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Research Article

METHOD VALIDATION FOR SPECTROPHOTOMETRIC ESTIMATION OF CILNIDIPINE

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ABSTRACT

The present study describes accurate, precise and reproducible spectrophotometric method for estimation of Cilnidipine. The method was validated by using various parameters as per ICH guidelines. Cilnidipine is a new dihydropyridine (DHP) calcium channel antagonist used as antihypertensive agent. Method was validated by checking parameters like linearity, precision, accuracy, sensitivity, recovery study. Cilnidipine showed maximum absorbance at 240 nm. Linearity was obeyed in concentration range of 3-18 µg/mL with R^2 0.9994. The assay result was found to be in good agreement with label claim. The recovery studies were carried out at three different levels. The method was validated statistically and by recovery studies.

Keywords: Cilnidipine, Spectrophotometry, Validation

INTRODUCTION

Cilnidipine (FRC-8653) is a dihydropyridine (DHP) type of calcium channel antagonist[1]. Unlike other calcium channel antagonists, Cilnidipine blocks the influx of Ca^{2+} ions into both vascular smooth muscle at the level of L-type Ca^{2+} channels and neuronal cells at the level of N-type Ca^{2+} channels[1,2]. Cilnidipine shows first pass metabolism[3].Literature review revealed that few methods are available for the determination of Cilnidipine in bulk.

The present study describes accurate, precise, reproducible, spectrophotometric method for estimation of Cilnidipine in tablet formulation. The method was validated by using various parameters as per ICH guidelines.

MATERIALS AND METHODS

Instrument and material

Cilnidipine was obtained as a gift sample from JB Chemicals, Mumbai, India. The Shimadzu UV-Visible spectrophotometer 1601 was used with spectral bandwidth 3 nm and wavelength accuracy (with automatic wavelength correction) of 0.5 nm. All the apparatus and instruments were calibrated and validated before starting the experimental work.

Method

Preparation of standard solution

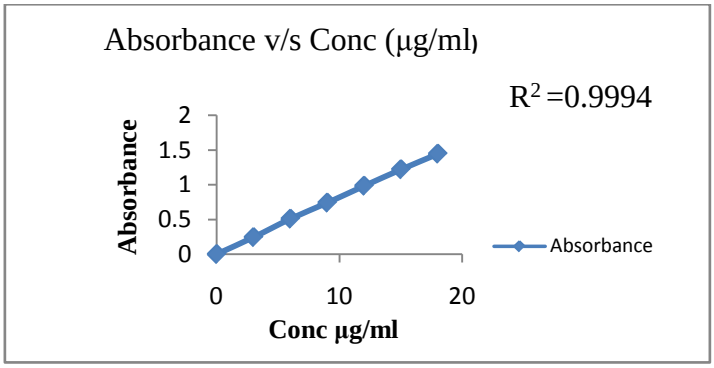
Stock solution of Cilnidipine (100µg/ml) was prepared in methanol and different standard solutions ranging from 3-18µg/ml were prepared by appropriately diluting stock solution.

Validation of analytical method

Validation is the process of establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.

Linearity[4]

The linearity of Cilnidipine was found to be within the range of 3-18 µg/ml. The linear regression value was found to be R^2= 0.9994 (Table 1).



Graph 1: Absorbance v/s Concentration (µg/ml) of Cilnidipine

Precision[5, 6]

Precision is the degree of agreement among individual test results when the procedure is applied repeatedly to multiple samplings of a homogeneous sample. Precision is usually expressed as the standard deviation or relative standard deviation. In the present study, developed method was validated for method, system, inter-day and intra-day precision. As the values of % RSD (relative standard deviation) of all precision study were within the acceptable limits (less than 2 %), both the method as well as the system provides good precision and reproducibility. Results of precision study are shown in Table1.

Sensitivity[4]

Absorbance of standard solutions of Cilnidipine was measured at 240 nm. Sandell's sensitivity for Cilnidipine drug was calculated from formula:

(μgcm^{-3}/ AU) = Conc. of drug ($\mu g100\ mL^{-1}$) X 0.001

Absorbance Sandell sensitivity for Cilnidipine (240nm) was found to be 0.0717 µgcm-3/AU.

Accuracy[4]

Accuracy of the method was determined in the terms of % recovery of standard Cilnidipine. Recovery studies were carried out by addition of standard drug solution at 3 different levels to the preanalyzed sample. Results of the recovery study were found to be within the acceptance criteria 100 ± 10 %, indicates sensitivity of the method towards detection of Cilnidipine and non interference of excipients in the method (Table 1).

Procedure for the analysis of tablet formulation

Sample: Cilnidipine Tablet
Brand name: Cilacar 10 (Cilnidipine 10 mg)
Manufacturer: J.B.Chemicals & Pharmaceuticals Ltd, Daman, India.

Table 1: Validation Parameters

S. No.	Parameters		Cilnidipine
1.	Linearity	µg/ml	3-18µg/ml
		Regression equation	0.0812 x + 0.0190
		R^2	0.9994
2.	Precision	Method	0.1994
	(%RSD)	Inter-day	0.1490
		Intra-day	0.2010
3.	Sensitivity (µg/cm-3/ A)		0.0717
4.	Accuracy(%Recovery) N=3		98.0%-102.0%

Preparation of sample solution[4]

Twenty tablets were accurately weighed, their average weight was determined, crushed to fine powder. An accurately weighed quantity of tablet powder equivalent to 10 mg of Cilnidipine was transferred to 100 ml volumetric flask, dissolved in 20 ml methanol, filtered and finally volume adjusted to 100ml with methanol.

RESULT AND DISCUSSION

Cilnidipine is new calcium channel antagonist used as antihypertensive agent. It showed maximum absorbance at 240 nm. Linearity was obeyed in concentration range of 3-18 µg/ml. As the values of % RSD of all precision study were within the acceptable limits (less than 2 %), the method provides good precision and reproducibility. The % RSD less than 2 indicated that the method was accurate. Results of the recovery study were found to be within the acceptance criteria linear, accurate, precise and reproducible.

Recovery study

To check the accuracy of the proposed method, recovery studies were carried out at three different levels i.e. 100 %, 120 % and 140 %. The standard bulk drug was added at 3 different levels to the preanalyzed sample solution and then reanalyzed. The developed method was found to be simple,

100 ± 10 % indicates sensitivity of the method towards detection of Cilnidipine.

CONCLUSION

A Spectrophotometric method has been developed for the determination of Cilnidipine in tablet formulation. The method was validated based on ICH analytical method validation guidelines.

Table 2: Analysis of tablet formulation

Label claim mg/tablet	Amount found*	% Amount found	SD	% RSD
Cilacar 10mg	10.16	101.6	0.0027	0.027

*Average of six determinations

Table 3: Recovery studies

S. No.	Conc. Of standard drug (µg/ml)	Conc. Of Marketed sample (µg/ml)	Total drug conc. (µg/ml)	Absorbance* at 240 nm	Total conc. Of Cilnidipine from standard curve(µg/ml)	Amount of sample (µg/ml)	% Recovery
1.	10	2	12	0.985	12.20	10.20	102
2.	10	4	14	1.129	13.99	9.99	99.9
3.	10	6	16	1.291	15.99	9.99	99.93

*Average of three readings.

The method was found to be accurate, linear, precise and reproducible. Hence the method can be used for routine analysis of Cilnidipine in bulk and tablet formulation.

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REFERENCES

1. T. Sakaki, H.Naruse, M. Masai et al."Cilnidipine as an agent to lower blood pressure without sympathetic nervous activation as demonstrated by iodine-123 metaiodobenzyl-guanidine imaging in rat hearts" Annals of Nuclear Medicine, Vol. 17,2003, 321–326.
2. H. Uneyama, H. Uchida, T. Konda, R.Yoshimoto,"Cilnidipine:Preclinic-al Profile and Clinical Evaluation", Cardiovascular Drug Reviews, Vol 17, No.4, pg no. 341-357.
3. L. Xiao-Quan, Z. Yang, I. Dan, Q. Zhi-Yu, W. Guang-Ji, "Metabolism and metabolic Inhibition of Cilnidipine in Human Liver microsomes" Acta Pharmacol Sin 2003 Mar; 24 (3): pg no. 263-268.
4. G. Mubeen, Rao D.S, Kadri .U, "Spectrophotometric Method for Determination of Lercanidipine in Tablets", International Journal of ChemTech Research, Vol.1, No.4, 1186-1188.

5. D. Tsvetkova, D. Obreshkova, "Validation of UV-Spectrophotometric Method for Identification and Determination of Angiotensin II Receptor Antagonist Losartan Potassium'', International journal Of Pharmacy and Pharmaceutical Sciences, Vol 4, Issue 1, 2012, pg no 428-432.

6. M. Reddy, A. Kumar, V. Reddy, S. Haque,"Stability-indicating HPLC method for Simultaneous estimation of low level impurities of Telmisartan and Hydrochlorothiazide in tablet dosage forms", International journal Of Pharmacy and Pharmaceutical Sciences, Vol 4, Issue 1, 2012, pg.no 497-504.