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Original Article

SPECTROPHOTOMETRIC ESTIMATION OF CILNIDIPINE IN BULK AND PHARMACEUTICAL DOSAGE FORM USING N-(1-NAPHTHYL) ETHYLENE DIAMINE DIHYDROCHLORIDE

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ABSTRACT

Objective: To develop a new, simple and sensitive visible spectrophotometric method for the estimation of Cilnidipine [CIL] in bulk and tablet dosage forms.

Methods: The visible spectrophotometric method was based on the color reaction of CIL with N-(1-Naphthyl) ethylene diamine dihydrochloride reagent [it is stable for 20 min] to form a purple coloured chromophore that has an absorption maxima at 554 nm. The method was validated as per ICH guidelines.

Results: Beer's law was obeyed over the concentration range of 16-24 µg/mL for Cilnidipine. Limit of detection [LOD] and limit of quantification [LOQ] are 0.4365 and 1.3228 respectively. The average recovery was found to be 100.43% w/w.

Conclusion: The method developed is precise, linear and accurate. Satisfactory results were obtained from validation of the method. Hence the proposed method is suitable in quality control of estimation Cilnidipine bulk and pharmaceutical dosage forms.

Keywords: Cilnidipine, Visible spectrophotometry, N-(1-Naphthyl) ethylene diamine dihydrochloride, Validation, ICH guidelines.

INTRODUCTION

Cilnidipine [CIL] is chemically, 1,4- Dihydro- 2,6- dimethyl- 4-(3-nitrophenyl)-3,5-pyridinecarboxylic acid 2-methoxyethyl(2E)-3-phenyl-propenyl ester. It 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[1,2].

The literature survey revealed the lack of a visible spectrophotometric method for the estimation of CIL. However estimation of the drug as a single molecule and in combination with other drugs by UV spectrophotometric, HPLC and HPTLC was available[3-17].

The aim of present work was to develop an improved spectrophotometric method with greater precision and accuracy. The proposed method is mainly based on the reaction of Cilnidipine with N-(1-Naphthyl) ethylene diamine dihydrochloride (NED) reagent which gives purple color chromophore that has an absorption maximum at 554 nm. The structural formula for CIL is shown in **Fig 1**.

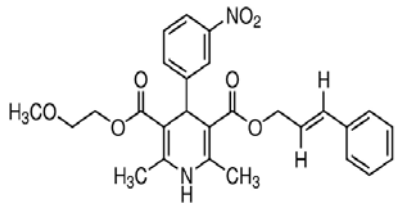

Fig. 1: Structure of Cilnidipine ($C_{27}H_{28}N_2O_7$)

MATERIALS AND METHODS

Instrumentation

A Shimadzu UV/visible double beam spectrophotometer (model Lambda 25) with 1 cm matched quartz cells were used for all the spectral measurements.

Chemicals and Reagents

Pharmaceutical grade Cilnidipine was obtained as gift samples from Ideal Analytical and Research Institute, India. The pharmaceutical dosage form used in this study was Cilacar tablets (J. B. Chemical and Pharmaceuticals Ltd., Mumbai, India) labeled to contain 20 mg of Cilnidipine was procured from the market. Double distilled methanol was used. All other chemicals used were of Analar grade. All the aqueous solutions were prepared in double distilled water. 2 M hydrochloric acid, Sodium nitrite (0.1%w/v), Ammonium sulphamate (0.5%w/v), NED reagent (0.1%w/v) solutions were prepared in double distilled water.

Preparation of stock solution

The stock solution was prepared by dissolving 100 mg pure Cilnidipine in 25 mL of methanol in to 100 mL volumetric flasks and sonicated for 15 min. Then volume was made up to 100 mL with distilled water to give a concentration of 1 mg/mL.

Recommended procedure and calibration graph

Transfer increasing volumes of the filtrate, covering the range 16 – 24 mg/mL into a series of 50 mL volumetric flasks. Add 5 mL of 2M HCl and the mixtures are shaken. Then 5 mL of 0.1 %w/v sodium nitrite solution is added and the mixtures are allowed to stand for 2 minutes. Then 5 mL of 0.5 %w/v ammonium sulphamate solution is added and is allowed to stand for 2 minutes. After that 5 mL of 0.1 %w/v NED was added and the volumes are made up to the mark with methanol. After 10 minutes, the absorbance of the Purple chromogen was measured against a reagent blank, prepared in the same manner but without CIL at 554 nm.

Procedure for the tablet dosage form

Ten tablets (20 mg / tablet) were weighed and finely powdered. A portion of the powder equivalent to 100 mg of the drug was weighed in to a 100 mL volumetric flask and dissolved in 25 mL of methanol and was sonicated for 15 minutes. Then the volume was madwe upto the mark with distilled water. The solution was shaken well, filtered and an aliquot of the filtered drug solution was the treated as done in the recommended procedure.

Method Validation

The developed method was validated as per the International Conference on Harmonization (ICH) [18-19] guidelines with respect to linearity and range, precision, accuracy, limit of detection (LOD) and limit of quantization (LOQ). The values were analyzed by statistical methods.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of CIL. Beer-Lambert's concentration range was found to be 16-24 µg/mL. The overlay spectra and calibration graph are shown in Figure 2 and 3 respectively. The optical parameters are given in Table 1.

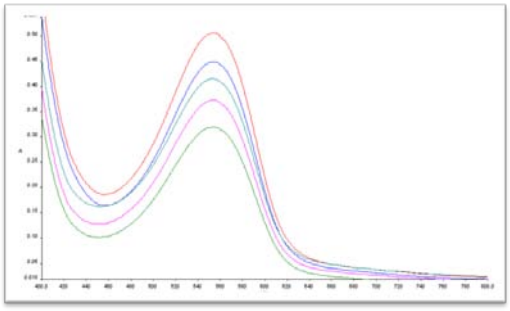

Fig. 2: Overlay spectrum of cilnidipine showing linearity

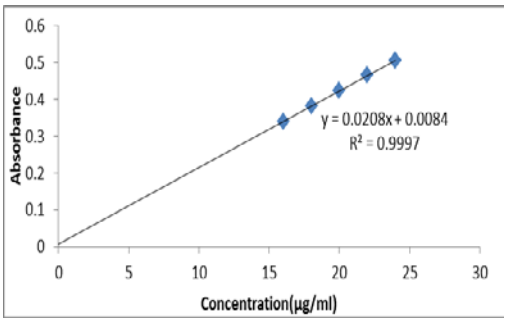

Fig. 3: Calibration curve of cilnidipine

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

The LOD and LOQ of CIL were determined by using standard deviation of the response and slope approach as defined in the International Conference on Harmonization (ICH) guidelines. The LOD and LOQ data presented in Table 1.

Accuracy

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 CIL was found in the range of 98.3 – 102 %w/w (Table 2).

Table 1: Optical Characteristics and Other Parameters

Parameter	Results
Regression equation	y = 0.0208X + 0.0084
λ_{max} (nm)	554
Beer's law limits (µg/mL)	16-24
Slope	0.02
Intercept	0.008
Correlation Coefficient	0.999
LOD (µg/mL)	0.4365
LOQ(µg/mL)	1.3228

Table 2: Recovery Study Data.

Preanalysed Quantity	Amount of pure drug added	Amount recovered (µg/mL)	% Recovery
6	10	16.15	101.00
10	10	20.22	102.00
14	10	23.83	98.30

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 1.08665 and 0.89205 for intraday and Interday respectively.

RESULTS AND DISCUSSION

CIL is a 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.

CONCLUSION

A visible Spectrophotometric method has been developed for the determination of CIL in bulk and tablet formulation. The method was validated based on ICH analytical method validation guidelines. The method was found to be accurate, linear, precise and reproducible. Hence the method can be used for routine analysis of CIL in bulk and tablet formulation.

CONFLICT OF INTERESTS

Declared None

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REFERENCES

1. Yoshimoto R, Dohmoto H, Yamada K, Goto A. Prolonged inhibition of vascular contraction and calcium influx by the novel 1,4-dihydropyridine calcium antagonist Cilnidipine (FRC-8653). Jpn J Pharmacol 1991;56;225–9.
2. http: //www.chemicalbook.com/ChemicalProductProperty_EN_CB2193117. htm.
3. Mohammed M. Safhi, Spectrophotometric method for the estimation of cilnidipine in bulk and pharmaceutical dosage forms. Orient J Chem 2013;29(1):131–4.
4. Pankaj P Chaudhari, AV Bhalerao. Method Validation for Spectrophotometric Estimation of Cilnidipine. Int J Pharm Pharm Sci 2013;4(5):96–8.
5. Parihar YP, Kotkar TA, Mahajan MP, Sawant SD. Development and validation of UV Spectrophotometric methods for the simultaneous estimation of Cilnidipine and Telmisartan in tablet and bulk dosage form by Simultaneous Equation and Absorbance Ratio method. Int J Pharm Integrated Life Sci 2014;2(3):59–74.
6. M Haripriya, Neethu Antony, P Jayasekhar. Development and validation of UV Spectrophotometric Method for the simultaneous estimation of Cilnidipine and Telmisartan in Tablet Dosage Form utilising Simultaneous Equation and Absorbance Ratio Method. Int J Pharm Biol Sci 2013;3(1):343–8.

7. Nilam K Patel, Jayvadan K Patel. Simultaneous UV Spectrophotometric methods for estimation of Cilnidipine and Telmisartan in Tablet Dosage Form. Inventi Rapid: Pharm Analysis & Quality Assurance, 2013. Available from http: //www.inventi.in/Article/ppaqa/576/12.aspx.
8. Isha J Soni, Hiral J Panchal. Development and validation of dual wavelength UV Spectrophotometric Method for simultaneous estimation of Cilnidipine and Olmesartan Medoxomil in Tablet dosage form. Indian J Pharm Biol Res 2014;2(1):76-81.
9. Shahin Vahora, Falgun Mehta, Usmangani Chhalotiya, Dimal Shah. Dual wavelength spectrophotometric method for estimation of cilnidipine and telmisartan in their combined dosage form. Res Rev: J Pharm Anal 2014;3(2):22–9.
10. Faimida Jahan, Avnish Jain, Sumeet Prachand, Arun Kumar Gupta. Simultaneous estimation of telmisartan and cilnidipine in solid dosage form. Int J Pharm Res Sci 2012;1(1):32–42.
11. Mohammed Safhi M, Nagaraj Manohara Yagaina. Development and validation of a rapid stability indicating chromatographic determination of cilnidipine in bulk and dosage form. Res J Pharm Technol 2013;6(3):296–9.
12. Xianhua Zhang, Suodi Zhai, Rongsheng Zhao, Jin Ouyang, Xiaoguang Li, Willy RG Baeyens. Determination of Cilnidipine, a new Calcium antagonist, in human plasma using high performance liquid chromatography with tandem mass spectrometric detection. Anal Chim Acta 2007;1(2):142–6.
13. HE Ling-yun, HU Gao-yun, ZHOU Yan-bin, LIU Jian-hao. Determination of Cilnidipine and its related substances by RP-HPLC. West China J Pharm Sci 2004;01.
14. Sidhdhapara Mital. Development and validation of RP-HPLC method for simultaneous estimation of Cilnidipine and Olmesartan Medoxomil in their Combined Tablet Dosage Form. Int J Pharm Biol Sci 2014;4(1):157–60.
15. Prajakta Pawar, Santosh V Gandhi, Padmanabh B Deshpande, Suvarna Vanjari, Swapnil U Shelar. Simultaneous RP-HPLC estimation of Cilnidipine and Telmisartan in combined tablet dosage form. Chem Sin 2013;4(2):6–10.
16. Reema H Rupareliya, Hitendra S Joshi. Stability indicating simultaneous validation of telmisartan and cilnidipine with forced degradation behavior study by RP-HPLC in tablet dosage form. ISRN Chromatogr; 2013. http: //dx.doi.org/ 10.1155/ 2013/461461.
17. Pawar Prajakta, Deshpande Padmanabh, Gandhi Santhosh, Bhavnani Vandana. high performance thin layer chromatographic determination of cilnidipine and telmisartan in combined tablet dosage form. Int Res J Pharm 2012;3(6):219–22.
18. International Conference on Harmonization Guidance for Industry, In: Q2A Text on Validation o f Analytical Methods, Switzerland, IFPMIA 1994:1–4.
19. International Conference on Harmonization Guidance for Industry, In: Q2B Text on Validation of Analytical Methods, Switzerland, IFPMI A 1996:1–8.