International Journal of Medicine and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijmpr

Research Article **Open Access**

Simple Validated UV method for Cinacalcetin Bulk and Its Tablets Dosage Form

Anilkumar P, Mohammed Ishaq B, Hindustan Abdul Ahad, Kalyani K, Khadeera C

Balaji College of Pharmacy, Rudrampeta bypass, Ananthapuramu, AP, India

A B S T R A C T

Cinacalcet is prescribed to Hyperparathyroidism patients. The present research work is to develop and validate Cinacalcet by UV spectrometric method. Simple, accurate, precise and cost efficient spectrophotometric method has been developed for the estimation of Cinacalcetin bulk and its tablets dosage form. The optimum condition for the analysis of the drug was established. The maximum wavelength (λ_{max}) was found to be 271.74nm in Methanol. The mean percentage recovery of Cinacalcet was found to be in range of 99.40-101.64%. Beers law was obeyed in the concentration range of 10-200µg/ml. Calibration curve shows a linear relationship between the absorbance and concentration. The line equation y = 0.0109x+0.123 with R^2 = 0.9982 was obtained. Validation was performed as ICH guidelines for linearity, accuracy, precision, LOD & LOQ. The proposed method may be suitable for analysis of Cinacalcet in bulk and tablets formulation for routine quality control purposes.

Keywords: Cinacalcet tablets, UV spectrophotometric, beers law

A R T I C L E I N F O

CONTENTS

Article History: Received 28 December 2015, **Accepted** 31 January2015, **Available Online** 10 June 2016

***Corresponding Author**
Hindustan Abdul Ahad
Balaji College of Pharmacy,
Ananthapuramu, Andhra Pradesh, India
Manuscript ID: IJMPR2970

PAPER-QR CODE

Citation: Hindustan Abdul Ahad, *et al.* Simple Validated UV method for Cinacalcetin Bulk andIts Tablets Dosage Form. *Int. J. Med. Pharm. Res.*, 2016, 4(3): 129-133.

1. Introduction

Cinacalcet (R)-Alpha-Methyl-N-[3- [3-(trifluoro methyl) phenyl] propyl]-1-naphthalenemethane amine (shown in fig.1). SHPT develops as a result of impaired calcium homeostasis when the failing kidneys disturb the complicated interactions between parathyroid hormone (PTH), calcium, phosphorus, and vitamin D. Cinacalcet hydrochloride, a first-in-class calcimimetic agent, offers a new therapeutic approach to the treatment of SHPT [1]. Cinacalcet puts forth its action by binding to the

parathyroid Ca sensing receptor (CaSR). This leads to a decrease in the circulation of parathyroid hormone (PTH) levels in CKD

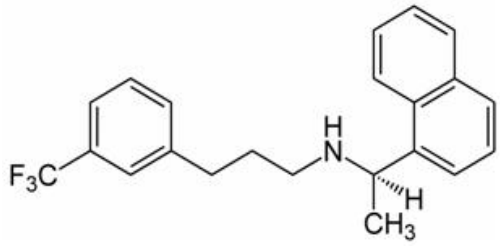

Figure1: Chemical Structure of Cinacalcet

2. Materials and Methods

Experimental methods:

An UV–Visible double beam spectrophotometer with 1cm matched quartz cells were used for the spectral and absorbance measurements. All the chemicals and reagents used were of analytical grade and the aqueous solutions were freshly prepared with triple distilled water [2-5].

Preparation of Stock solution

Accurately weighed 10 mg of Cinacalcet was transferred into 100 ml volumetric flask, dissolved in 10ml of methanol. Take 0.1 ml from above solution and make up to 10ml. Take 0.4 ml from the above solution and make up to 10 ml to get a concentration of 40µg/ml. working standard solution of 1µg/ml for10ml with water. The working standard solution was daily prepared by diluting stock solution in water [6].

Preparation of test sample

Ten tablets of Cinacalcet were weighed and powdered. The quantity of the powder equivalent to 10 mg (31.1mg) of Cinacalcet was transferred in to 10ml of volumetric flask. Methanol was added up to 10ml and mixed for 5-10 min, filtered the solution and first few ml was discarded. 0.4 ml from the above stock solution was transferred to 10 ml volumetric flask along with methanol. From the above solution 0.4ml was transferred to 10 ml volumetric flask along with methanol to get 40µg/ml concentration [6].

Solubility Studies

Cinacalcet was tested for solubility in various solvents at room temperature [7, 8].

λ_{max} Determination:

The absorbance of the solutions containing Cinacalcet at 10µg/ml was determined in the UV range 200-400nm using an appropriate blank [9].

Accuracy

The accuracy of the method was checked by recovery determinations and percentage bias. The determination was done over three concentration levels in triplicate according to the ICH guidelines. The concentration levels selected as QC samples were 5µg/ml, 10µg/ml and 15µg/ml of Cinacalcet [10].

Precision

The precision was evaluated on the basis of repeatability and intermediate precision. On at least three occasions, six replicates of each QC sample pool at low, three replicates middle, and six replicates at high concentrations were assayed. Percentage relative standard deviation (%RSD) was calculated [11].

Linearity

The linearity of the described spectrophotometric method was studied in the concentration range 10-100µg/ml for Cinacalcet. The calibration curves were constructed by plotting concentration versus intensities. In the overall concentration range examined, the linearity was evaluated by linear regression analysis that was calculated by the least square regression method [11].

Limit of Detection

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value [11].

Limit of Quantification

The Quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy [11].

Degradation studies

The degradation studies were performed for the Cinacalcet in Methanol [12].

3. Results and Discussion

Cinacalcetper formed in various solvents like carbon tetra chloride, aniline, chloroform, acetone, nitro benzeneand toluene. The λ max was found to be 271.74nm. The λ_{max} of Cinacalcet pure drug and in tablets were shown in fig 2 and 3 respectively. The Molar Absorptivity was found to be 7.5 x 10^{-6} by using the formula (e= A / c l), (A= absorbance, c = sample concentration in moles/liter &l = length of light path through the sample in cm). The Sandell's sensitivity (Sandell's sensitivity = mol. wt / molar absorvitity) was found to be 2.96 X 10^{7}µg cm^{-2}.The Accuracy results were shown in table 1. The precision was carried out for 10µg/ml. The intraday precision for 10µg/ml was found to be 0.8933% RSD, while it gave a value of 1.339% RSD at interday (intermediate precision). The accuracy of the method was calculated as percent bias. The Intraday Precision and Inter-day precision of Cinacalcet tablets were shown in table 2 and 3 respectively.

The spectrum of standard solution of Cinacalcet in Methanol was given in Fig. 2 and 3.The λ_{max} was found to be 271.74 nm. The calibration curve was prepared by plotting concentration (in µg/ml) on the abscissa and absorbance in ordinate axis in the range of 10-100µg/ml. Good linearity was obtained in the concentration range considered. The linearity equation was developed by using least square regression analysis.

The Limit of detection and Limit of quantitation was calculated according to the ICH guidelines. The Beer-Lamberts limit was found to be10-100µg/ml (table 4). Calibration curve of Cinacalcet was plotted (shown in fig. 4) and the linearity, regression, LOD and LOQ were shown in table 5.The LOD was found to be 1.927µg/ml and the LOQ was found to be 6.422µg/ml. The acid, base, heat and peroxide degradation spectrums of Cinacalcet tablets were shown in fig 5, 6, 7 and 8 respectively. The summary of these degradation results were shown in table 6.

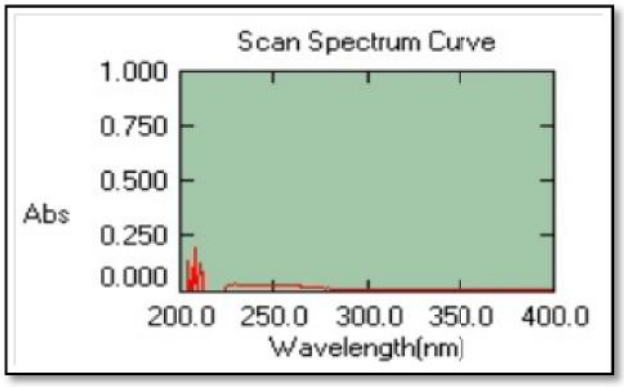

Figure 2: λ_{max} of Cinacalcet pure drug

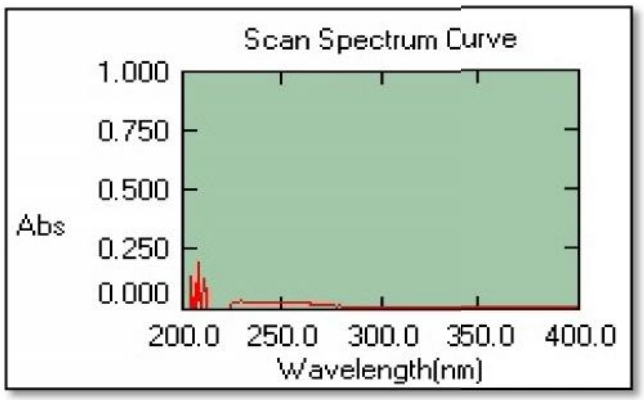

Figure 3: λ_{max} of Cinacalcet tablet powder

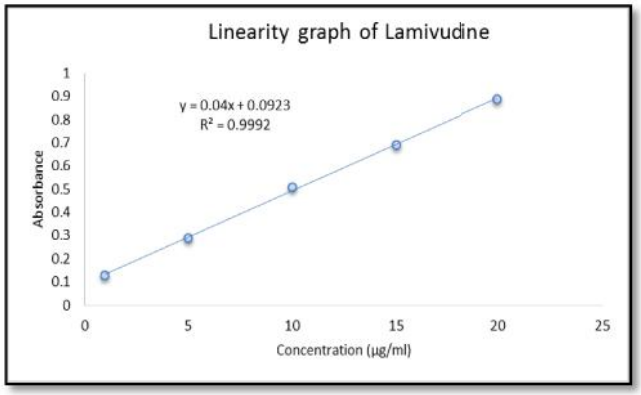

Figure 4: Calibration curve of Cinacalcet

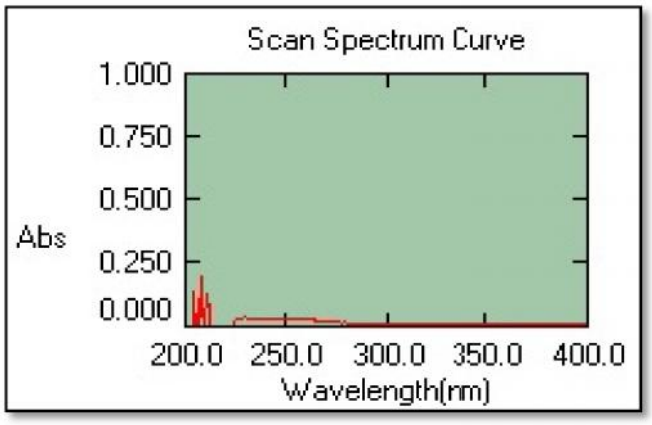

Figure 5: Acid degradation Spectrum of Cinacalcet tablets

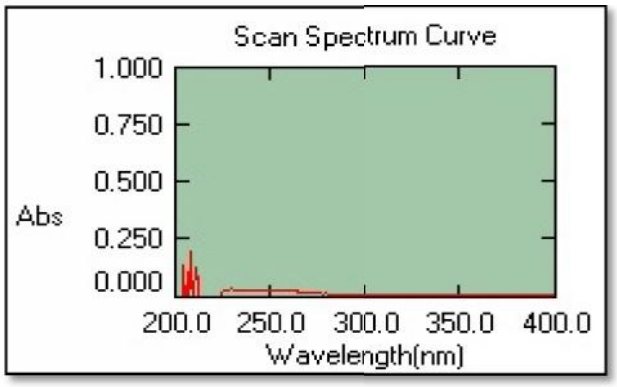

Figure 6: Base degradation Spectrum of Cinacalcet tablets

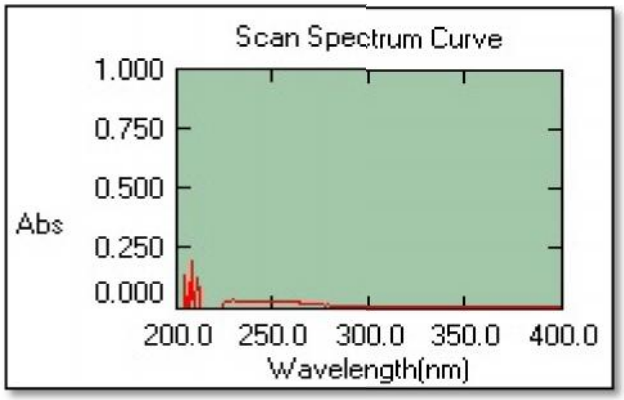

Figure 7: Heat degradation Spectrum of Cinacalcet tablets

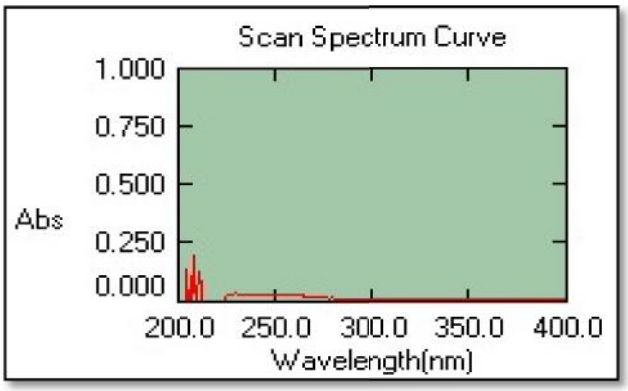

Fig. 8: Peroxide degradation Spectrum of Cinacalcet tablets

4. Conclusion

In this study simple, fast and reliable UV spectrophotometric method was developed and validated for the determination of Cinacalcet in tablet formulation. The method was applied directly to the analysis of pharmaceutical dosage forms without the need for separation such as extraction steps prior to the drug analysis. As these proposed methods have the lowest LOD value and wider linear range so these methods were more sensitive methods. From the results obtained, we concluded that the suggested methods showed high sensitivity, accuracy, reproducibility and specificity. Moreover, these methodswere simple and inexpensive and they can be employed for the routine quality control analysis of Cinacalcet in pharmaceutical formulations.

Table 1: Accuracy results of Cinacalcet tablets

S. No	Conc. Level	Amount of the sample	Absorbance	Amount Added	Amount found	% Recovery	Mean % Recovery
1	50%	32.5	0.256	20.102	19.505	97.031	99.684
2			0.257	20.102	19.581	97.410	
3			0.275	20.102	20.952	104.232	
4			0.263	20.102	20.038	99.684	
5			0.263	20.102	20.038	99.684	
6			0.264	20.102	20.114	100.063	
7	100%	65	0.520	40.203	39.619	98.547	99.494
8			0.528	40.203	40.229	100.063	
9			0.527	40.203	40.152	99.873	
10	150%	97.5	0.793	60.305	60.419	100.189	99.494
11			0.774	60.305	58.971	97.789	
12			0.789	60.305	60.114	99.684	
13			0.789	60.305	60.114	99.684	
14			0.795	60.305	60.571	100.442	
15			0.785	60.305	59.810	99.179	

Table 2: Intraday Precision of Cinacalcet tablets

S. No	Concentration (µg/ml)	Absorbance		
		9.3 AM	1.3 PM	5.3 PM
1	40	0.524	0.544	0.517
2		0.529	0.543	0.516
3		0.526	0.543	0.514
4		0.523	0.543	0.533
5		0.519	0.547	0.511
6		0.518	0.547	0.514
Average		0.523	0.545	0.518
SD		0.004	0.002	0.008
% RSD		0.797	0.363	1.520

Table 3:Inter-day precision of Cinacalcet tablets

S. No	Concentration (µg/ml)	Absorbance		
		Day-I	Day-II	Day-III
1	10	0.548	0.523	0.509
2		0.544	0.528	0.505
3		0.547	0.521	0.513
4		0.566	0.536	0.517
5		0.545	0.539	0.514
6		0.543	0.534	0.528
Average		0.549	0.530	0.514
SD		0.009	0.007	0.008
% RSD		1.569	1.378	1.534
Limit% RSD must be less than 2%.				

Table 4: Slope, Linearity, LOD and LOQ of Cinacalcet tablets

Slope	Linearity (R^2)	LOD(µg/ml)	LOQ(µg/ml)
0.0109x+0.123	0.9982	1.927	6.422

Table 5: Calibration (Linearity) of Cinacalcet tablets

Concentration (µg)	Absorbance
10	0.235
25	0.962
40	1.552
60	1.730
80	3.488

Table 6: Degradation studies of Cinacalcet tablets

Parameter	Results
Acid degradation	0.150
Base degradation	0.148
Peroxide degradation	0.129
Heating degradation	0.149
UV degradation	0.204

5. References

[1] Drug monograph- Cinacalcet. Available from www.drugbank.ca/drugs/db00997.

[2] Shalini S, Shanooja VP, AbdulJameel S, Basima, Harilal KK, Harish R, et al. Application of UV-spectrophotometric methods for estimation of lamivudine in tablets. Dig J Nanomater Biol Struct. **2009**, 4: 357–60.

[3] Basavaiah K, Somashekar BC. Titrimetric and spectrophotometric determination of lamivudine in pharmaceuticals. Indian J Chem Technol. **2009**, 13: 7–12.

[4] Kumar CHA, Kumar TA, Gurupadayya BM, Sloka SN, Reddy BMR. Novel spectrophotometric determination of valacyclovir and cefotaxime using 1, 2-napthaquinone-4-sulfonic acid sodium in bulk and pharmaceutical dosage form. Arch Appl Sci Res. **2010**, 2: 278–287

[5] Sigala A, Raghunath V, and Varma M, Balaswamy G A: NewValidated Liquid Chromatographic Method for TheDetermination Of Impurities In Cinacalcet Hydrochloride. Analytical chemistry-An Indian Journal. **2009**: 8-15

[6] Mohammed Ishaq B, Muneer S, Hindustan Abdul Ahad,A Simple UV Spectroscopic Method for the Determination of Ritonavir inBulk and Tablets, JPBMAL, **2014,** 2(2): 118-122.

[7] Beckett, A.H. and Stenlake, J.B. Practical Pharmaceutical Chemistry. 4th Ed Part 2. New Delhi: CBS Publishers and Distributors; **2002**. p. 275-78.

[8] Residual Solvents, 1997.Solli, Chou, Jalali B et al. "Amplified wavelength–time transformation for real-time spectroscopy," Nature Photonics, **2008**, 2, pp.48-51.

[9] Ishaq BM, Hindustan Abdul Ahad, UV Spectroscopic Method for Estimation of Enalapril Maleate in Bulk andin its Tablets, AMCL, **2014,** 1(1): p.31–35

[10] Loni, Amruta B.; Ghante, Minal R.; Sawant SD. Spectrophotometric estimation of Cinacalcet hydrochloride in bulk and tablet dosage form, International Journal of Pharmacy and Pharmaceutical Sciences. **2012**, 4(3): 513.

[11] Text on validation analytical procedures, international conference on harmonization of technical requirements for registration of pharmaceuticals for human use, ICH harmonized tripartite guidelines, **1996**

[12] ICH, Q2B. Harmonised Tripartite Guideline, Validation of Analytical Procedure Methodology, IFPMA, In: Proceedings of The International Conference on Harmonization, Geneva **1999**.