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ESTIMATION OF CANDESARTAN CILEXETIL IN BULK AND TABLET DOSAGE FORM BY UV SPECTROPHOTOMETRIC METHOD

Patil Basawaraj S[1]*, Rao Raghavendra NG[2], Jadhav Suvarna[1], Kulkarni Upendra[1], Gada Mahesh M[1]
[1]R.M.E.S College of Pharmacy, Gulbarga– 585 102, Karnataka, India
[2]Luqman College of Pharmacy, Gulbarga – 585 102, Karnataka, India

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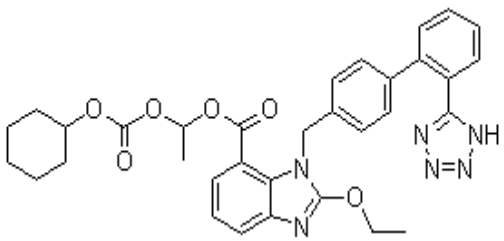
ABSTRACT
Candesartan cilexetil is a prodrug of Candesartan – a compound that inhibits binding of angiotensin II to the AT_1 – receptor. It is mainly used in the treatment of hypertension. It is available in oral dosage formulation. Candesartan cilexetil is a white to off white powder. It is soluble in dimethyl formamide, acetone, methanol, 0.1N sodium hydroxide solution and insoluble in water. A simple spectrophotometric method was developed for the determination of Candesartan cilexetil in pharmaceutical tablet dosage form. Candesartan cilexetil exhibited maximum absorbance at 255 nm in methanol and obeyed Beer's law in the concentration range of 5-25 mcg/ml. The proposed method was statistically validated.
KEY WORDS: Candesartan cilexetil, UV-spectrophotometry, Absorbance.

***Author for correspondence**
Basawaraj S.Patil, Professor, Department of Pharmaceutics, RMES College of Pharmacy, Old Jewargi road, Balaji Nager, Gulbaraga. (Karnatka) India E-mail:bspatilglb17@rediffmail.com

INTRODUCTION

Candesartan cilexetil is chemically 2-Ethoxy-3-[21-(1H-tetrazol-5-yl) biphenyl-4-ylmethyl] -3Hbenzoimidazole-4-carboxylic acid 1- cyclohexyloxycarbonyloxy ethyl ester.[1] Candesartan cilexetil is a prodrug of Candesartan – a compound that inhibits binding of angiotensin II to the AT_1 – receptor. Candesartan cilexetil is hydrolyzed to candesartan during absorption from the gastrointestinal tract.[2] It is mainly used in the treatment of hypertension. The typical dose of Candesartan cilexetil is 16 mg per day in patients who are not volume depleted. It may be given once or twice daily with total daily doses ranging from 8 mg to 32 mg.[3]. Tablet formulation containing 4 mg and 8 mg Candesartan cilexetil are available in market. Literature survey revealed that various analytical methods such as Q-Analysis spectrophotometric methods for estimation of Candesartan cilexetil and Hydrochlorothiazide in tablet dosage form.[4] HPTLC-densitometric analysis of Candesartan cilexetil and Hydrochlorothiazide in tablets.[5] HPLC, RP-HPLC, and LC-UV re used for estimation of Candesartan cilexetil.[6-8] No spectrophotometric method has been reported for estimation of Candesartan cilexetil in tablet dosage form. Its empirical formula is $C_{33}H_{34}N_6O_6$, Molecular weight is 610.7 and its structural formula is;



In the present investigation an attempt was made to develop a simple and economical spectrophotometric method with greater precision, accuracy and sensitivity for the analysis of Candesartan cilexetil in bulk and pharmaceutical formulation.

MATERIALS AND METHODS

Instruments

- A PG instrument UV-spectrophotometer T_{80} model with
- Spectral bandwidth (resolution) of 3 nm.
- Wavelength accuracy (with automatic wavelength correction) of 0.5 nm.
- Ultrasonicator. (Bath sonicator 1.5 lts. PCI Labs Mumbai).
- Shimadzu digital balance (1mg sensitive).

Chemicals and reagents

Methanol (SD Fine Chemicals Ltd.) and Candesartan cilexetil, gift sample from Hetero Labs. Ltd. Medak district. (AP)

Procedure

Candesartan cilexetil (100 mg) was accurately weighed and dissolved in 100 ml of methanol to give stock solution (1000 mcg/ml). Aliquots of 1000 mcg/ml solution were suitably diluted with methanol to give final concentrations of 5, 10, 15, 20 and 25 mcg/ml. The λ_{max} was found by UV spectrum of Candesartan cilexetil in methanol, in the range of 200-400 nm, and it was found to be 255 nm (**Fig. 1**). Absorbance was measured at 255 nm against methanol as a blank. Spectral characteristics of Candesartan cilexetil and linearity data are given in **table 1 & 2**.

Procedure for analysis of tablets

Two commercial brands of Candesartan cilexetil were procured from the local market. Each brand contained a label claim of 8 mg of Candesartan cilexetil per tablet. Twenty such tablets of each brand were weighed and powdered for analysis. The tablet powder equivalent to 8 mg of Candesartan cilexetil was weighed accurately, dissolved in methanol and the volume was made up to 100 ml with methanol. The solution was filtered through whatmann filter paper No. 40. An aliquot corresponding to 10 mcg/ml was analyzed by the method described above. The result of the analysis of the tablets is presented in **table 3**.

Recovery Studies

Recovery Studies were carried out at three different levels by adding 2.0, 4.0 and 6.0 mcg/ml of standard drug solution to different samples of tablet powder solution containing the equivalent of 10 mcg/ml of drug. Percentage recovery was calculated from the amount of drug found in the solution (**table 4**).

RESULS AND DISCUSSION

Candesartan cilexetil exhibited maximum absorption at 255 nm and obeyed Beer's law in the concentration range of 5-25 mcg/ml. The proposed method for determination of Candesartan cilexetil showed molar absorptivity of 2.0275304×10^4 calculated based on the exact purity of the drug), linear regression $Y = 0.03401x - 0.00847$ with a correlation coefficient (r^2) 0.9998 (**Fig.2**). A relative standard deviation of 0.313 and 0.461 was observed on analysis of five replicate samples of the two brands I and II respectively. The percentage recovery revealed that the values lie between 98.34 and 99.13 which indicate that the proposed method is accurate and also reveals that the commonly use excipients and additives in the pharmaceutical formulation were not interfering in the proposed method.

CONCLUSION

The developed method for determination of Candesartan cilexetil in tablet formulation was found to be simple, accurate, economical, rapid, precise, reproducible and stable, which indicated that this method could be used for the routine determination of Candesartan cilexetil in pure and pharmaceutical formulation.

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Table 1: Spectral characteristics of Candesartan cilexetil

Parameters	Value
λ_{max} (nm)	255
Beer's law limits (mcg/ml) (c)	5 - 25
Molar absorptivity (lit/mol^{-1} cm^{-1})	2.0275304×10^4
Regression equation (Y*)	$Y = 0.03401x - 0.00847$
Slope (m)	3.4011×10^{-2}
Y - intercept (c)	8.4761×10^{-3}
Correlation coefficient (r^2)	0.9998

Table 2: Linearity table of Candesartan cilexetil in working standard

Concentration (mcg/ml)	Absorbance (nm)
0	0.000
5	0.155
10	0.329
15	0.498
20	0.671
25	0.847

Table 3: Analysis of Candesartan cilexetil in tablets

Tablet code	Label claim	Amount found (%)	% Label claim found ± SD
Brand I	8 mg	99.14 99.68 99.01 98.78 98.84	99.09 ± 0.313
Brand II	8 mg	98.29 98.24 99.33 98.83 98.61	98.66 ± 0.461

Table 4: Recovery studies

Concentration of drug added to the formulation (mcg/ml)	% Recovery ± SD	Coefficient of variance
2	99.13 ± 0.317	0.398
4	98.45 ± 0.578	0.459
6	98.34 ± 0.441	0.527

% Recovery = Amount /Amount added x 100
SD stands for standard deviation, the results are mean of three readings (n=3)

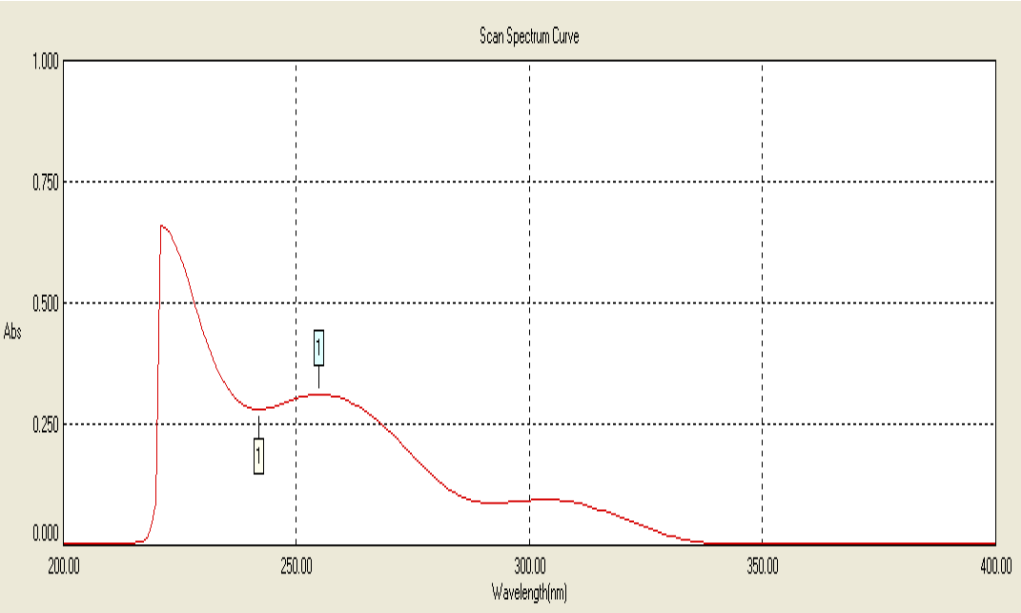

Fig. 1: UV spectrum of Candesartan cilexetil in methanol

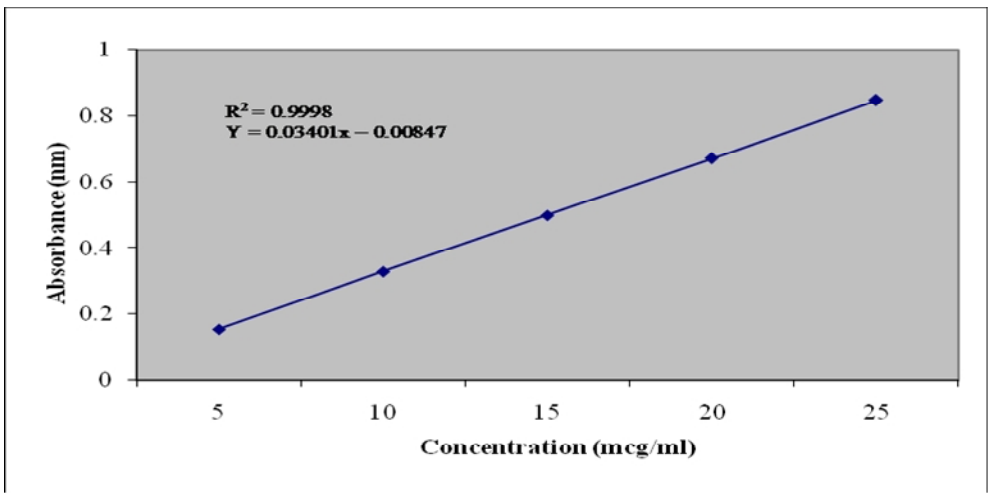

Fig. 2: Linearity curve of Candesartan cilexetil in working standard

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