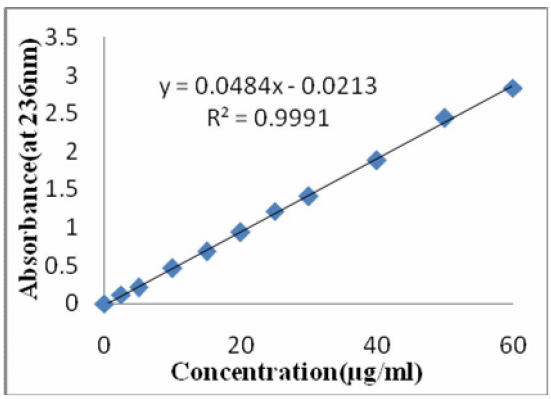


Figure-5: Linearity graph at 238nm (D_2)

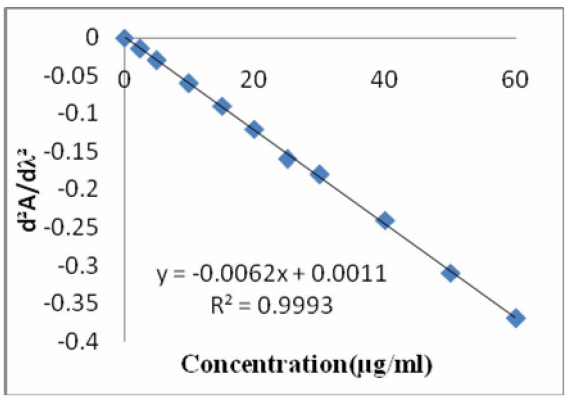
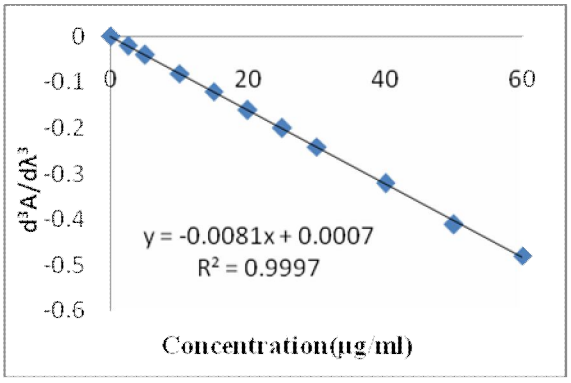


Figure-6: Linearity graph at 234nm (D_3)



CONCLUSION

Proposed methods are sensitive, accurate and reproducible. The D_0 method is useful for tablet formulations where there is no interference of excipients in the absorbance of Lercanidipine Hydrochloride and method D_2 and D_3 can be utilized for formulations containing any interfering excipients.

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