INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF CILNIDIPINE AND TELMISARTAN IN COMBINED PHARMACEUTICAL DOSAGE FORM

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Article Received on: 12/08/17 Approved for publication: 09/09/17

DOI: 10.7897/2230-8407.089166

ABSTRACT

A specific, accurate, precise and reproducible RP-HPLC method development validation for simultaneous estimation of cilnidipine and telmisartan in combined pharmaceutical dosage form. The proposed HPLC method utilizes Youglin C18 column (250 mm x 4.6 mm) 5 µm particle sizes and mobile phase consisting of Acetonitrile: 0.05% ortho phosphoric acid (60: 40) at a flow rate of 0.7 ml/min with UV detection 236 nm. The retention time of cilnidipine and telmisartan were found to be 4.650 min and 8.050 min respectively. The method was validated in terms of accuracy, precision, Linearity and robustness and was successfully applied for the determination of investigated drugs in combined dosage form.

Keywords: RP-HPLC, Cilnidipine, Telmisartan, Pharmaceutical Dosage form.

INTRODUCTION

Cilnidipine (CIL) is chemically 2-Methoxyethyl (2E)-3-phenyl-2-propen-1-yl 2, 6-dimethyl-4(3-nitrophenyl)-1, 4-dihydro-3,5 pyridinedicarboxylate and it belongs to calcium channel blocker class of oral antihypertensive drugs . CIL acts as anti-hypertensive and lowers the blood pressure level by blocking calcium channel and increasing contraction of heart.[1,2,3]

Telmisartan is 4'-[1, 4'-dimethyl-2-propyl [2, 6'- bi-benzimidazole]-1'-yl] methyl 1, 1'- biphenyl 2-carboxylic acid. It is an angiotensin receptor blocker (ARB) that shows high affinity for the angiotensin II type 1 (AT1) receptors.[4]

Telmisartan is practically insoluble in water; sparingly soluble in strong acid; soluble in strong bases. It blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland.[5] Telmisartan acts as a selective modulator of peroxisome proliferator activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose.[6]

MATERIALS AND METHODS

Cilnidipine and Telmisartan were obtained as gift sample from Macleods Pharmaceutical Pvt. Ltd. Mumbai. Market formulation of this combination Telista-CL was procured from the local market HPLC grade acetonitrile; ortho phosphoric acid and methanol were obtained from Merck (India).

The analysis was carried out on a HPLC system (Youglin) equipped with UV detector. Other apparatus and instruments used were a micro analytical balance (citizen, Cyloa). Ultrasonic (Met. Lab. 1.5L50). Nylon Membrane filters (0.22 µcm, 47 mmD). All instruments and glass-wares were calibrated.

Chromatographic Condition

Instrument: - High Performance liquid chromatography equipped with UV detector.
Column: - C18 250 x 4.6 mm, (YMC)
Column oven temperature: - Ambient
Wave length: - 236 nm
Flow rate: - 0.7 ml/min
Injection Volume: - 20□l
Runtime: - 11 min.
Mobile phase: - Acetonitrile: 0.05% ortho phosphoric acid (60: 40)

Preparation of Mobile Phase

The mixture of Acetonitrile: 0.05% ortho phosphoric acid was prepared. Filtered and degassed the mobile phase.

Preparation of Cilnidipine and Telmisartan Standard Solution

Accurately weighted quantity 10mg and 40mg of Cilnidipine and Telmisartan was dissolved in Methanol Volume was made up to 10ml mark to get final concentration of about 1000µg/ml of Cilnidipine and 4000µg/ml Telmisartan. Telmisartan was soluble in alkali so we have used triethyleamine to solublise the telmisartan.

Preparation of Standard Stock Solution
Cilnidipine Standard Solution

Accurately weighed Cilnidipine 10mg was dissolved in mobile phase and volume was make up to 10ml Methanol. The stock Solution was diluted further with mobile phase to get final concentration of about 1000µg/ml of cilnidipine.

Telmisartan Standard Solution

Accurately weighed Telmisartan 40mg was dissolved in mobile phase and volume was make up to 10ml Methanol. The stock Solution was diluted further with mobile phase to get final concentration of about 4000µg/ml of Telmisartan.

RESULT AND DISCUSSION

Development and validation of RP-HPLC for the simultaneous estimation of Cilnidipine and Telmisartan in bulk and combined tablet dosage form.

RP-HPLC method was developed for simultaneous estimation of Cilnidipine and Telmisartan in tablet dosage form. The separation was achieved by C18 (PriCILNIil) column of (4.6×250 mm) with particle size packing 5 µm and Acetonitrile: 0.05% OPA (0.05ML OPA in 100 ML): (60:40) as mobile phase at a flow rate of 0.7 ml/min. The detection was carried out at 236 nm. The retention time of was found to be 4.65 min and 8.05 min respectively.

METHOD OF VALIDATION

System suitability

To determine the adequate resolution and repeatability of the proposed method, system suitability test were carried out. The parameters like retention time, no. of theoretical plates, asymmetry factors we studied by injecting standard solutions of the drug five times. The values given in table 1 were obtained within the limits.

Accuracy

The accuracy of the method was evaluated in triplicates by recovery studies at three different concentration levels of 80%, 100% and 120% known amounts of standard drug concentration were added to the sample. The accuracy data and the corresponding results are as shown in table 2 and 3.

Precision

The precision of this method is determined by intra-day and inter-day precision. The % RSD was found less than 2, this indicate that the method is precise. The results of precision study are shown in table 4.

Robustness

The Robustness of a method is its ability to remain unaffected by small deliberate changes in parameters. To evaluate the robustness of the proposed method, small but deliberate variations in the optimized method parameters were done. The effect of changes in mobile phase composition and flow rate on retention time and tailing factor of drug peak was studied.

The mobile phase composition was changed in ± 1 ml proportion and the flow rate was varied by ± 0.1 ml min-1, of optimized chromatographic condition. The results of robustness studies are shown in Table No.5 & 6. System suitability parameters were also found satisfactory hence the analytical method would be concluded.

Table 1 System suitability parameters for Cilnidipine and Telmisartan

Parameters	Cilnidipine	Telmisartan
Retention time	4.70	8.01
Tailing factor	1.23	1.39
Theoretical plate	5022.04	9437.1

Table 2 Recovery studies of Cilnidipine and Telmisartan

Level of Recovery (%)	80		100		120	
	CIL	TEL	CIL	TEL	CIL	TEL
Amount present (mg)	8.87 8.97	35.78 35.92	10.04 10.07	40.18 40.05	11.11 11.07	43.83 43.79
Amount of Std. Added (mg)	4 4	16 16	5 5	20 20	6 6	24 24
Amount Recovered (mg)	3.87 3.97	15.78 15.92	5.04 5.07	20.18 20.05	6.11 6.07	23.83 23.79
% Recovery	96.96 99.25	98.65 99.50	100.80 101.43	100.94 100.28	101.84 101.25	99.31 99.15

Table 3. Statistical Validation of Recovery Studies

Level of Recovery (%)	Drug	Mean % Recovery	Standard Deviation*	% RSD
80	Cilnidipine	98.11	1.62	1.65
	Telmisartan	99.08	0.60	0.61
100	Cilnidipine	101.12	0.45	0.44
	Telmisartan	100.61	0.47	0.46
120	Cilnidipine	101.55	0.42	0.41
	Telmisartan	99.23	0.11	0.11

Table 4 Precision data of cilnidipine and telmisartan

Compound (n=6)	Intraday Precision		Interday precision	
	% Amt. found	% RSD	% Amt. found	% RSD
Cilnidipine	100.40	1.27	100.14	1.21
Telmisartan	99.81	0.54	100.29	0.64

Table 5 Result of Robustness Study of Cilnidipine

Parameters	Conc.	Amount of detected(mean ±SD)	%RSD
Mobile phase composition-(61+39)	10	533.12 ± 2.06	1.03
Mobile phase composition-(59+41)	10	501.92 ± 0.47	0.09
Wavelength change235nm	10	562.31 ± 6.10	1.08
Wavelength Change 237nm	10	593.35 ± 1.89	0.32
Flow rate change(0.6ml)	10	583.79 ± 5.99	1.03
Flow rate change(0.8ml)	10	589.02 ± 0.69	0.12

Table 6 Result of Robustness Study of Telmisartan

Parameters	Conc.	Amount of detected(mean ±SD)	%RSD
Mobile phase composition-(61+39)	40	1714.53 ± 3.71	0.22
Mobile phase composition-(59+41)	40	1720.56 ± 7.42	0.43
Wavelength change235nm	40	1667.55 ± 4.53	0.27
Wavelength Change 237nm	40	1770.70 ± 11.60	0.65
Flow rate change(0.6ml)	40	1717.70 ± 5.69	0.33
Flow rate change(0.8ml)	40	1812.21 ± 4.68	0.26

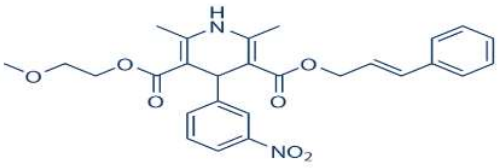

Figure 1: Structure of Cilnidipine

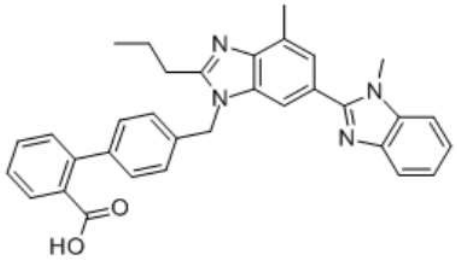

Figure 2: Structure of Telmisartan

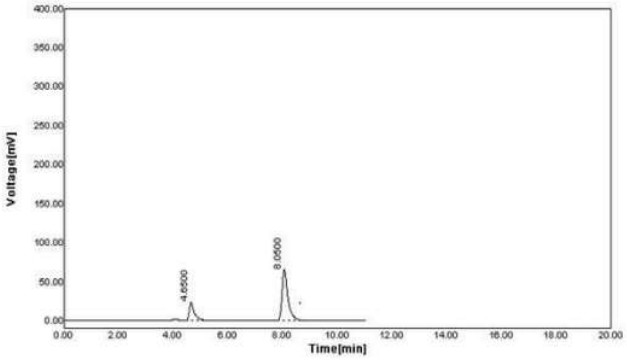

Figure 3: Chromatogram of Cilnidipine and Telmisartan

SUMMARY & CONCLUSION

The method provides selective quantification of Cilnidipine and Telmisartan. This developed RP-HPLC method for estimation Cilnidipine and Telmisartan is accurate, precise and robust. The method has been found to be better than previously reported method, because of its less retention time, gradient mode and use of economical readily available mobile phase, readily available column, UV detection and better resolution of peaks. The run time is relatively short, which will enable rapid quantification many samples in routine and quality controlled analysis of various formulations containing Cilnidipine and Telmisartan. All these factors make this method suitable for quantification of Cilnidipine and Telmisartan pharmaceutical dosage forms without any interference. The method was completely validated showing satisfactory data for all the method validation parameters tested. Hence this method can be introduced into routine use for determination of Cilnidipine and Telmisartan.

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Cite this article as:

Pravin Y. Khandagale *et al*. RP-HPLC method development and validation for simultaneous estimation of Cilnidipine and Telmisartan in combined pharmaceutical dosage form. Int. Res. J. Pharm. 2017;8(9):118-121 http://dx.doi.org/10.7897/2230-8407.089166

Source of support: Nil, Conflict of interest: None Declared