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Simultaneous Estimation Of Telmisartan And Cilnidipine In Combined Tablet Dosage Form By Rp-Hplc

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Abstract: This paper describes a simple, accurate, and validated reverse-phase high-performance liquid chromatographic method for the simultaneous quantification of Telmisartan and Cilnidipine as the bulk drug and in tablet dosage forms. Separation was carried out on Waters HPLC system equipped with SUPLECO C_{18} column (150 × 4.6 mm i.d.) and PDA detector using Methanol: Sodium dihydrogen phosphate buffer (pH 7) (70:30, v/v)) as the mobile phase, and detection was carried out at 273 nm. Results were linear in the range of 50-150 µg mL^{-1} for Cilnidipine and 50-150 µg mL^{-1} for Telmisartan. The method was successfully applied for the analysis of drugs in pharmaceutical formulation. Results of the analysis were validated statistically and by recovery studies.

Keywords: Telmisartan, Cilnidipine Rp-Hplc

I. Introduction

Cilnidipine (CILNI), chemically, 1,4-Dihydro- 2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinecarboxylic acid 2- methoxyethyl(2E)-3-phenyl-propenyl ester 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]. Telmisartan (TELMI), 4′-[1(1,4′ -Dimethyl-2′-propyl [2,6′-bi-1H-benzimidazol]-1′-yl) methyl] - [1,1′-biphenyl] -2- carboxylic acid is an angiotensin II receptor blocker that shows high affinity for the angiotensin II receptor [2].

Literature survey reveals reverse phase high-performance liquid chromatographic (RP-HPLC) [3], LC-MS [4, 5] and high performance thin layer chromatographic (HPTLC) [6] methods for the determination of CILNI either as a single or in combination with other drugs in human plasma and in pharmaceutical preparations. Analytical methods reported for TELMI includes HPLC [7-12], Spectrophotometric [13-16], UPLC [17] and HPTLC [18] either as a single drug or in combination with other drugs.

To the best of our knowledge no HPLC method of analysis has yet been reported for simultaneous analysis of CILNI and TELMI. This paper describes a simple, accurate, and validated reverse-phase high-performance liquid chromatographic (RP-HPLC) method for the simultaneous quantification of these compounds as a bulk drug and in tablet dosage forms. The proposed method is optimized and validated as per the International Conference on Harmonization (ICH) guidelines [19].

II. Materials And Methods

Chemicals and reagents

Pharmaceutical grade working standards CILNI and TELMI were obtained from J. B. Chemicals and Pharmaceuticals Ltd. (Mumbai) and FDC Ltd. (Goa), India respectively used as such without further purification. The pharmaceutical dosage form used in this study was Cilacar T tablets (J. B. Chemical and Pharmaceuticals Ltd., Mumbai, India)**,** labeled to contain 10 mg of CILNI and 40 mg of TELMI were procured from the local market. Methanol (HPLC grade), sodium dihydrogen phosphate (AR grade), Ortho phosphoric acid (AR grade) purchased from Merck specialties Pvt. Ltd. (Mumbai, India) and double distilled water were used in analysis.

Instrumentation and chromatographic conditions

` Waters HPLC system consisting of waters 2695, photo diode array detector(PDA),with an automated sample injector using Empower2 software was used for analysis. Separation was carried out on SUPLECO C_{18} (150 x 4.6 mm i.d.) column using as mobile phase methanol: sodium dihydrogen phosphate buffer (pH 7) (70:30, v/v) at flow rate of 1 mL min^{-1} .Samples were injected and detection was carried out at 273 nm.

Preparation of standard stock solutions

Standard stock solution of CILNI and TELMI was prepared separately by dissolving 10mg of drug in 50 mL methanol to get concentration of 1000 µg mL^{-1} from which 1 ml of solution was further diluted to 10 mL with mobile phase to get a working standard solution having concentration 100 µg mL^{-1} for both the drugs.

Procedure for analysis of tablet formulation

Twenty tablets were weighed accurately and powdered. A quantity of tablet powder equivalent to 40 mg of TELMI (10 mg of CILNI) was weighed and transferred to 100 mL volumetric flask containing about 50 mL of methanol and ultrasonicated for 20 min and volume was made upto the mark with the methanol. One millilitre of this solution was transferred to 10 mL calibrated volumetric flask and volume was made up to the mark with the mobile phase. After setting the chromatographic conditions and stabilizing the instrument to obtain a steady baseline the tablet sample solution was injected, chromatogram was obtained and the peak areas were recorded. The injections were repeated six times and the amount of each drug present per tablet was estimated from the respective calibration curves.

Method development

Lots of mobile phase and three different proportions were tried and finally was selected as sodium dihydrogen phosphate: methanol in the ratio of 70:30(v/v) at pH 7 appropriate mobile phase which gave good resolution and acceptable system suitability parameters. The chromatogram of working standard solution is shown in fig 1.

Calibration curve

Accurately measured volumes of working standard solution of TELMI and CILNI were transferred into a series of 10ml volumetric flasks and diluted appropriately with mobile phase.10µl of each solution was injected at same chromatographic conditions. Calibration curves were obtained by plotting the peak area versus concentration of drug. Regression equations were calculated. The method was found linear over a concentration range 50-150µg/ml of TELMI and 50-150µg/ml of CILNI. (Fig 2,3)

Precision

The repeatability studies were carried out by estimating response of TELMI (100µg/m) and CILNI (100µg/m) five times and results are reported in terms of %CV. It is expressed as the percentage coefficient of variation (%CV) which is calculated as per the following expression.

%CV= (standard deviation / mean) x 100.

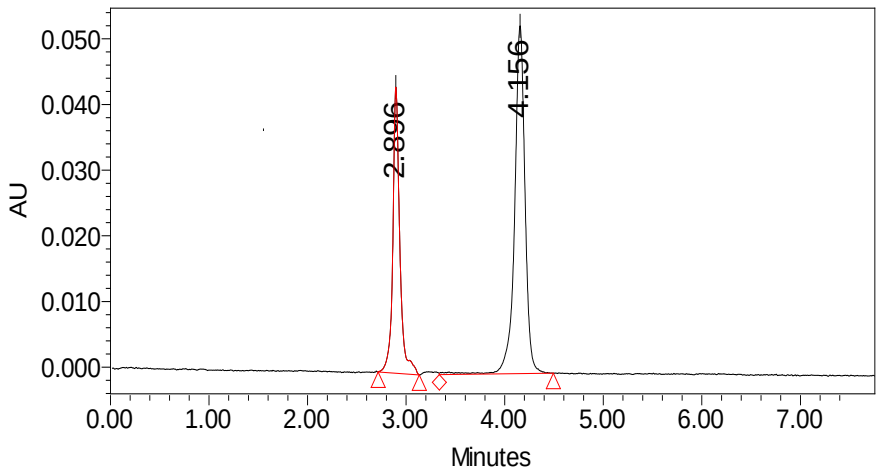

Fig 1: **A typical chromatogram shows sharp peaks of TELMI and CILNI**

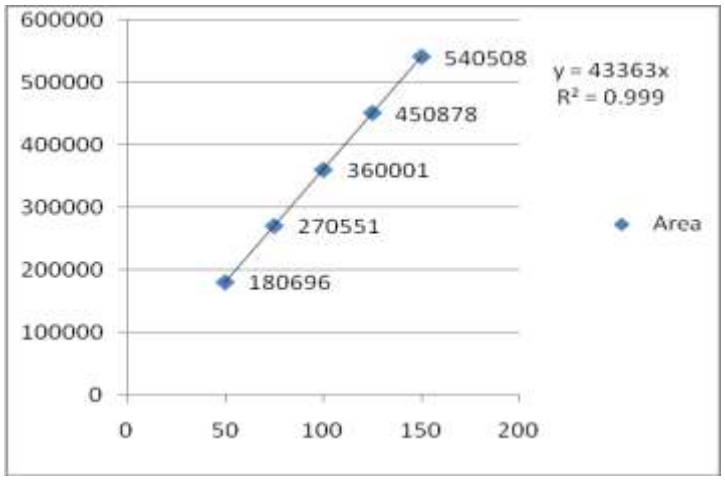

Fig 2: Calibration curve of telmisartan

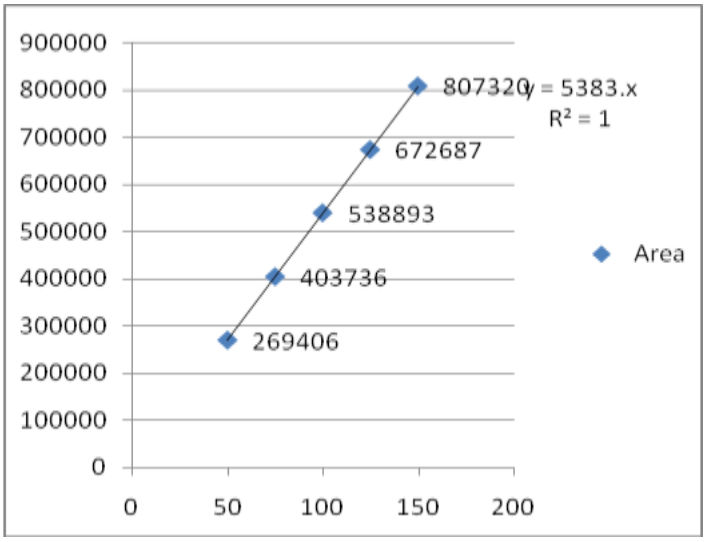

Fig 3: Calibration curve of cilnidipine

Accuracy

to pre-analyzed sample solution at three different levels 50, 100 and 150 %. The percentages of recoveries were calculated which sense to confirmation that the proposed method was accurate.

Limit of detection and Limit of quantification

Limit of detection and Limit of quantification were calculated as 3.3 σ /S and 10 σ /S respectively; where σ is the standard deviation of the response (y-intercept) and S is the slope of the calibration plot.

III. Results And Discussion

The present work done on this combination comprises a simple, precise and accurate method by reverse phase high performance liquid chromatography. The present combination of TELMI and CILNI was marketed as one formulation. An attempt has been made to estimate TELMI and CILNI by RP-HPLC. Calibration curve depicting the linearity and range for TELMI and CILNI were determined from mixed standards were found to be order 50-150µg/ ml of TELMI and CILNI. The formulation was diluted in the linearity range and peak areas were determined, the concentrations of both TELMI and CILNI were determined by comparing the peak areas of sample with that of standard peak areas this can be identified by their retention times 2.89min for TELMI and 4.15min for CILNI. The results obtained from HPLC method were reproducible. The values percentage deviation was within limit (>2%) and recovery close to 100% indicating reproducibility and accuracy of method.

Parameters	TELMI	CILNI
Linearity range (µg mL^{-1})	50-150	50-150
Correlation co-efficient	0.999	1
LOD (µg mL^{-1})	3.06	3.10
LOQ (µg mL^{-1})	10.17	10.37
Accuracy (% Recovery)	99	98
Precision (% R.S.D.)[2]	0.14	0.23

Table: Summary of validation parameters

IV. Conclusion

The validated RP-HPLC method employed here proved to be simple, fast, accurate, and precise, thus can be used for routine analysis of TELMI and CILNI in combined tablet dosage form.

V. Acknowledgement

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VI. References

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