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DEVELOPMENT AND VALIDATION OF UV-SPECTROSCOPIC METHOD FOR THE ESTIMATION OF CILNIDIPINE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

The present work has been developed for the estimation of Cilnidipine in bulk and pharmaceutical dosage form under UV- Spectroscopic method. Methanol was used as solvent. Cilnidipine attains maximum wavelength at 240nm. This method complies Beer's law in the concentration range of 1-5µg/ml. A linear plot with a regression coefficient of 0.993was obtained. The proposed method was validated according to International Conference on Harmonization (ICH) guidelines and the validation parameters like Accuracy, Precision, Linearity, Ruggedness, Limit of Detection (LOD) and Limit of Quantitation (LOQ). The % Recovery range was found to be 100.05% to 100.50%. The method developed and validated was found to be simple, accurate and precise, and it was successfully performed for the estimation of Cilnidipine in bulk and pharmaceutical dosage form.

KEYWORDS: Cilnidipine, UV- Spectroscopic method, Validation, UV – VIS Spectrophotometer.

1. INTRODUCTION

Cilnidipine is [1,4 – dihydro – 2,6 – dimethyl – 4 – (3 nitrophenyl) 3,5 – pyridinedicarboxylic acid 2 – methoxy ethyl (2E) – 3 – phenyl – 2 – propenyl ester] fourth generation drug of dihydropyridine calcium antagonist.[1] It is used in the treatment of Hypertension, Hypertension associated vascular diseases, Angina Pectoris, Heart attack and Stroke. It is a class II drug of BCS with low aqueous solubility and poor dissolution rate. But it is highly lipophillic in nature.[2] Cilnidipine is a dual activity drug, it acts on both L and N type calcium channel. It blocks both L and N type calcium channel and dilates both arterioles and venules. It results in lowering the blood pressure in capillary bed.[3] The L type voltage gated calcium channel is in smooth muscles and the N type calcium channel are in sympathetic nerve terminals. Cilnidipine suppresses the cardiovascular neurohormonal regulation, sympathetic nervous system as well as rennin – angiotensin – aldosterone.[4]

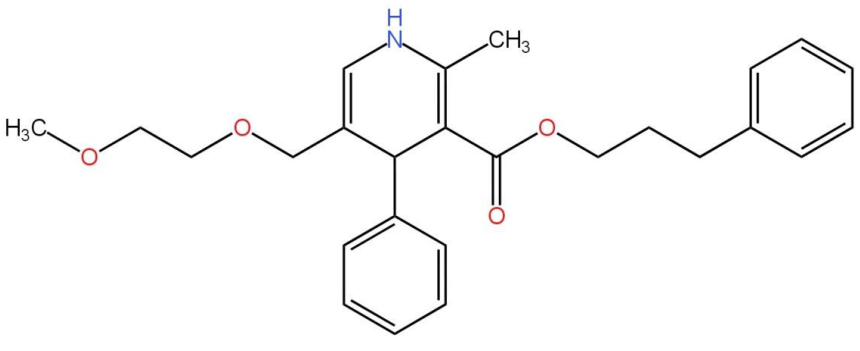

Fig. No: 1 Structure of Cilnidipine.

This paper describes about the simple and accurately developed and validated spectroscopic method for the quantification of drug in bulk and in pharmaceutical dosage form. The preferred method was developed and validated as per the International Conference on Harmonization (ICH) guidelines.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

Cilnidipine as a raw material was obtained from NEBULAE HI-TECH LABORATORIES, Chennai. The pharmaceutical dosage form used in this research was CILINI-10 with labelled claim 10mg of Cilnidipine was procured from the market. All the chemicals and solvents used were of analytical grade. The solvent used for this study was Methanol (Analytical Grade). The Methanol AR grade was procured from THE PRECISION SCIENTIFIC CO., Coimbatore.

2.2 Instrumentation

The Double beam UV – Visible spectrophotometer (Shimadzu 1900i) with 1cm matched Quartz cells were used for this proposed method.

2.3 Methodology

2.3.1 Preparation of standard stock solution

The amount of 0.01g of Cilnidipine standard substance was weighed and dissolved in 10ml of Methanol. From this 10ml stock solution 1ml was taken and made up to 10ml of methanol. Aliquots of diluted solution was further diluted to 10ml with methanol to get the concentration of 12µg/ml and the solution was scanned between 200 – 400nm. From that spectra λmax was found.

Fig. No: 2 Spectrum of Cilnidipine.

2.3.2 Preparation of Calibration graph

From the standard stock solution 1-5ml were transferred into a series of 10ml volumetric flask and made upto the volume with methanol. The absorbance of different concentration solution were measured. The calibration curve was constructed by plotting concentration Vs absorbance. Cilnidipine was linear with concentration range of 1-5µg/ml.

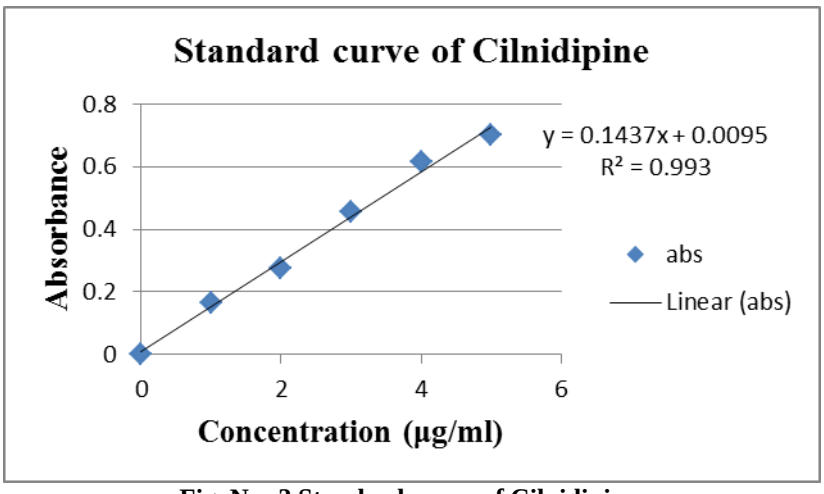

Fig. No: 3 Standard curve of Cilnidipine.

2.3.3 Preparation of sample solution

Twenty tablets (CILINI-10 containing 10mg of Cilnidipine) were accurately weighed and the average weight was found. The powdered tablet of Cilnidipine 0.121g was weighed accurately and diluted with 100ml of methanol. The solution was sonicated for 10minutes and it was filtered to Whatmann filter paper grade no: 1. From the clear solution, further dilution were made. 1ml was pipette out into a series of six and made upto the mark with methanol to get the concentration of 10µg/ml.

The absorbance of six solutions were measured and amount found by using regression equation.

3. VALIDATION

The method was validated with respect to linearity, precision, accuracy, ruggedness, Limit of Detection (LOD) and Limit of Quantitation (LOQ). The values were examined by statistical methods.

3.1 Linearity

A calibration curve was plotted between concentration and absorbance. Cilnidipine was linear with the concentration range of 1-5µg/ml. The optical characteristics were calculated.

3.2 Precision

The repeatability of the method was confirmed by the analysis of formulation was repeated for six times with the same concentration. The amount of drug present in the tablet formulation was calculated. The %RSD was calculated. The intermediate precision of the method was confirmed by interday and intraday analysis. The analysis of formulation was repeated for three times in a day and one time on three successive days, the amount of drug was determined.

3.3 Accuracy

The amount of 0.01g of cilnidipine was accurately weighed and diluted with 10ml of methanol to dissolve the substance. This solution contains 1000µg/ml, to the pre-analysed formulation a known quantity of raw material of cilnidipine was added and the procedure was followed as per the analysis of formulation. The amount of drug was calculated and this procedure was repeated for three times for each concentration. The %RSD were calculated.

3.4 Ruggedness

Ruggedness of method was confirmed by the analysis of formulation was done by using different analysts. The amount was calculated and the %RSD were calculated.

3.5 LOD and LOQ

The limit of detection (LOD) is the lowest concentration at which the results still satisfy some predetermined acceptance criteria. Below the LOD, the results fail to meet these criteria (analysis is not feasible). It may expressed as,

$$LOD = \frac{3.3 \times \sigma}{S}$$

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in sample which can be quantitatively determined with suitable precision and accuracy. It is a parameter of quantitative assays for low levels of compounds in sample matrices and is used particularly for the determination of impurities and degradation products.[5]

$$LOQ = \frac{10 \times \sigma}{S}$$

4. RESULTS AND DISCUSSION

The optical characteristics of cilnidipine by UV method such as maximum wavelength, Beer's law limits, are presented in table 1. The correlation coefficient value for the calibration graph was found to be 0.993 which indicates that the absorbance was linear with the concentration range of 1-5µg/ml are presented in table 2. The percentage amount of cilnidipine was found to be 99.90 ± 0.690 are presented in the table 3. The percentage label claim in tablet formulation was found to be 99.76 ± 0.891 and the %RSD value was found to be 0.893 are presented in table 4. The percentage RSD value for intraday and interday analysis of cilnidipine was found to be 0.458 and 0.555 respectively are presented in table 5 & 6. The developed method was validated for Ruggedness. The percentage RSD value for analyst 1 and analyst 2 were found to be 1.015 and 0.923 are presented in table 7. The accuracy of the method was confirmed by recovery studies. The percentage recovery was found to be in the range of 100.05 to 100.50% are presented in table 8. Hence, the method was found to be accurate.

Table 1: Optical Characteristics of Cilnidipine by UV method.

PARAMETERS	VALUES
λmax(nm)	240nm
Beer's law limit (µg/ml)	1 - 5µg/ml
Correlation Coefficient (r^2)	0.993
Regression equation (Y = mx+c)	y = 0.143x + 0.009
Slope (m)	0.143
Intercept	0.009
LOD (µg/ml)	0.188
LOQ (µg/ml)	0.572
Standard error	0.0183

Table 2: Linearity of Cilnidipine by UV method.

CONCENTRATION (µg/ml)	ABSORBANCE
0	0
1	0.165
2	0.277
3	0.455
4	0.615
5	0.700

Table 3: Quantification of raw material by UV method.

S.no	Absorbance	Amount found (µg/ml)	Percentage Obtained (%)	Mean(%)	SD	RSD
1	1.705	11.86	98.83%			
2	1.715	11.93	99.43%			
3	1.726	12.01	100.08%	99.90%	0.690	0.691
4	1.723	11.99	99.91%			
5	1.737	12.09	100.75%			
6	1.732	12.05	100.41%			

Table 4: Quantification of formulation by UV method.

Labelled amount (µg/tab)	Absorbance	Amount found (µg/ml)	Percentage Obtained (%)	Mean (%)	SD	%RSD
10	1.413	9.82	98.2%			
10	1.441	10.02	100.2%			
10	1.437	9.99	99.9%	99.76%	0.891	0.893
10	1.451	10.09	100.9%			
10	1.433	9.96	99.6%			
10	1.436	9.98	99.8%			

Table 5: Intraday analysis of formulation by UV method.

Labelled amount (µg/ml)	Amount found (µg/ml)	Percentage obtained (%)	Mean (%)	SD	%RSD
10	9.96	99.6%	100%	0.458	0.458
10	10.05	100.5%			
10	9.99	99.9%			

Table 6: Interday analysis of formulation by UV method.

Labelled amount (µg/ml)	Amount found (µg/ml)	Percentage obtained (%)	Mean (%)	SD	%RSD
10	9.98	99.8%	100.4%	0.557	0.555
10	10.09	100.9%			
10	10.05	100.5%			

Table 7: Ruggedness study by UV method (Different Analysts).

Condition	Labelled amount (µg/ml)	Amount found (µg/tab)	Percentage obtained (%)	Mean (%)	SD	%RSD
Analyst 1	10	9.90	99%	99.1%	1.007	1.015
		10.02	100.2%			
		9.82	98.2%			
Analyst 2	10	9.83	98.3%	99.3%	0.917	0.923
		10.01	100.1%			
		9.95	99.5%			

Table 8: Recovery analysis of formulation by UV method.

Amount present (µg/ml)	Amount added (µg/ml)	Amount found (µg/ml)	Amount recovered (µg/ml)	% Recovery	Average % Recovery	Mean %	SD	%RSD
	8	17.80	7.97	99.62%				
9.83	8	17.89	8.06	100.75%	100.49%			
	8	17.92	8.09	101.12%				
	10	19.88	10.05	100.5%				
9.83	10	19.92	10.09	100.9%	100.46%	100.34%	0.229	0.228
	10	19.83	10	100%				
	12	21.86	12.03	100.25%				
9.83	12	21.77	11.94	99.5%	100.08%			
	12	21.89	12.06	100.5%				

5. SUMMARY AND CONCLUSION

The preferred method was found to be a simple, rapid, precise and accurate. The solvent selected for solubility was Methanol. The λmax of Cilnidipine was 240nm. Cilnidipine was linear with the concentration range of 1-5µg/ml. The correlation coefficient value for the calibration graph was found to be 0.993. The percentage of cilnidipine present in prepared raw material solution was found to be 99.90 ± 0.690. CILINI-10 containing 10mg of Cilnidipine were selected for analysis, the percentage label claim present in tablet formulation was found to be 99.76 ± 0.891. The precision method was confirmed by repeated analysis of formulation. The %RSD was found to be 0.893. And the precision method was further confirmed by intraday and interday analysis. The %RSD was found to be 0.458 and 0.555 respectively. The developed method was validated for ruggedness. The %RSD value of analyst 1 and analyst 2 were found to be 1.015 and 0.923 respectively. The %RSD value indicate that the developed method was more rugged. The accuracy method was confirmed, the percentage was found to be in the range of 100.05 to 100.50% of Cilnidipine. This UV spectroscopic method were developed and validated for the estimation of Cilnidipine in bulk and in its pharmaceutical dosage form (tablets) can be used routinely.

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