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Research Article

SPECTROPHOTOMETRIC ESTIMATION OF CINACALCET HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Two simple, precise and economical UV methods have been developed for the estimation of Cinacalcet hydrochloride in bulk and pharmaceutical dosage form. Method A is Absorbance maxima method, which is based on measurement of absorption at maximum wavelength, 281.0 nm. Method B is area under curve (AUC), in the wavelength range of 249-299 nm. Linearity for detector response was observed in the concentration range of 5-50µg/ml for the two methods. The accuracy of the methods was assessed by recovery studies and was found to be 99.87 and 99.30% respectively.The developed method were validated with respect to linearity, accuracy (recovery), precision and specificity. The results were validated statistically as per ICH Q2 R1 guideline and were found to be satisfactory. The proposed methods were successfully applied for the determination of Cinacalcet hydrochloride in commercial pharmaceutical dosage form.

Keywords: Cinacalcet hydrochloride, UV Spectrophotometry, Absorbance maxima method, Area under curve.

INTRODUCTION

Cinacalcet hydrochloride is an oral calcimimetic indicated for the treatment of secondary hyperparathyroidism (HPT) in patients on dialysis with endstage renal disease (ESRD), and in patients with parathyroid carcinoma to reduce hypercalcaemia. Cinacalcet hydrochloride is the first of a new class of drugs, the calcimimetics, which act by increasing the sensitivity of calcium sensing receptors in the parathyroid gland[1, 2, 3]. Chemically Cinacalcet hydrochloride is N-((1R)-1-(1-Naphthyl) ethyl)-3-(3-(trifluoromethyl) phenyl) propan-1-amine hydrochloride (Fig.1).

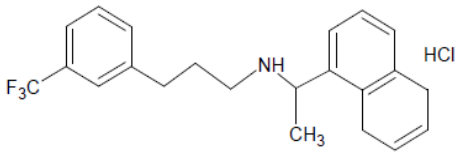

Fig. 1: It shows structure of Cinacalcet hydrochloride[4]

The literature survey reveals that several analytical methods have been reported for the quantification and determination of the drug individually in human plasma by liquid chromatography/tandem mass spectrometry[4, 5, 6]. From literature, no spectrophotometric method has been reported for the estimation of Cinacalcet hydrochloride by the two simple methods. Hence, a simple, rapid, precise and accurate method for the estimation of Cinacalcet hydrochloride in bulk and pharmaceutical formulation is developed and validated.

MATERIAL AND METHODS

Materials

Cinacalcet hydrochloride was generous gift samples from Watson Pharma Limited (Ambernath, Mumbai, India). A commercial PTH tablets (Intas Pharma) containing 30mg was purchased from local market and used within their shelf-life period. All other chemicals used were of pharmaceutical or analytical grade.

Instrumentation

A Jasco double beam UV–visible spectrophotometer, Model: V-630, with a fixed bandwidth (1.5nm) and 1-cm quartz cell was used for Spectral and absorbance measurements. In addition, electronic balance, micropipette and sonicator were used in this study.

Procedure

Preparation of standard stock solution

Standard stock solutions of Cinacalcet hydrochloride (CIN) were prepared by dissolving 25 mg of drug in 25 ml of methanol to get standard stock solution of 1000 µg/ml. This solution was further diluted to get standard solution of concentration 100 µg/ml of CIN.

Method A: Absorption Maxima Method

For the selection of analytical wavelength, standard solution of CIN was scanned in the spectrum mode from 400 nm to 200 nm. From the spectra of drug [Fig.2], λ_{max} of CIN, 281 nm was selected for the analysis. Aliquots of standard stock solution were made and calibration curve was prepared in the concentration range of 5-50µg/ml at 281 nm.

Method B: Area under Curve Method

From the spectra of drug obtained after scanning of standard solution of CIN, area under curve in the range of 249-299 nm was selected for the analysis. The calibration curve was prepared in the concentration range of 5-50 µg/ml at their respective AUC range.

The drug followed the Beer-Lambert's law in the concentration range of 5-50 µg/ml. The calibration curve was plotted as absorbance against concentration of Cinacalcet hydrochloride. The coefficient of correlation (r), slope and intercept values of these methods are given in Table .1 Six concentrations of sample solutions were determined from calibration curve.

Application of the proposed methods for the determination of CIN in tablet dosage form

For the estimation of drug in the tablet formulation, 20 tablets were weighed and weight equivalent to 25 mg of CIN was transferred to 25 ml volumetric flask and ultrasonicated for 20 minutes and volume was made up to the mark with methanol. The solution was then filtered through a Whatmann filter paper (No. 42). The filtrate was appropriately diluted further. In Method-A, the concentration of CIN was determined by measuring the absorbance of the sample at 281 nm in zero order spectra mode. By using the calibration curve, the concentration of the sample solution can be determined.

In Method-B, the concentration of CIN was determined by measuring area under curve in the range of 249-299nm. By using the calibration curve, the concentration of the sample solution can be determined.

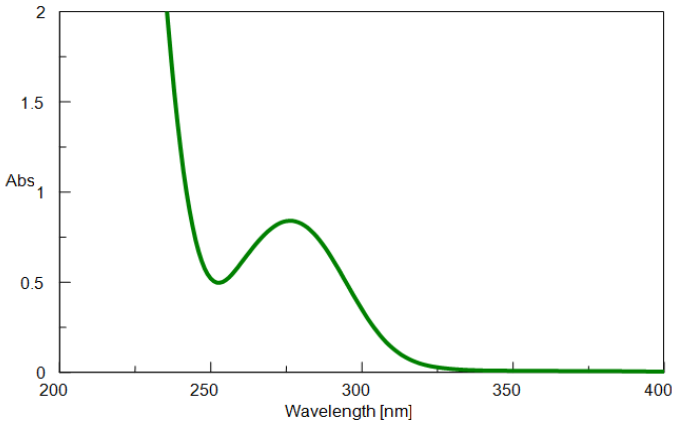

Fig. 2: It shows λ_{max} of Cinacalcet hydrochloride

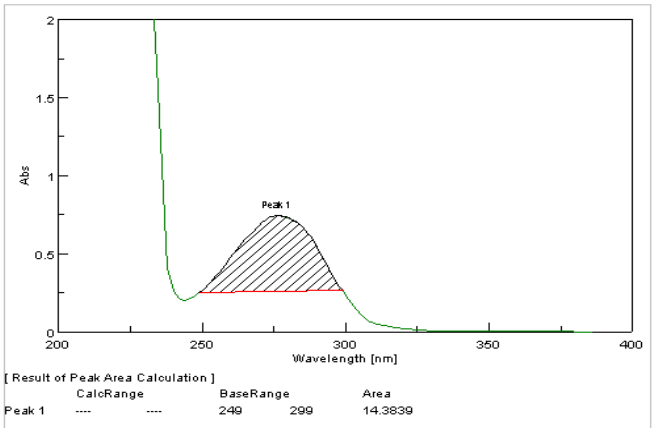

Fig. 3: It shows AUC of Cinacalcet hydrochloride

Validation of the developed methods[7]

The methods were validated with respect to accuracy, linearity, precision and selectivity.

Accuracy

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% & 120%).

Linearity

The linearity of measurement was evaluated by analyzing different concentration of the standard solution of CIN.

Precision

The reproducibility of the proposed method was determined by performing tablet assay at different time intervals (morning, afternoon and evening) on same day (Intra-day precision) and on three different days (Inter-day precision). Result of intra-day and inter-day precision is expressed in % RSD.

Table 1: Table shows Optical characteristics and precision

S. No.	Parameter	Method- A	Method- B
1.	**λ-** max / wavelength range (nm)	281	249-299
2	Beer's law limit (µg/ml)	5-50	5-50
3.	Molar absorptivity (L/mol.cm)	8314.79	2639.32
4.	Sandell's sensitivity (µg/Sq.cm/0.001)	0.04737	0.02141
5.	Correlation coefficient (r)	0.999	0.999
6.	Slope (m)	0.021109	0.086701
7.	Intercept	0.007685	0.095681

Table 2: Table shows Results of Analysis of Tablet Formulation (N*=6)

Method	Label Claim mg	Amount of drug estimated (mg/tab)	% Label Claim*± S.D.	% Recovery
A	30	99.87	99.87±0.09987	99.87
B	30	99.30	99.30±0.00852	99.30

Table 3: Table shows Result of Recovery studies

Excess drug added to the analyte (%)	% Recovery		%RSD		SE	
	Method A	Method B	Method A	Method B	Method A	Method B
80	99.65	100.01	0.409	0.289	0.673	0.154
100	100.56	100.56	0.102	0.194	0.417	0.198
120	100.78	100.78	0.094	0.127	0.792	0.129

a) RSD: Relative Standard deviation b) SE: Standard error

Table 4: Table shows Result of Intra-day and Inter-day precision

Method	Intra-day precision			Inter-day precision		
	SD	%RSD	SE	SD	%RSD	SE
Method A	0.1097	0.412	0.853	0.1766	0.987	0.137
Method B	0.3451	1.078	0.1134	0.1427	0.876	0.198

RESULT AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for analysis of Cinacalcet hydrochloride in its pharmaceutical dosage form. Absorbance maxima of CIN at 281 nm for Method A and Wavelength range of 249-299 nm for Method B was selected for the analysis. Linearity for detector response was observed in the concentration range of 5-50 µg/ml for the two methods. Percent label claim for CIN in tablet analysis was found in the range of 99.87 % and 99.30% [Table 2]. The standard deviation, % RSD and standard error calculated for both the methods were low, indicating high degree of precision. Accuracy of proposed methods was ascertained by recovery studies and the results are expressed as % recovery. % recovery for CIN was found in the range of 99.65% to 100.78 % Results of the recovery studies exhibited high degree of accuracy of the proposed methods [Table 3]. % RSD for Intraday assay precision was found to be 0.412 and 1.078 for Method A and B. Interday assay precision was found to be 0.987 and 0.876 for Method A and B [Table 4]. Based on the results obtained, it is found that the proposed methods are accurate, precise, reproducible & economical and can be employed for routine quality control of Cinacalcet hydrochloride in bulk drug and its pharmaceutical dosage form.

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