Available Online through
www.ijpbs.com (or) www.ijpbsonline.com

IJPBS |Volume 3| Issue 1 |JAN-MAR |2013|343-348

Research Article
Pharmaceutical Sciences

DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF CILNIDIPINE AND TELMISARTAN IN TABLET DOSAGE FORM UTILISING SIMULTANEOUS EQUATION AND ABSORBANCE RATIO METHOD

*M.Haripriya[1], Neethu Antony[1], P. Jayasekhar [2]

*[1]College of Pharmaceutical Sciences, Government Medical College, Trivandrum, Kerala-695011

[2] Oman Medical College, Azaiba, Post box 620, Postal code.130 Muscat , Sultanate of Oman

*Corresponding Author Email: riyasiva@yahoo.co.in

ABSTRACT

Two validated uv spectrophotometric methods for the simultaneous estimation of Cilnidipine and Telmisartan in pure powder and in two component dosage forms have been developed, utilising simultaneous equation and absorbance ratio method. The method is based on the measurement of absorbance of Cilnidipine and Telmisartan at their respective wavelengths of 240 nm and 297nm and at the iso absorptive wavelength of 270 nm in methanol. Cilnidipine and Telmisartan at their respective λ_{max}240 nm and 297nm obeyed Beer's law in the concentration range 4-10µg/ml and 6-18µg/ml respectively with correlation coefficient 0.9998 and 0.9992 for Cilnidipine and 0.9998 and 0.9991 for Telmisartan. The results have been validated statistically as per ICH guidelines.

KEY WORDS

Cilnidipine; Telmisartan; Simultaneous estimation; absorbance ratio, Validation.

INTRODUCTION

Cilnidipine (CIL) O3-(2-methoxyethyl) *O*5-[(*E*)-3-phenylprop-2-enyl] 2, 6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine- 3,5-dicarboxylate is a novel and unique dihydropyridine calcium channel blocker that possesses a slow-onset, long-lasting vasodilating effect[1].

Telmisartan (TEL), 4-((2-n-propyl-4-methyl-6-(1-methylbenzimidazol – 2 – yl) – benzimidazol – 1 -yl) methyl) biphenyl-2- carboxylic acid, is an angiotensin II receptor antagonist that shows high affinity for the angiotensin II receptor type 1 (AT_1), with a binding affinity 3000 times greater for AT_1 than AT_2[2].

Literature review revealed only one method for the simultaneous estimation of Cilnidipine and Telmisartan in two component dosage forms, which is an HPTLC method[3].Hence it was proposed to develop economical, rapid and simple uv spectrophotometric methods for the simultaneous estimation of these drugs in dosage forms.

MATERIALS

All the chemicals and reagents used were of analytical grade. Cilnidipine and Telmisartan hydrochloride were obtained as gift samples from J B Chemicals and Pharmaceuticals,Daman and Akums Drugs and Pharmaceuticals limited, Hardwar. The combined dosage form was purchased from local market.Methanol HPLC was procured from SD Fine-Chem limited, Mumbai.

EQUIPMENT

The Jasco double beam uv- vis spectrophotometer with spectral band width 2.0 nm wavelength accuracy 0.5nm and matched quartz cells of 1 cm path length were used for all spectral and absorbance measurements. Class A volumetric glass wares were used.

EXPERIMENTAL METHODS

Standard solutions and Calibration curves

Stock solutions for spectrophotometric measurements were prepared by dissolving CIL and TEL in methanol to obtain concentration of 1mg/ml for each compound. For calibration, series of above solutions were prepared containing CIL4.0, 5.0,6.0,7.0,8.0.9.0,10.0 µg/ml and TEL 6.0,8.0,10.0,12.0,14.0,16.0,18.0 µg/ml by diluting the stock standard solution with methanol in standard volumetric flasks(10ml).The solutions were scanned in the range of 220-350nm.

Selection of wavelengths

Method I. Simultaneous equation method

Overlain spectra for both the drugs are shown in Fig.1.Two wavelengths selected for the use of simultaneous equation were 240 and 297nm. The absorbance was recorded at the selected wavelengths and the absorptivity values were determined for Cilnidipine and Telmisartan. Statistical parameters like slope, intercept, coefficient of correlation and SD were determined. (Table 1).

Method II. Absorbance ratio/Q value method

From the overlain spectra of the two drugs, the isoabsorptive wavelength of 270nm and the λ max of telmisartan at 297 nm were selected for this method. The absorptivity values were calculated at 270nm and 297nm. Statistical parameters like slope, intercept, coefficient of correlation and SD were determined. (**Table 1**)

DERIVATION OF EQUATIONS

METHOD I

Simultaneous equation method

From the absorptivity values determined for CIL and TEL, simultaneous equations are derived for determination of these two drugs in combination in their pharmaceutical formulations.

A_1=0.0850Cx+0.0605Cy …… at 240nm (1)

A_2=0.0146C_x+0.0494Cy ……..at 297 nm (2)

The absorbance and the absorptivity values at the particular wavelength were calculated and substituted in the following equation, to obtain the concentration.

$Cx = (A_1ax_2 – A_2ax_1) / (ax_2ay_1 – ax_1ay_2)$.

$Cy = (A_2ay_1 – A_1ay_2) / (ax_2ay_1 – ax_1ay_2)$.

Where,

Cx = Concentration of CIL

Cy = Concentration of TEL

A_1&A_2 absorbance of sample at 240 nm and 297 nm respectively

ax_1&ax_2 absorptivity of CIL at 240 nm and 297 nm respectively

ay_1&ay_2 absorptivity of TEL at 240 nm and 297 nm respectively.

METHOD II

Absorbance ratio/Q value method

In Q analysis method, from the overlay spectra of CIL and TEL absorbances were measured at selected wavelength i.e.270 nm (isoabsorptive point) and at 297 nm (λ max of TEL).The absorptivity coefficient of each drug at both the wavelengths were determined. The concentration of each drug in the tablet formulation were determined by substituting the absorbances and absorptivity coefficients in the equation

$Cx = (Qm - Qy)/(Qx - Qy)\times A_1/ax_1$

$Cy = (Qm – Qx)/(Qy - Qx)\times A1/ay1$

Where,

Qm = Absorbance of sample at 297 nm / Absorbance of the sample at 270 nm

Qx = Absorptivity of CIL at 297 nm / Absorptivity of CIL at 270 nm

Qy = Absorptivity of TEL at 297 nm / Absorptivity of TEL at 270 nm

A1 = Absorbance of the sample of sample at 270nm (isoabsorptive point)

ax_1= Absorptivity of CIL at 270 nm

ay_1 = Absorptivity of TEL at 270 nm

ANALYSIS OF FORMULATION

Twenty tablets of brand Cilacar T (J B Chemicals and Pharmaceuticals) containing 10 mg of CIL and 40 mg of TEL were weighed, average weight determined and finely powdered. Appropriate quantity of powder equivalent to 10 mg of CIL and 40 mg TEL was accurately weighed, transferred to a 100 ml volumetric flask and volume was made up to 100 ml with methanol and shaken vigorously for 15 minutes. The solution was then sonicated for 5 minutes and filtered through the Whatman filter paper no.41. Necessary dilutions of filtrate were made with methanol to get final concentration 10 µg/ml of CIL and 40 µg/ml of TEL. Absorbance of this solution was measured at 240 nm (λ max of CIL) 297nm ((λ max of TEL), and 270 nm (Isoabsorptive Point), The values obtained were substituted in the respective formulae of **Method 1 & 2** to obtain concentrations of CIL and TEL. The results are shown in **Table 3**.

Method Validation[4]

Calibration curve (linearity of the method)

Calibration curves were constructed by plotting absorbance vs. concentrations of CIL and TEL,at their respective λmax and the regression equations were calculated. The calibration curves were plotted over the seven different concentrations in the range 4-10 µg/mL and 6-18 µg/mL for CIL and TEL, respectively (**Fig.2 and Fig.3**). The optical parameters and statistical parameters are depicted in **Table 1**.

Accuracy (% Recovery)

The accuracy of the method was determined by calculating recoveries of CIL and TEL by the standard addition method. Known amount of standard of CIL and TEL (80%, 100%, and 120%) were added to the sample solutions of tablet dosage forms. The amounts of CIL and TEL were estimated by equations in method I and II. The results are shown in **Table 2**. The values prove that the method is accurate.

5.3. Method Precision (Repeatability) The precision of the instruments was checked by repeatedly scanning (n = 5) standard solutions of CIL and TEL (10 µg/ml). The RSD values were found to be below 2% which indicate that the proposed methods are repeatable (**Table 2**).

Intermediate Precision (Reproducibility) The intermediate precision for the proposed method was determined by estimating standard solution of CIL and TEL for three different concentrations for three times on the same day(intraday) and on three different days(interday). The results are reported in terms of relative standard deviation (RSD). The RSD values were found to be below 2% which indicate that the proposed methods are reproducible (Table 2).

Robustness Solutions of both the drugs in methanol were studied for their stability at ambient temperature for 24 h. Absorbance variation was found to be less than 1%.

Fig. 1: Overlain Absorption spectra of Cilnidipine and Telmisartan

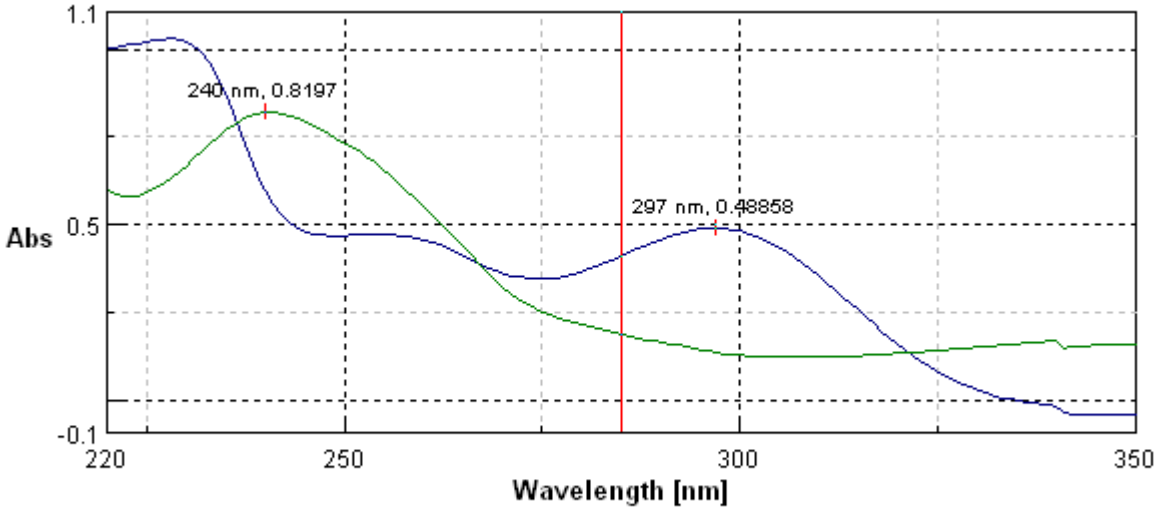

Fig.2 Calibration plot of fundamental spectra of CIL

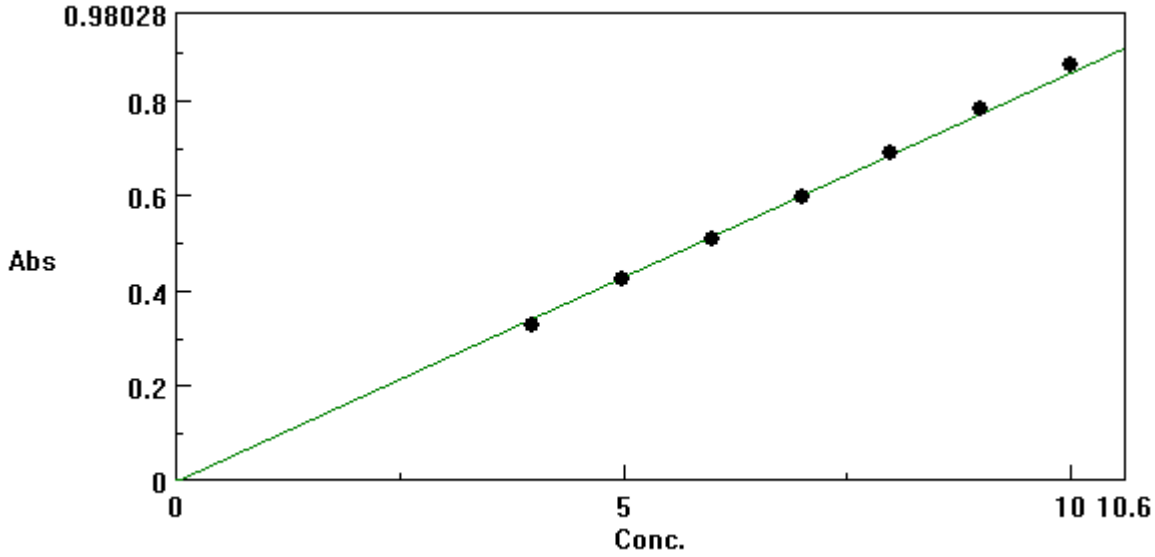

Fig.3. Calibration plot of fundamental spectra of TEL

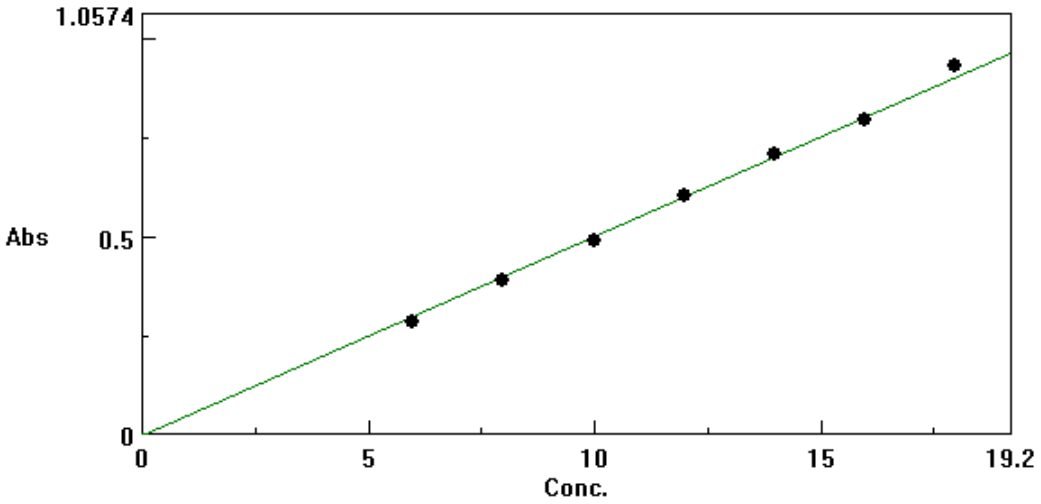

Table 1: Optical characteristics Data

Parameters	Method I Simultaneous equation method		Method II Q Absorbance ratio method	
	CIL	**TEL**	**CIL**	**TEL**
Working λmax	240nm	297 nm	270 nm	270 nm
Beer's law limit	4-10µg/ml	6-18µg/ml	4-10µg/ml	6-18µ/ml
Correlation coefficient	0.999892	0.999179	0.999876	0.999071
Intercept	-0.03717	-0.03736	0.057311	-0.04226
Slope	0.090775	0.0528680	0.029225	0.040509
Regression equation	Y=0.090775x -0.03717	Y=0.052868x -0.03736	Y=.029225x+ 0.057311	Y=0.040509x -0.04226

Table 2: Summary of validation parameters for the proposed methods

Parameter	CIL		TEL	
	Method I	**Method II**	**Method I**	**Method II**
Accuracy %	99.72	98.94	100.10	98.95
Precision (RSD, %)				
Repeatability(n=5)	0.19	0.2	0.25	0.16
Intraday(n=3)	0.46-0.56	0.21-0.39	0.22-0.84	0.35-0.78
Interday(n=3)	0.88-1.24	0.98-1.10	1.02-1.06	0.85-0.93
Robustness	Robust	Robust	Robust	Robust

Table 3.Compilation of results of commercial formulation

Brand name	Company	Formulation	Label Claim	Amount found (mg)	
				Method I	**Method II**
Cilacar T	J B Chemicals & Pharmaceuticals	Tablet	**CIL 10mg** **TEL 40mg**	9.89±0.10 39.91±0.45	10.11±0.12 39.87±0.38

CONCLUSION

The methods discussed in the present work provide a convenient and accurate way for simultaneous estimation of CIL and TEL. In simultaneous equation method, wavelengths selected for analysis were 240 nm (λ_{max} of CIL) and 297 nm (λ_{max} of TEL).

In Q-analysis method wavelengths selected were 270 nm (isoabsorptiv e point) and 297 nm (λ_{max} of (TEL). In both the methods linearity for detector response was observed in the concentration range of 4-10 µg/ml (for CIL) and 6-18 µg/ml (for TEL). Absorptivity coefficient were calculated for both the drugs at selected wavelengths and substituted in equations for determining concentration of CIL and TEL in its tablet dosage form. Percent label claim for CIL and TEL in tablets was found by simultaneous equation method and by Q-analysis method. Accuracy of proposed methods was ascertained by recovery studies. Hence the proposed methods can be employed for routine quality control of Cilnidipine and Telmisartan in its combined dose formulations.

REFERENCES

1. Yoshimoto R, Dohmoto H, Yamada K, Goto A. Prolonged inhibition of vascular contraction and calcium influx by the novel 1,4-dihydropyridine calcium antagonist cilnidipine (FRC-8653) Jpn J Pharmacol. 1991; 56:225–229.
2. Benson, S. C.; Pershadsingh, H.; Ho, C.; Chittiboyina, A.; Desai, P.; Pravenec, M.; Qi, N.; Wang, J. et al. (2004). "Identification of Telmisartan as a Unique Angiotensin II Receptor Antagonist with Selective PPAR - Modulating Activity". *Hypertension* **43** (5): 993.
3. Pawar Prajakta, et al. "HPTLC Determination of Cilnidipine and Telmisartan in combined tablet dosage forms" . International Research Journal of Pharmacy. 2012:3(6) 219-222
4. ICH Harmonized Tripartite Guidelines, Validation of analytical procedures: Text and Methodology, Q2 (R1), 2005, Geneva.

***Corresponding Author:**
M. Haripriya*
College of Pharmaceutical Sciences, Government Medical College, Trivandrum, Kerala-695011