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Stability study of Lacidipine Bulk drug and it's Marketed Formulation by UV-Spectrophotometer

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ABSTRACT

A simple, sensitive, precise and stability indicating UV spectrophotometric method of analysis of lacidipine in bulk as well as formulation was developed and validated.The solvent used was a methanol and absorption maxima were found to be 281nm. Linear response was found to be in the range of 2-12ug/ml. The drug was subjected to stress degradation conditions like acid, alkaline, oxidative, photo and thermal degradation. The method was validated for specificity, linearity, precision, accuracy, robustness and solution stability. Method was found to be linear with correlation coefficient 0.998 and also found to be robust as %RSD values are less than 2%. Stress degradation study shows that lacidipine undergoes degradation in acid, base, oxidation, thermal and photo (17.06%, 4.60%, 10.61%, 2.82%, and 2.12% respectively). Degradation products which are formed during studies did not interfere in detection of lacidipine and thus assay can be considered stability indicating.

KEYWORDS: *Lacidipine, Stability indicating assay, UV-Spectrophotometry, Stress degradation condition.*

INTRODUCTION [1]

Lacidipine is a calcium channel blocker and used as antihypertensive agent. It dilates peripheral arterioles resulting in reduced peripheral vascular resistance and blood pressure. Literature survey reveals that no UV Spectrophotometric stability indicating assay methods have been reported for determination of lacidipine in bulk and formulation. Structure of lacidipine shown in **Fig. 1**.

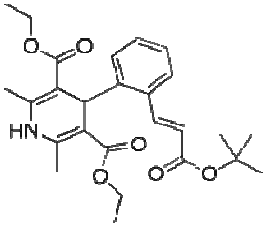

Fig. 1: Structure of lacidipine

MATERIALS AND METHODS [2-9]

Lacidipine was obtained from Sun Pharma, Hyderabad. Lacidipine tablet was purchased from local market. The solvents used are Methanol (AR grade), HCL(AR grade), Hydrogen peroxide(AR grade), NaOH(AR grade).Chemicals were purchased from Merck chemicals(Mumbai, India). Instrument used for present study was Jasco V-630 UV-visible double beam spectrophotometer.

Preparation of standard stock solution:

10mg of pure Lacidipine was accurately weighed and transferred to 100ml volumetric flask. Drug was dissolve in Methanol and volume was made upto 100ml using methanol to get the concentration 100ug/ml**.** From that stock solution working standards are prepared.

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Selection of wavelength:

From standard stock solution further dilutions are carried out using methanol and scanned over range of 200-400. Lacidipine shows considerable absorbance at 281nm. "**Fig. 2**"

Degradation study:

According to International Conference on Harmonization (ICH) guidelines, stability testing of drug substance requires stress testing carried out to find out stability of active substance. The aim of this work is to develop and validate High Performance Liquid Chromatographic stability indicating assay Method for estimation of Lacidipine in bulk as well as marketed formulation using proposed method.

Acidic hydrolysis:

2ml of working standard solution was mixed with 5ml of 2 N HCl and kept for 3 hours. After 3hours solution was neutralized with NaOH then solution was diluted to 10ml with methanol and scanned Under UV, degradation was observed. Result shown in "**Fig. 3** & **Table 1**".

Alkaline hydrolysis:

2ml of working standard solution was mixed with 5ml of 1.2N NaOH and kept for 3 hours. After 3 hours solution was neutralized with HCl then solution was diluted to 10ml with methanol and scanned under UV & degradation was observed. Results are shown in "**Fig. 4** & **Table 1**".

Oxidation:

2ml of working standard solution was mixed with 3ml 6% solution of Hydrogen peroxide. The solution was diluted to 10ml with methanol and refluxed for 3 hours. The solution was scanned under UV. Results are shown in "**Table 1** & **Fig. 5**".

Thermal degradation:

Thermal degradation study was performed by keeping drug sample in oven at temperature 100^0C for 48 hours. 10 mg of exposed drug weighed accurately and transferred to a 100ml of volumetric flask and dissolved in methanol, the volume was made up with methanol to get concentration of 100µg/ml. 1.2ml of standard stock solution was diluted with methanol to get conc. of 12ug/ml. This solution is then scanned under UV. Results are shown in "**Fig. 6** & **Table 1**".

Photo degradation:

Photo degradation study was performed by exposing drug sample to long UV (366nm) for 48 hours. 10mg of exposed drug accurately weighed and transferred to 100ml volumetric flask to get conc. of 100ug/ml. 1.2ml of standard stock solution of lacidipine was then diluted with methanol to get conc. of 12ug/ml. This solution is then scanned under UV. Results are shown in "**Fig. 7** & **Table 1**".

Validation of analytical method:

Validation was performed by using parameters like Linearity, Precision, Accuracy, Limit of detection (LOD), Limit of quantification (LOQ) and Robustness.

Linearity:

The standard stock solution of 100µg/ml of Lacidipine was prepared, from that standard solution dilution of 2-12ug/ml was prepared. Results obtained are shown in "**Table 2** & **Fig. 8**".The peak absorbance was plotted against the corresponding concentrations to obtain the calibration curve "**Fig. 8**"

Precision:

The precision of the method was performed by intra-day and inter-day variation studies. In the interday and intraday studies, 3 different concentrations 4, 6 and 8µg/ml were analysed in triplicate under UV. The percentage RSD was calculated. The result obtained for intraday and interdayvariations shown in "**Table 3, 4** respectively".

Accuracy:

To check accuracy of the method, recovery studies were carried out by mixing standard drug solution to pre-analyzed sample solution at three different levels 80, 100 and 120%. Basic concentration of sample chosen was 10µg/ml of Lacidipine bulk drug solution to which 8, 10 and 12µg/ml of Lacidipine tablet solution wasadded. These solutions were scanned under UV in triplicate. "Results are shown in **Table 5** & **8**".

Limit of detection (LOD):

LOD is calculated from the formula: - **LOD = 3.3 SD/ S**

Where,

SD = standard deviation , 3.3= Standard factor, S = Slope of the calibration curve.

LOD ofLacidipine was found to be 2.57µg/ml.

Limit of quantification (LOQ)

The quantitation limit (QL) may be expressed as: **LOQ= 10 x SD/S**

LOQ of lacidipinewas found to be 4.83µg /ml.

Range

Lacidipine: 2-12µg/ml

Robustness:

Robustness of the method was determined by carrying out the analysis under different temperature condition i.e. at room temperature and at 18°C. The respective absorbances of 12µg/ml were noted and the result was indicated as %RSD. "Results are shown in **Table 6** & **8**".

Ruggedness:

Ruggedness of the method was determined by carrying out the analysis by different analyst and the respective absorbance of 12µg/ml was noted. The result was indicated as %RSD. "Results are shown in **Table 7** & **8**"

RESULTS AND DISCUSSION

The developed and validated method was found to be precise and accurate as %RSD values are less than 2. Percent recovery was found to be 100.23%, 99.40%, 98.81% of each added drug concentration. LOD and LOQ were found to be 2.57ug/ml and 4.83ug/ml respectively indicating the sensitivity of the method.

Method was found to be robust as %RSD values are less than 2%. The summary of validation parameters is shown in "**Table 8**". The stress degradation study showed that lacidipine undergoes degradation in acid, base, oxidation, thermal and photo (17.06%, 4.60%, 10.61%, 2.82% and 2.12%respectively). Summary of stress degradation study of lacidipine are shown in "**Table 1**".

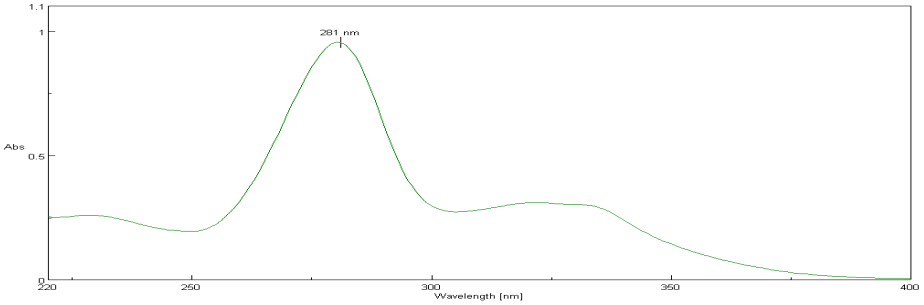

Fig. 2: UV spectrum of Lacidipine (12ug/ml)

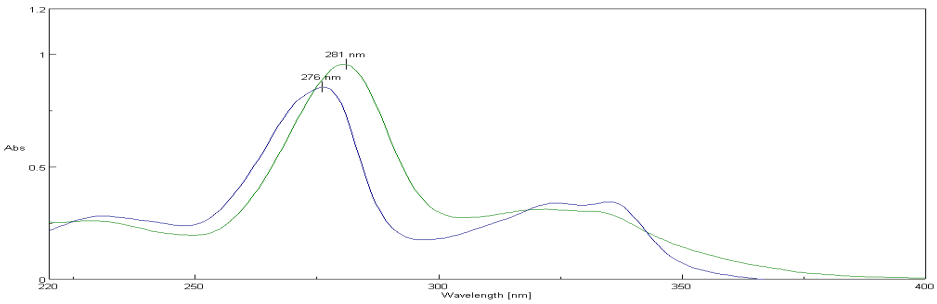

Fig. 3: UV spectrum of lacidipine after acidic degradation (12ug/ml). Drug got degraded and λmax shifted.

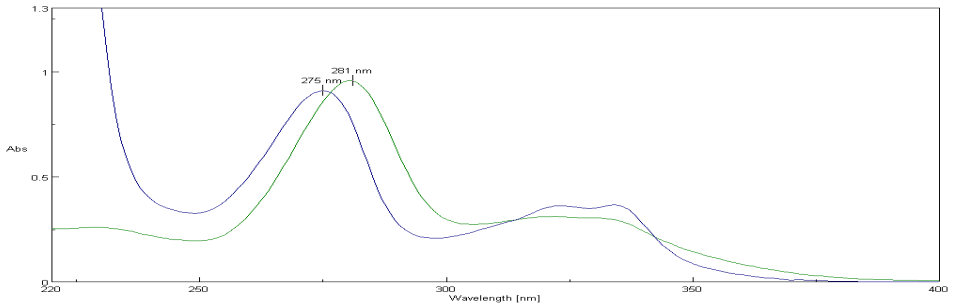

Fig. 4: UV spectrum of lacidipine after alkali degradation (12ug/ml). Drug got degraded and λmax shifted.

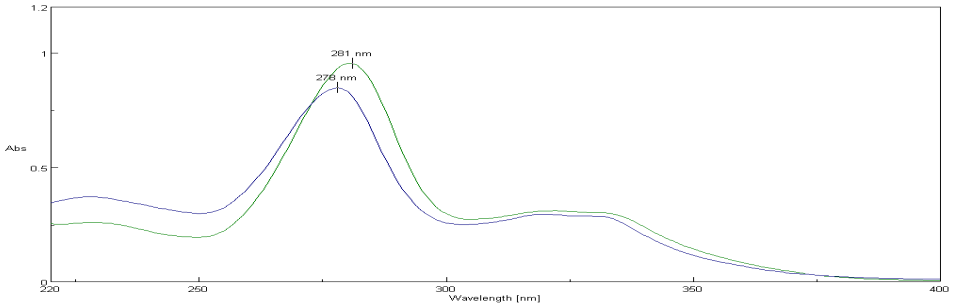

Fig. 5: UV spectrum of lacidipine after oxidative degradation (12ug/ml). Drug got degraded and λmax shifted.

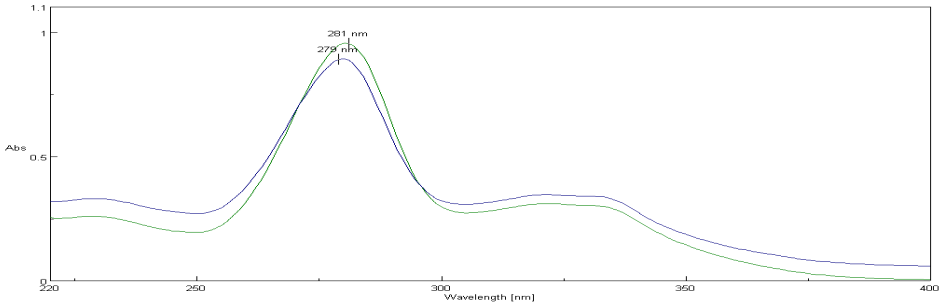

Fig. 6: UV spectrum of lacidipine after thermal degradation (12ug/ml). Drug got degraded and λmax shifted.

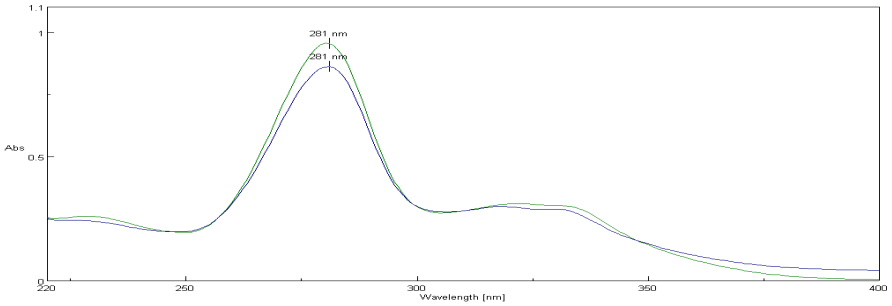

Fig. 7: UV spectrum of lacidipine after photo degradation (12ug/ml)

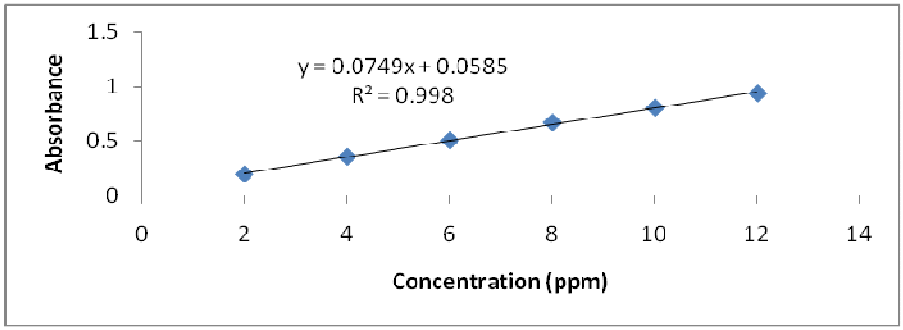

Fig. 8: Standard calibration curve for Lacidipine

Table No. 1: Summary of stress degradation study of Lacidipine bulk drug

Stress condition	Time	Observation	% Degradation	Concentration of Lacidipine Degraded µg/ml
Acidic Degradation	3hours	λmax shifted	17.06	2.05
Alkali Degradation	3hours	λmax shifted	4.60	0.56
Oxidative degradation	3hours	λmax shifted	10.61	1.28
Thermal degradation	48 hours	λmax shifted	2.82	0.34
Photo degradation	48 hours	λmax not shifted	2.12	0.25

Table No. 2: Linearity study of Lacidipine

Sr. no.	Concentration	Absorbance
1	2µg/ml	0.199
2	4 µg/ml	0.359
3	6 µg/ml	0.509
4	8 µg/ml	0.675
5	10 µg/ml	0.811
6	12 µg/ml	0.943

Table No. 3: Intraday precision study for Lacidipine

Conc. (µg/ml)	Absorbances			Mean	SD	% RSD
	Trial 1	Trial 2	Trial 3			
4	0.359	0.360	0.359	0.3593	0.00057	1.58%
6	0.509	0.509	0.511	0.5096	0.001	0.21%
8	0.675	0.673	0.674	0.6740	0.0015	0.14%
Average OF % RSD = 0.6433%						

Table No. 4: Interday precision study for Lacidipine

Conc. (µg/ml)	Absorbances			Mean	SD	% RSD
	Trial 1	Trial 2	Trial 3			
4	0.356	0.359	0.358	0.3576	±0.0015	0.41%
6	0.509	0.508	0.510	0.5090	±0.0010	0.19%
8	0.676	0.674	0.673	0.6743	±0.0015	0.22%
Average OF % RSD = 0.2733%						

Table No. 5: Recovery study of Lacidipine

No.of Preparation	Concentration(µg/ml)		% Recovery	Mean
	Formulation	Pure drug		
S_1:80%	10	8	100.41	**100.23%**
S_2: 80%	10	8	100.32	
S_3: 80%	10	8	99.98	
S_4:100%	10	10	99.12	**99.40%**
S_5:100%	10	10	99.68	
S_6:100%	10	10	99.40	
S_7:120%	10	12	98.73	**98.81%**
S_8:120%	10	12	99.05	
S_9:120%	10	12	98.66	

Table No. 6: Robustness Studies of Lacidipine

Sr. no	Concentration (ppm)	Absorbance	
		At Room temperature	At 18^{0}C
1	12	0.943	0.932
2	12	0.939	0.947
3	12	0.927	0.935
4	12	0.944	0.941
5	12	0.938	0.940
6	12	0.941	0.944
7	**Mean**	0.938	0.939
8	**SD**	±0.0061	±0.0055
9	**%RSD**	0.6503	0.5857
Average % RSD = 0.618			

Table No. 7: Ruggedness studies of Lacidipine

Sr no	Conc (ppm)	Absorbance		
		Analyst 1	Analyst 2	Analyst 3
1	12	0.942	0.937	0.945
2	12	0.951	0.947	0.943

3	12	0.943	0.949	0.942
4	12	0.941	0.939	0.929
5	12	0.945	0.935	0.940
6	12	0.932	0.938	0.944
7	**Mean**	0.942	0.941	0.940
8	**SD**	±0.0061	±0.0057	±0.0058
9	**% RSD**	0.6475%	0.6063%	0.6170%
Average% RSD = 0.6236				

Table No. 8: Summary of validation parameters of Lacidipine

Sr. No.	Parameter	Result
1	Linearity indicated by correlation coefficient	0.998
2	Linear regression equation	0.0749x+0.0585
3	Range	2-12µg/ml
4	Interday Precision (%RSD)	0.6433%
5	Intraday Precision (%RSD)	0.2733%
6	Limit of Detection	2.57µg/ml
7	Limit of Quantification	4.83µg/ml
8	Robustness indicated by % RSD	0.6180%
9	Ruggedness indicated by % RSD	0.6236%

CONCLUSIONS

A validated stability indicating UV-Spectrophotometric analytical method has been developed for determination of lacidipine drug. The results of stress degradation study undertaken according to ICH guidelines, reveals that method is selective and stability indicating. The proposed method is simple, accurate, precise and specific. The method is suitable for routine analysis of lacidipine in bulk as well as pharmaceutical dosage form.

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