Int. J. Chem. Sci. : 6(2), 2008, 975-981

STABILITY INDICATING HPLC METHOD FOR THE DETERMINATION OF TELMISARTAN AS BULK DRUG AND IN PHARMACEUTICAL DOSAGE FORM

B. UDAYKUMAR RAO, DEVANAND B. SHINDE[a] and ANNA PRATIMA NIKALJE[*]

Y. B. Chavan College of Pharmacy, Dr. Rafiq Zakaria Campus, Rauza Bagh, AURANGABAD (M. S.) INDIA
[a]Department of Chemical Technology, Dr. B. A. M. University, AURANGABAD (M. S.) INDIA

ABSTRACT

This paper describes the validation of an isocratic HPLC method for the assay of telmisartan as bulk and pharmaceutical dosage forms. The solubility of drug is very poor in all solvents. Diluent has been developed to dissolve the drug substance first. The mixture of methanol and acetonitrile 1.5 : 1 was used as a diluent for dissolving the drug substance. The method employs Phenomenex luna ODS, (25 cm x 4.6 mm OD , 5µ, pore size 100A^{o}) column with a mobile phase with composition phosphate buffer and acetonitrile. 60 : 40. Quantitations was achieved by UV detection at 230 nm.A linear response ($r > 0.999$) was observed in the range of 300 –1500 µg mL^{-1}. The method shows good recoveries (Average 98.69%) and the relative standard deviation intra and inter-day were found to be 0.57% and 0.05%. Validation parameters as specificity, and robustness were also determined. The method can be used for quality control assay of telmisartan as bulk and in finished dosage form and for the stability studies as the method separates telmisartan from its degration products and exipients

Key words : Telmisartan, HPLC, Diluents, UV.

INTRODUCTION

Chemically, telmisartan is 4'-{ [4-methyl-6-(1-methyl –2-benzimidazoyl)-2 –propyl-1- benzimidazoyl]methyl} –2-biphenyl carboxylic acid. (Fig. 1). Telmisartan[1,2] is an angiotensin II receptor antagonist with actions similar to those of losartan. It is used in the management of hypertension. Telmisartan is given by mouth. After an oral dose, the hypotensive effect peaks within 3 hours and persists at least 24 hours. The maximum hypotensive effect is achieved within about 4 to 8 weeks after initiating therapy. Its

[*] Author for correspondence

structure is given in Fig. 1. The present work illustrates a development of simple and accurate isocratic HPLC method for quantitation of telmisartan in solid dosage form using the mixture of solvent and buffer[3-5]. The method was validated using ICH guidelines[6,7].

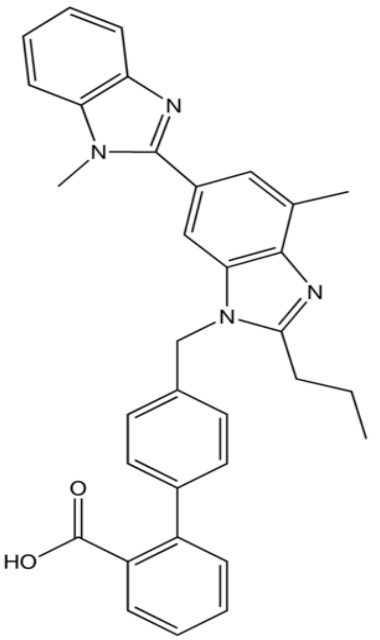

Fig. 1 Chemical structure of telmisartan

EXPRIMENTAL

Materials and reagents

Samples of telmisartan (assigned purity 99.68%) of pharmaceutical grade was received from Torrent Pharmaceuticals, Ahemadabad, India. Telmisartan tablets of strength 20 mg and 40 mg were procured from the market. Potassium dihydrogen orthophosphate of analytical grade was purchased from Merck India. HPLC grade acetonitrile and methanol were purchased from Qualigens –India. High purity water was prepared by Millipore milli Q plus purification system.

Equipment

The M/S Shimadzu HPLC system with a photodiode array detector system (SPD – M20A) was used for the method development and forced degradation studies. The out put signal was monitored and processed using LC-solution (Shimadzu). The LC system used for method validation was Shimadzu HPLC LC- 2010CHT with quaternary gradient

pumps. The out put signal was monitored and processed using LC-solution (Shimadzu) on Pentium computer (HCL)

Chromatographic conditions

The chromatographic column used was Phenomenex luna 250 mm x 4.6 mm ODS column with 5µ particle size The mobile phase comprised of 1% potassium dihydrogen orthophosphate buffer in water adjusted the pH to 3.5 with orthophosphoric acid and acetonitrile (60 : 40) .The diluent used was acetonitrile and methanol (1 : 1.5) .The mobile phase was filtered through 0.45 micron membrane filter, degassed in ultrasonic bath and pumped from the respective solvent reservoir to the column at a flow rate of 1.5 mL min^{-1}. The column temperature was maintained at 25 ºC and the detection wavelength was 230 nm. The run time was 30 minutes. Prior to the injection of the drug solution, the column was equilibrated for 60 minutes.

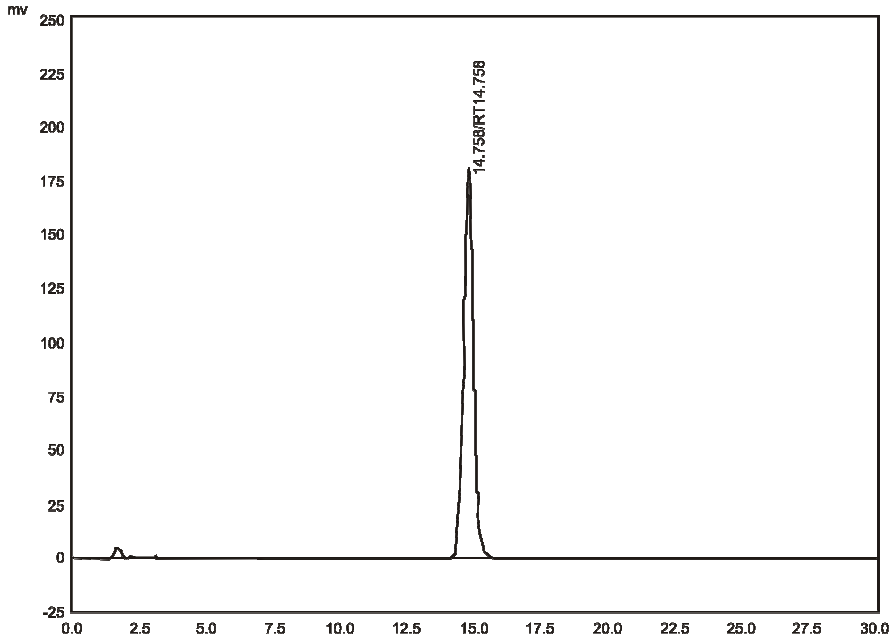

Fig. 2: Typical chromatogram of telmisartan (Conc. 1 mg/mL)

Preparation of standard solution

The stock solution of drug was prepared by dissolving telmisartan reference substance 25 mg in 25 mL volumetric flask and diluted with diluent.(1.0 mg mL^{-1})

Sonicated for 10 minutes and then made up to volume with diluent. Working standards solution of telmisartan of concentration 1 mg/mL was prepared by using diluent. Linearity solution was prepared in diluent containing telmisartan concentration in the range of 300 mcg/mL to 1500 mcg/mL. Each of these drug solutions (10 μL) was injected into the column and the peak area and retention times were recorded.

Preparation of sample solution

Twenty tablets were weighed and transferred into a clean and dry mortar. The average tablet weight was Calculated, then crushed and mixed well to give a homogeneous mixture. A sample of the mixed material containing 25 mg of the active material was taken in 25 ml volumetric flask. The mixture was diluted with 20 mL diluents. The mixture was soniccated for 10 minutes to ensure the complete solubility of the drug, followed by the addition of diluents to obtain a solution of 1.0 mg mL^{-1}. All the experiments were conducted in triplicate. The chromatogram of drug substance is shown in Fig .2

RESULTS AND DISCUSSION

Method validation

Precision

Method repeatability (intra-day precision) was evaluated by assaying six samples, prepared as described in the sample preparation. The mean % assay and percentage R.S.D. for assay values were found to be 99.08% and 0.57%, respectively, which is well within the acceptance criteria i.e. assay value should be between 97.0 and 103.0% and R.S.D. should be not more than 2.0%. The intermediate precision (inter-day precision) was performed by assaying six samples prepared by different analyst, different HPLC system and different HPLC column in different days as described in the sample preparation. The mean % assay and percentage R.S.D. for assay values were found to be 99.74 and 0.05%, respectively. The results of intra-day precision and inter-day precision were evaluated with respect to student's t- test and found that t-test was passed. The result shows good precision of the method (Table 1)

Linearity

Linear calibration curve for assay method was obtained over the calibration ranges tested, i.e. 0.3-1.5 mg mL^{-1} and the correlation coefficient was found to be greater than 0.999. Linearity was checked over the same concentration range for three consecutive

days. The result shows that an excellent correlation existed between the peak area and concentration of the analyte.

Table 1. Results of precision of test method

Sample No.	Assay of telmisartan as % of labled amount	
	Analyst 1 (intra-day precision)	**Analyst 2 (inter-day precision)**
1	99.00	99.7
2	10.40	99.7
3	98.70	99.7
4	98.80	99.7
5	98.70	99.8
6	98.90	99.7
Mean	99.10	99.7
RSD	0.58	0.05

Accuracy

The percentage recovery of telmisartan in pharmaceutical dosage forms ranged from 97 to 105% (Table 2).

Table 2. Recovery results of telmisartan in pharmaceutical dosage form

Spike level (%)	Average 'mg' added	Average 'mg' found	Mean % recovery	Percentage R. S. D.
80	32.02	30.99	96.8	0.45
100	39.52	40.5	102.5	0.09
120	47.84	49.92	104.3	0.02

Robustness

In all the deliberate varied chromatographic condition carried out i.e. flow rate,

column temperature, pH of the buffer in mobile phase and organic phase composition in mobile phase, the tailing factor and the % R.S.D. for the telmisartan peak area from the five replicate injections of standard was found to be within the acceptable limits; thus, illustrating the robustness of the method (Table 3).

Table 3. Results of robustness study

Parameter	observed value		
	Variation	**Tailing factor**	**RSD for five injections of standard (%)**
Flow rate	1.4 mL^{-1}	0.9	0.15
	1.6 mL^{-1}	0.9	0.38
Column temperature	20°C	0.9	0.07
	30 °C	0.9	0.06
pH (±0.2units of the set pH)	3.3	0.9	0.09
	3.5	0.9	0.06
Mobile phase composition	90% organic	1.1	0.08
	110% organic	0.9	0.15

Solution stability and mobile phase stability

The R.S.D. of assay of telmisartan during solution stability and mobile phase stability experiments was within 1%. The solution stability and mobile phase stability experiments data confirm that sample solutions and mobile phase used during assay determination was stable up to 72 h.

Results of forced degradation studies

All the stressed samples prepared, were injected into the HPLC system with photodiode array detector as per the described chromatographic conditions. Degradation was not observed in light exposure and water hydrolysis. In heat, moisture, acid hydrolysis and oxidative conditions degradation were found to be very less. Only in base hydrolysis, a significant degradation was observed. All degradants peaks were resolved from telmisartan peak in the chromatograms of all stressed samples. In all the forced degradation samples, impurity was not detected in the telmisartan peak. Peak purity of telmisartan is almost

1.0000. Single point threshold is less than 1.0 for the telmisartan peak. This indicates that there is no interference from degradants quantitating in stressed samples.

CONCLUSION

An isocratic reversed phase HPLC method has been developed and validated for the determination of telmisartan as bulk drug and in pharmaceutical dosage form. This chromatographic assay fulfilled all the requirements to be identified as reliable and feasible method, including accuracy, recovery and precision data. It is highly specific and precise analytical procedure and its chromatographic run time of 30 min., therefore this HPLC method can be used for routine sample analysis.

ACKNOWLEDGMENTS

The authors wish to thank the Honorable Chairman Maulana Azad Education Trust and Principal Maqdoom Faruqui, Maulana Azad Research Center and Principal, M.H. Dehghan, Y.B.Chavan College of Pharmacy for their encouragement. We are also thankful to M/S Torrent Pharmaceuticals Ltd. for providing samples of telmisartan and Mr. Jayaprakash Sangshetty for providing support.

REFERENCES

1. Martindale The Complete Drug Reference, Thirty fourth Edition, pp.1010.
2. The Merck Index, Thirteenth Edition, pp. 1628-1629
3. Julienne K. Kirk, Angiotensin II Receptor Antagonists,- Their Place in Therapy, American Family Physicians, **59** 3140 (1999).
4. Norman M. Kalpan, Angiotensin II Receptor Antagonists in the Treatment of Hypertension, American Family Physicians, **60** 1185 (1999)
5. United State Pharmacopoea, 29 Method < 1225 > -.
6. ICH Draft Guidelines on Validation of Analytical Procedure, Text and Methodology. Q2 (R1) November (2005).
7. J. N. Done, Practical High performance Liquid Chromatography, C. F. Simson (Ed.). London. 69.

Accepted : 04.03.2008