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Spectrophotometric Method for the Estimation of Cilnidipine in Bulk and Pharmaceutical Dosage forms

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ABSTRACT

A new, simple and sensitive Spectrophotometric Method in ultraviolet region has been developed for the determination of cilnidipine in bulk and in pharmaceutical formulations. Cilnidipine exhibits absorption maxima at 240 nm. The method obeys the Beer's law in the concentration range of 2 - 30 µg/ml. The method is accurate, precise and economical. The % recovery is greater than 99.86 - 100.67%. This shows that the method was free from the interference of excepients. The results of the tablet analysis were validated with respect to accuracy (recovery), linearity, limit of detection and limit of quantization were found to be satisfactory. The proposed method has been applied successfully for the analysis of the drug in pure and in its tablet dosage forms.

Key words: Spectrophotometeric method, Ultraviolet region, Clinidipine, Pharmaceutics.

INTRODUCTION

Cilnidipine is chemically, 1,4- Dihydro- 2,6-dimethyl- 4-(3-nitrophenyl)-3,5-pyridinecarboxylic acid 2-methoxyethyl(2E)-3-phenyl-propenyl ester. Cilnidipine is a dual blocker of L-type voltage-gated calcium channels in vascular smooth muscle and N-type calcium channels in sympathetic nerve terminals that supply blood vessels[1]. Literature survey reveals reverse phase high-performance liquid chromatographic (RP-HPLC)[2], LC-MS[3,4] and high performance thin layer chromatographic (HPTLC)[5] methods for the determination of Cilnidipine either as single or in combination with other drugs in human plasma and in pharmaceutical preparations.

This paper describes a simple, accurate and validated spectrophotometric method for the quantification of the compound as a bulk drug and in tablet dosage form. The proposed method is optimized and validated as per the International Conference on Harmonization (ICH) guidelines[6].

MATERIALS AND METHODS

Chemicals and Reagents

Pharmaceutical grade Cilnidipine was obtained as gift samples from J. B. Chemicals and Pharmaceuticals Ltd. (Mumbai, India). The pharmaceutical dosage form used in this study was Cilacar tablets (J. B. Chemical and Pharmaceuticals Ltd., Mumbai, India) labelled to contain 10 mg of Cilnidipine was procured from the market. Solvents Ethanol AR grade were obtained from Sigma.

Instrumentation

A Shimadzu UV/visible double beam spectrophotometer (model 1700) with 1 cm matched quartz cells were used for all the spectral measurements.

Reagents

Double distilled ethyl alcohol was used. Authentic sample of Cilnidipine was gifted by J.B.Chemicals and Pharmaceutical Ltd.(Mumbai, India). The commercial product was purchased from the local market.

Preparation of Standard Stock Solutions and calibration Curve

100 mg of Cilnidipine (pure) was accurately weighed and dissolved in 30 ml ethanol. The solution was sonicated for 30 minutes. The solution was filtered through Whatman filter Paper No. 41, volume of the filtrate was made up to 100 ml with ethanol (1 mg/ml). 10 ml of the stock solution was diluted to 100ml with ethanol. Aliquots of the diluted solution was further diluted to 10 ml with ethanol and the absorbance was measured at 240nm using ethanol as blank (Fig. 1 overlain spectra).

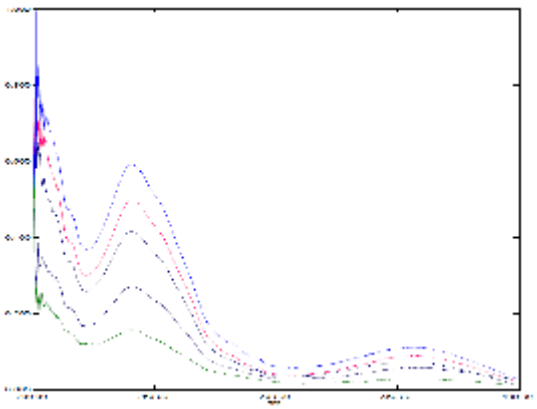

Fig. 1: Overlain spectra of standard sample

Preparation of Sample Solution and analysis

Twenty tablets of Cilnidipine containing 10 mg were accurately weighed and powdered. Weigh accurately a quantity of the powder equivalent to 0.1 gm of Cilnidipine, suspended in 30 ml of ethanol. The solution was sonicated for 30 minutes. The solution was filtered through Whatmann filter paper No- 41. The residue was washed with 10 ml portions of ethanol three times and the total volume of the filtrate was made up to 100 ml with ethanol (1 mg/ml). 10 ml of the above solution is diluted to 100 ml with ethanol. Volume of sample equal to beer's law range was taken and diluted to 10 ml and absorbance measured at 240 nm. The amount of Cilnidipine present in the sample was computed from the calibration curve (Table 1) The experiments were repeated six times to check its reproducibility.

The results obtained by One-way ANOVA, found that P value is < 0.0001. Hence the method is considered extremely significant.

Table 1: Result of Analysis in Marketed Formulation

Name	Labelclaim	Amount found	% Estimated*	S.D*	R.S.D*
CILACAR	10 mgm	9.965mgm	99.65	1.094	1.00

Where * indicates mean of six determinations by Absorption Maxima method.

Validation

The method was validated with respect to linearity, accuracy, precision, limit of detection (LOD) and limit of quantization (LOQ). The values were analyzed by statistical methods using Graph pad Instat software.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of Cilnidipine. Beer-Lambert's concentration range was found to be 02 - 30 µg/Ml. The results obtained by One-way ANOVA, found

that P value is < 0.0001. Hence the method is considered extremely significant. The optical parameters are given in Table 2.

Accuracys

To ascertain the accuracy of proposed method, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). Percent recovery of Cilnidipine, was found in the range of 99.86 – 100.67% (Table 3).

The results obtained by One-way ANOVA, found that P value is < 0.0001. Hence the method is considered extremely significant.

Table 2: Optical Characterstics and Other Parameters

No	Parameter	Results
1	λ max (nm)	240
2	Beer's law limits (µg/ml)	2 – 30
3	Sandell's sensitivity(µg / cm^2/ 0.001 absorbance unit)	0.0151
4	Slope	0.06555
5	Y- Intercept	0.01439
6	X- Intercept	-0.2196
7	Correlation coefficient (r2)	0.9996
8	LOD(µg/ml)	0.0255
9	LOQ(µg/ml)	0.0772

Table 3: Recovery study data.(Absorption Maxima Method)

S. No	Pre analysed quantity. (mcg/ml)	Amount of pure drug added.(mcg/ml	Total amount found. (mcg/ml)	S.D*	R.S.D*
1	10	8	17.95	0.05	0.278
2	10	10	20.04	0.0721	0.359
3	10	12	21.89	0.1442	0.658

Where * indicates mean of six determinations.

Precision

Precision is determined by using the same method used to assay the sample and repeated for a sufficient number of times to obtain statistically valid result. The experimental values were determined by Intra and Interday. The values are validated by statistical analysis. The precision is then expressed as the relative standard deviation. % RSD was found to be 0.5745. The results obtained by One-way ANOVA, found that P value is < 0.0001. Hence the method is considered extremely significant.

Limit of detection (LOD) and limit of quantitation (LOQ)

The LOD and LOQ of Cilnidipine were determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines. The LOD and LOQ data presented in Table 2.

Selectivity and Specificity

A study of interferences of excipients has been made during the determination of Cilnidipine. It was observed that starch, glucose and lactose were added to the powder of Cilnidipine tablet and results obtained showed that in the proposed method excipients are not interfered in the estimation. So the proposed method is more selective and specific for the drug.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, and Sandell's sensitivity are presented in Table 2. The regression analysis using method of least squares was made for the slope, intercept and correlation coefficient(r) obtained from different concentrations and the results are summarized in Table 2. The percent relative standard deviation were calculated from the six measurements are shown in Table 3. The

result showed that the above method has a reasonable precision. The result obtained with the proposed methods for the dosage forms (Table 1) confirms the suitability of the method. Interference studies revealed that the common excipients and other additives are usually present in the tablet dosage forms did not interfered at their regularly added levels.

CONCLUSION

The proposed method was found to be simple, sensitive, selective, accurate, precise and economical. This UV method can be used in the determination of Cilnidipine in bulk drug and its pharmaceutical dosage forms (tablets) in a routine manner.

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