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# Q-Analysis spectrophotometric methods for estimation of Candesartan Cilexetil and Hydrochlorothiazide in tablet dosage form

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## ABSTRACT

*A method for simultaneous estimation of Candesartan Cilexetil and Hydrochlorothiazide in tablet dosage form has been described. The method is based on UV-Spectrophotometric determination using Q-absorbance method. It involves, formation of Q-absorbance equation at 258.14nm (isoabsorptive point) and 271 nm λ max of Hydrochlorothiazide in methanol. Linearity was obtained in the range 2-24µg/ml for Candesartan and 2-24 µg/ml for Hydrochlorothiazide. The method allows rapid analysis of binary pharmaceutical formulation with accuracy. The % recovery lies in the range of 101.2 – 102.1 for CAN and 99.2 – 99.7 for HCTZ. Result were validated statistically and were found satisfactory.*

**Key words:** Candesartan cilexetil(CAN); Hydrochlorothiazide(HCTZ); UV- Spectrometry.

## INTRODUCTION

Candesartan Cilexetil(CAN) is Angiotensin II receptor Antagonist. It is used in anti-hypertensive. Chemically it is 2-Ethoxy-3-[21-(1H-tetrazol-5-yl)biphenyl-4-ylmethyl]-3H-benzoimidazole-4-carboxylic acid 1- cyclohexyloxycarbonyloxy ethyl ester [1].The typical dose of CAN is 16 mg per day. Hydrochlorothiazide(HCTZ) is diuretic and antihypertensive, which inhibits the reabsorption of sodium and calcium at the beginning of distal convoluted. It is the 3,4 dihydroderivetive of chlorothiazide. It is chemically 6-chloro-3,4-dihydro-2*H*-1, 2, 4-benzothiadi- azine-7-sulphonamide-1,1-dioxide[2]. The typical dose of HCTZ is 12.5 mg per day [3-6]. HPLC, HPTLC, LC-MS and spectrophotometric method have been reported for the estimation of CAN and HCTZ in combination as well as indivisual [7-15]. The extensive literature survey revealed that no UV spectroscopic method using Q- analysis method is reported

for simultaneous estimation of both the drug in tablet formulation. Therefore, it was thought to estimate CAN and HCTZ simultaneously by Q- analysis method.

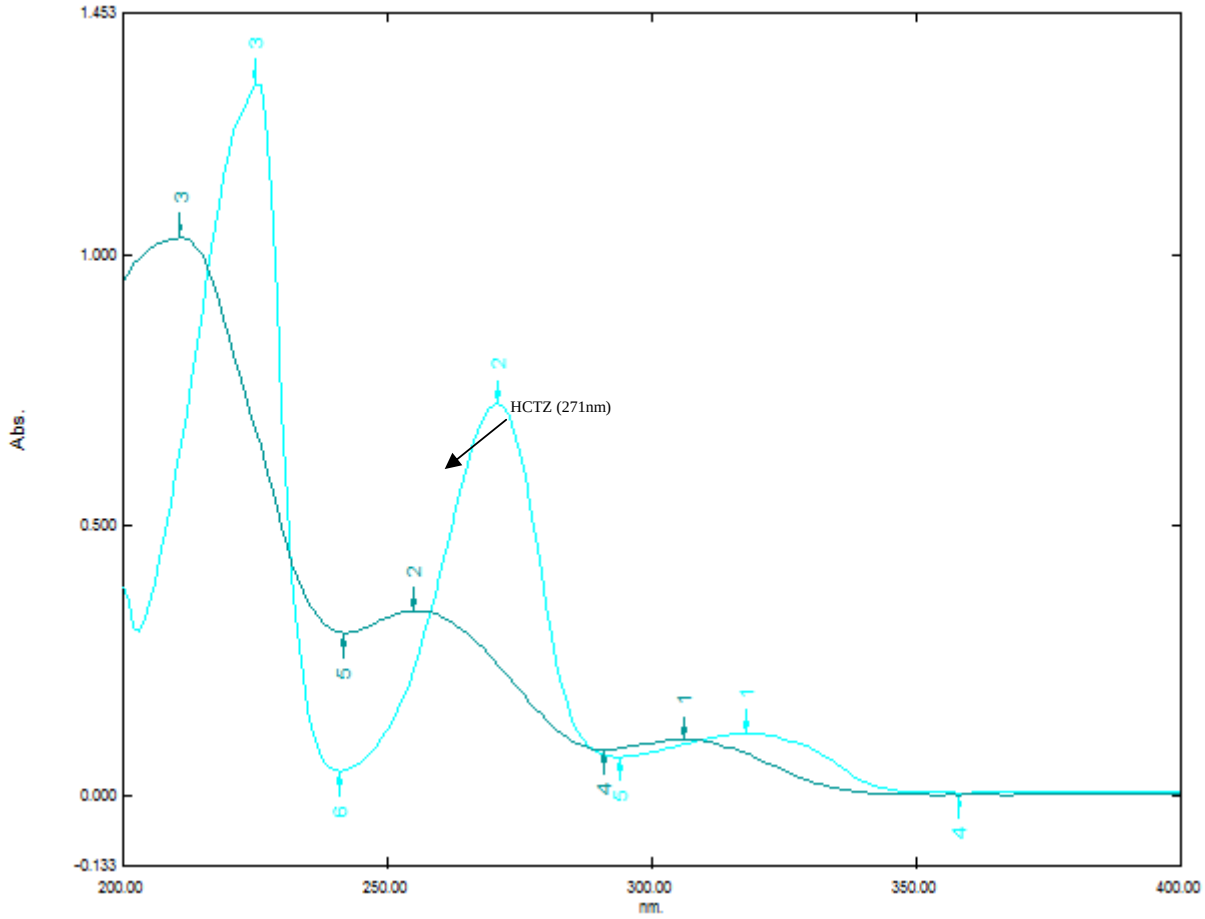
## MATERIALS AND METHODS

Pure drug sample of CAN and HCTZ were kindly gifted by Matrix Laboratories Ltd, Hydrabad. Methanol analytical reagent grade (E-Merck, Mumbai, India) was used as solvent in this work. Marketed formulations used (Candesar – H, Renbexy Laboratories Ltd.) was procured from local market. UV- Visible double beam Spectrophotometer, model: Simadazu 1700 with a pair of 10mm Quartz cell was used.

### UV-Visible Spectrophotometric method

Standard stock solution of 100 µg/mL were prepared by 10 mg of each in 100 mL of methanol. From these stock solutions, working standard solutions having concentration 10 µg/mL each were prepared by appropriate dilutions. They were scanned in the wavelengths range of 200-400 nm and the overlain spectrum was obtained (Fig 1) to determine the maximum absorbance (λ max) and isoabsorptive point.

**Fig. 1: Overlain UV Spectrum of CAN and HCTZ (each 10µg/mL) in methanol**




### Method

Q-Absorbance method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and other being the λ max of one of the two compounds. CAN and HCTZ have λ max at 254 nm and at 271 nm, respectively. Both the drugs were found to have same absorbance at 258.14 nm (isoabsorptive point). The wavelengths selected for analysis were

258.14 nm and 271 nm respectively (Fig.1). The calibration curve were found to be linear in the concentration range of 2-24 µg/mL for both the drug and the absorbance of solutions was recorded at 258.14 and 271 nm to plot a calibration curve of absorbance versus concentration. The calibration curves were found to be linear in the concentration range under study. Absorptivity values of CAN and HCTZ were determined at selected wavelengths and are presented in Table-1.

**Table 1: Absorptivity values (E 1%, 1 cm) of Candesartan (CAN) and Hydrochlorothiazide (HCTZ) at 258.14 nm (isoabsorptive point) and 271 nm**

| S. NO. | Absorptivity at 258.14 nm | | Absorptivity at 271 nm | |
|---|---|---|---|---|
| | CAN | HCTZ | CAN | HCTZ |
| 1 | 338.04 | 338.06 | 238.89 | 669.38 |
| 2 | 338.14 | 338.19 | 238.75 | 669.19 |
| 3 | 338.09 | 338.12 | 238.92 | 669.46 |
| 4 | 338.07 | 338.1 | 238.94 | 669.54 |
| 5 | 338.1 | 338.15 | 238.81 | 669.25 |
| 6 | 338.19 | 338.24 | 238.96 | 669.57 |
| Mean | 338.105 | 338.1433333 | 238.8783333 | 669.3983333 |
| S.D | 0.053197744 | 0.064704456 | 0.081833164 | 0.154326494 |
| RSD(%) | 0.01573409 | 0.019135216 | 0.034257257 | 0.023054508 |

The concentration of two drugs in mixture was calculated by using following equations:

$$C_{CAN} = \frac{Qm - Qy}{Qx - Qy} \times \frac{A1}{ax1} \quad (1)$$

$$C_{HCTZ} = \frac{Qm - Qx}{Qy - Qx} \times \frac{A2}{ay1} \quad (2)$$

Where,

$$Qm = \frac{\text{Absorbance of sample at 271 nm}}{\text{Absorbance of sample at 258.14 nm}}$$

$$Qx = \frac{\text{Absorptivity of Candesartan at 271 nm}}{\text{Absorptivity of Candesartan at 258.14.14 nm}}$$

$$Qy = \frac{\text{Absorptivity of Hydrochlorothiazide at 271 nm}}{\text{Absorptivity of Hydrochlorothiazide at 258.14 nm}}$$

A1 and A2 are the absorbances of mixture at 258.14 nm and 271 nm and ax1 (338.105), ax2 (239.96) and ay1 (338.143), ay2 (669.398) are absorptivities E (1%, 1 cm) of CAN and HCTZ at 258.14 nm and 271 nm and Qm= A2/A1, Qy = ay2/ay1 and Qx = ax2/ax1.

**Analysis of Tablet Formulation**

Twenty tablets weighed accurately. The average weight was determined and then ground to a fine power. A quantity equivalent to 16 mg of CAN and 12.5 mg of HCTZ was taken in 100 ml volumetric flask. The contents were ultrasonicated for 10 min with methanol (60ml), made the volume (100 ml) and filtered through whatmann filter paper. The solution was further diluted with methanol to give the concentration within the Beer's Law range. Absorbance of this solution was measured at 258.14 nm and 271 nm as A1 and A2 respectively and concentrations of these two drugs in the sample were calculated using equation (1) and equation (2). Results of the analysis of the tablet formulations are reported in Table 2.

**Table 2: Estimation of Candesartan and hydrochlorothiazide in Tablet(Candesar – H, Ranbexy Lab ltd.)**

| Tablet Content | Label Claim (mg/Tab) | Amount Found* (mg/Tab) | Percentage of Labeled Claim* | S.D* | Coefficient of variation* |
|---|---|---|---|---|---|
| CAN | 16 | 16.1 | 100.62 | 0.12 | 0.12 |
| HCTZ | 12.5 | 12.39 | 99.12 | 0.19 | 0.188 |

** Mean of six estimations*

**Table 3: Result for Recovery studies**

| Level of % Recovery | % Recovery found* | | S.D* | |
|---|---|---|---|---|
| | CAN | HCTZ | CAN | HCTZ |
| 50 | 102.1 | 99.7 | 0.145 | 0.122 |
| 100 | 101.6 | 99.4 | 0.198 | 0.186 |
| 150 | 101.2 | 99.2 | 0.205 | 0.154 |

** Mean of six estimations*

## RESULTS AND DISCUSSION

Absorbance was determined at both the wavelengths. CAN obeyed linearity in the concentration range of 2-24 µg/mL, HCTZ in the concentration range of 2-24 µg/mL and the correlation coefficient was < 1 in both the case. The absorptivity was then calculated and along with absorbance, these values were submitted in equation 1 and 2 to obtain concentration of drugs. The proposed methods were validated as per ICH guideline [16]. The experiment was repeated six times a day for intra-day and on six different days for inter-day precision. The reproducibility was determined by using methanol from three different manufacturers for preparation of stock solution of standard drugs. The accuracy was determined by performing recovery studies by standard addition method in which reanalyzed samples were taken and standard drug was added at three different levels. The % recovery lies in the range of 101.2 – 102.1 for CAN and 99.2 – 99.7 for HCTZ. The method was successfully used to estimate the amounts Candesartan Cilexetil and Hydrochlorothiazide in marketed tablet formulation containing Candesartan Cilexetil 16 mg and Hydrochlorothiazide 12.5 mg. By using this analytical method the amount of CAN was found 16.1 mg HCTZ was found 12.39 mg both are 100.62% and 99.12% w/w label claim, respectively. Precision was calculated as repeatability (% RSD is less than 1) and inter and intraday variations (%RSD is less than 1) for both drugs. The repeatability data, ruggedness data are presented in Table-3.

## CONCLUSION

The new q-analysis spectrophotometric method for quantitative determination of Candesartan Cilexetil and Hydrochlorothiazide is precise and accurate. The method was completely validated showing satisfactory data for all the method validation parameters tested. The developed method

can be used for assessing the combination formulation of Candesartan Cilexetil and Hydrochlorothiazide.

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