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UV Spectrophotometric method for the estimation of candesartan cilexetil in bulk and pharmaceutical dosage form

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ABSTRACT

A simple, accurate, specific and sensitive UV spectrophotometric method has been developed and validated for determination of Candesartan Cilexetil in bulk and tablet dosage form. The method is based on the measurement of absorbance of Candesartan Cilexetil in isopropyl alcohol at 306 nm. Beer's law was obeyed over the concentration range of 10-90 µg/ml with correlation coefficient (r^2) 0.999. As per ICH guidelines the method was validated for linearity, accuracy, precision, limits of detection (LOD), Limits of quantification (LOQ), and robustness and ruggedness. The proposed method was successfully applied for determination of Candesartan Cilexetil in tablets with good accuracy, precision and without any detectable interference from tablet excipients. The validity and reliability of the proposed method was assed by recovery studies.

Key words: Candesartan Cilexetil, Isopropyl alcohol, UV Spectrophotometric, Validation.

INTRODUCTION

Candesartan Cilexetil[1-3], a nonpeptide, is chemically described as (±)-1-Hydroxyethyl 2-ethoxy-1-[p-(o-1H-tetrazol-5ylphenyl)benzyl]-7-benzimidazolecarboxylate, cyclohexyl carbonate (ester).

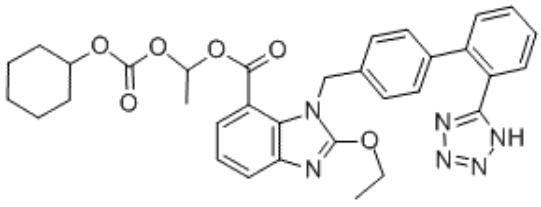

Fig.1 Chemical structure of Candesartan Cilexetil

Candesartan Cilexetil is a white to off-white powder with a molecular weight of 610.67 g/mol. It is practically insoluble in water and sparingly soluble in methanol. Candesartan Cilexetil is hydrolysed to Candesartan during absorption from the gastrointestinal tract. It is mainly used in the treatment of hypertention[4-7]. It may be given once or twice daily with total daily dosage forms ranging from 8 mg to 32 mg. Literature survey reveals various methods like Spectrophotometric[8-10], HPLC[11-13], LC-MS[14-15] were developed for determination of Candesartan Cilexetil in bulk, pharmaceutical formulation and in plasma in single and combined dosage form. Only few UV spectrophotometric methods were reported till now in its single dosage form. Hence an attempt was made to

develop a rapid, accurate, sensitive and economical UV spectrophotometric method for estimation of Candesartan Cilexetil from the tablet formulation.

MATERIALS AND METHODS

Instrumentation

An ELICO UV/Visible spectrophotometer model SL 210 with 10 mm matched quartz cells was used for all spectral measurements equipped with Spectral Treats software. Keeroy balance (1 mg sensitivity) was used for weighing purpose.

Chemicals and Reagents

Isopropyl alcohol was used as a solvent in the present study was of Merck made. Pure Candesartan Cilexetil obtained as gifted sample. Tablet formulation Atacand^{TM}-32 (Candesartan Cilexetil Tablets) contains Candesartan 32 mg was procured from local pharmacy.

Preparation of standard stock solution

Weighed accurately 100 mg of pure Candesartan Cilexetil and transferred it to 100 ml volumetric flask. The content in the flask was dissolved in 20 ml of isopropyl alcohol and volume was made upto the mark with isopropyl alcohol to get a concentration of 1000 µg/ml. From this 10 ml was transferred to 100 ml volumetric flask and volume was made upto the mark with isopropyl alcohol to get a concentration of 100 µg/ml.

Procedure for calibration curve

Aliquots of (1-9 ml) standard stock solution (100 µg/ml) of Candesartan Cilexetil were transferred into a series of 10 ml calibrated volumetric flask. The volumes were made up to 10 ml with Isopropyl Alcohol and the absorbance of each solution was measured at 306 nm against the blank. The UV spectrum was shown in Fig.1.

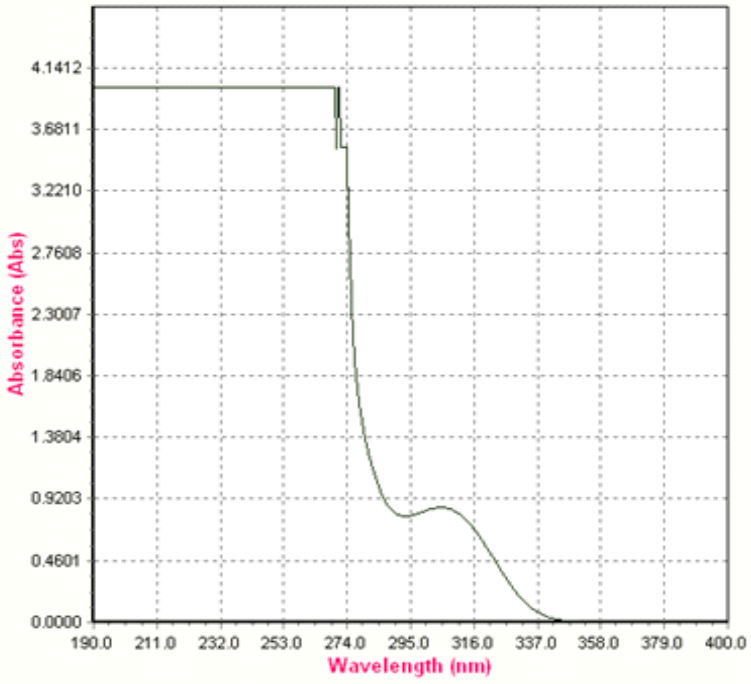

Fig.1 UV spectrum of Candeartan Cilexetil

Estimation of Candeartan Cilexetil in tablet formulation

Accurately about 20 tablets of Candeartan Cilexetil were weighed and triturated to fine powder. Tablet powder equivalent to 100 mg of Candesartan Cilexetil was taken and dissolved in 100 ml of isopropyl alcohol with shaking.

This was then filtered through whatmann's filter paper No.41 to get concentration of 1 mg/ml solution. It was then diluted to make the concentration of 100 µg/ml with isopropyl alcohol. From this solution 50 µg/ml was prepared for analysis. Absorbance was read and concentration of Candeartan Cilexetil determined using the calibration curve. Calculations were then made with the dilution factor to find out the concentration of the drug in tablets. The experiments were repeated six times to check its reproducibility.

RESULTS AND DISCUSSION

Method Validation[16]

Linearity

Calibration curve was obtained in a concentration range from 10-90 µg/ml for Candesartan Cilexetil. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.0143x + 0.0003 with correlation coefficient 0.999 (Table 1, Figure 2).

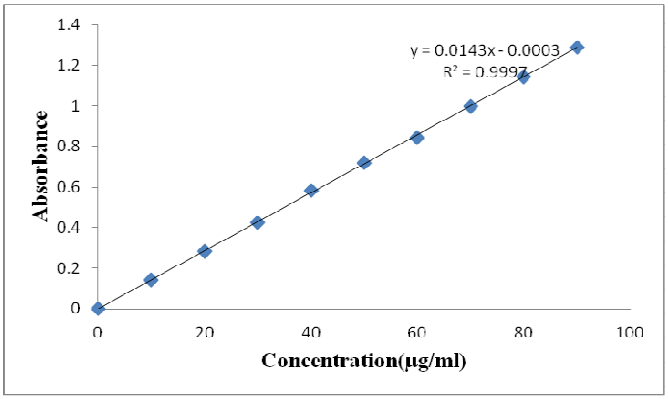

Fig.2 Calibration curve of Candesartan Cilexetil

Table 1: Optical characteristics and Regression parameters

Parameters		
λ_{max} (nm)		306
Beer's law limits (µg/ml)		10 – 90
Molar absorptivity (lit mol^{-1} cm^{-1})		8.8 x10^4
Limit of Detection (LOD/ µg/ml)		0.466
Limit of Quantification(LOQ/ µg/ml)		1.412
Sandell's sensitivity (µg/cm^2/ 0.001 A.U.)		0.0069
Regression equation (Y*)		
Slope (b)	0.0143	
Intercept (a)	0.0003	
Correlation coefficient (r^2)		0.999
% RSD**		0.778
Confidence limits with 0.01 level		0.9624

** Y= bX+a, where X is the concentration of Candeartan Cilexetil in µg/ml and Y is the absorbance at respective λmax*

*** For six replicate samples.*

Precision

The precision of analytical procedure expresses the closeness of agreement between a series of measurement obtained from multiple sampling of the same homogenous sample under the prescribed condition. System precision, intraday precision and interday precision were done. The system precision was analysed by 6 different solutions of same concentration and absorbances were noted. The result was indicated by % RSD. The results are shown in Table 1.

Repeatability or Intra-day precision was investigated on six replicate sample solutions on the same day. Inter-day precision was assessed by analyzing newly prepared sample solutions in triplicate over three consecutive days. Both inter day and intraday precision was expressed as % RSD. The % RSD values for intraday precision was found as

0.98. The % RSD for inter day precision was 0.79. The results were summarized in Table 2 & 3. The low value of % RSD for both methods indicates the high precision of the both methods.

Table 2: Precision (repeatability) data

S.No	Conc. (µg/ml)	Absorbance
1	50	0.7121
2	50	0.7135
3	50	0.7142
4	50	0.7104
5	50	0.7121
6	50	0.7112
SD=0.001409		% RSD=0.19

Table 3: Interday and Intraday precision

Sample No. Set	% Assay	
	Intraday	Interday
1	101.8	99.3
2	101.2	98.2
3	101.3	99.0
4	101.5	99.0
5	100.6	98.6
6	99.1	100.5
Mean	101.1	99.1
SD	0.79	0.78
%RSD	0.78	0.79

Accuracy

Accuracy of the method was ascertained by recovery studies at three levels. Standard quantity equivalent to 80%, 100% and 120% was to be added in sample. The result shown that best recoveries (99.35 - 99.71 %) of the spiked drug were obtained at each added concentration, indicating that the method was accurate (Table 4).

Table 4: Accuracy results by recovery method

% Level	% Recovery	Mean % Recovery ± SD
80	99.63 99.13 99.45	99.40 ±0.0054
100	99.54 99.23 99.61	99.46±0.0063
120	99.56 99.67 99.84	99.69±0.0047

Robustness

The evaluation of robustness should be considered during the development phase and depends on the type of procedure under study. It should show the reliability of an analysis with respect to deliberate variations in method parameters.

If measurements are susceptible to variation in analytical conditions, the analytical condition should be suitably controlled or a precautionary statement should be included in the procedure. The result of robustness study of the developed assay method was established in Table 6. The result shown that during all variance conditions, assay value of the test preparation solution was

not affected and it was in accordance with that of actual. Hence the analytical method would be concluded as robust.

Table 5: Robustness studies

S No.	304 nm	306 nm	308 nm
1	0.6954	0.7121	0.6945
2	0.6849	0.7135	0.6934
3	0.6899	0.7142	0.6967
4	0.6912	0.7104	0.6954
5	0.6944	0.7121	0.6884
6	0.6991	0.7112	0.6945
Mean	0.692	0.7122	0.6938
SD	0.0049	0.0014	0.0028
%RSD	0.70	0.19	0.40

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogeneous slot by two analysts using same operational and environmental conditions (Table 6).

Table: 6 Results for Ruggedness studies

Formulation	Amount of drug taken from tablet(mg)	Analyst 1 (n=3)%assay±%RSD	Analyst 2 (n=3)%assay±%RSD
Candesartan Celixitil Capsules	60	100.01±0.732	99.92±0.457

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

The LOD and LOQ of the method were determined by using standard deviation of the response and slope. LOD and LOQ values were calculated using the relation,

LOD=3.3δ/S
LOQ=10 δ/S

Where, δ= standard deviation of residuals from the curve; S=slope of the curve

The results are shown in Table 4.

Solution stability study

The solution stability was studied at different time intervals for test preparation. It was concluded that the test preparation solution was found stable up to 10 hr at room temperature, as during this time the result was not decrease below the minimum percentage. The result was summarized in Table 7.

Table 7: Stability studies

Time (Hrs.)	Standard	Sample
0	0.7121	0.7119
2	0.7119	0.7116
4	0.7103	0.7115
6	0.7099	0.7115
8	0. 7098	0.7096
10	0.7090	0.7093

Application of Method to dosage form

The developed method was used for the quantitative estimation of Candesartan Cilexetil in commercial Tablet dosage form. The sample was analyzed in triplicate after extracting the drugs. None of the tablet ingredients were interfered with the analyte peak for both methods. Result for assay was shown in Table 8**.**

Table.8 Estimation of Candesartan Cilexetil in Tablets

Brand Name	Labeled Amount(mg)	Amount found*(mg)	%Purity ± SD*
Atacand™-32	32	31.2	99.22±0.152

**Average of six determinations*

CONCLUSION

The proposed method was simple, sensitive and reliable with good precision and accuracy. The method was specific while estimating the commercial formulation without interference of excipients and the other additives. Hence it can be used for routine analysis of Candesartan Cilexetil in bulk and pharmaceutical formulations.

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