International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.3, No.4, pp 2001-2005, Oct-Dec 2011

Novel HPLC Method Development, Validation and Estimation of Telmisartan in Bulk and its Pharmaceutical Formulation

V. Bhaskara Raju[1] and A. Lakshmana Rao[2*]

[1]Sri Vasavi Institute of Pharmaceutical Sciences, Tadepalligudem- 534 101, A.P., India.
[2*]V.V. Institute of Pharmaceutical Sciences, Gudlavalleru- 521 356, A.P., India.

Corres. Author: dralrao@gmail.com

Abstract: An accurate and precise HPLC method was developed for the determination of telmisartan. Separation of the drug was achieved on a reverse phase C_8 column using a mobile phase consisting of phosphate buffer and acetonitrile in the ratio of 40:60 v/v. The flow rate was 0.9 ml/min and the detection wavelength was 229 nm. The linearity was observed in the range of 20-60 µg/ml with a correlation coefficient of 0.9996. The proposed method was validated for its linearity, accuracy, precision and robustness. This method can be employed for routine quality control analysis of telmisartan in tablet dosage forms.
Keywords: Telmisartan, Estimation, RP-HPLC, Validation, Tablets.

Introduction

Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. Generally, angiotensin II receptor blockers (ARBs) such as telmisartan bind to the angiotensin II type 1 (AT1) receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, ultimately leading to a reduction in arterial blood pressure. Recent studies suggest that telmisartan may also have PPAR-gamma agonistic properties that could potentially confer beneficial metabolic effects. Chemically described as 2-(4-{[4-methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl]methyl} phenyl)benzoic acid[1] (Fig. 1). A few spectroscopic[2,3], HPLC[4-8], HPTLC[9] and LC-MS[10] methods were reported earlier for the determination of telmisartan in bulk and pharmaceutical dosage forms. In the present study the authors report a rapid, sensitive, accurate and precise HPLC method for the estimation of telmisartan in bulk samples and in tablet dosage forms.

Experimental

Chromatographic conditions

The analysis of the drug was carried out on a Waters HPLC system equipped with a reverse phase Xterra C_8 column (150 mmx4.6mm; 3µm), a 2695 binary pump, a 20 µl injection loop and a 2487 dual absorbance detector and running on Waters Empower software.

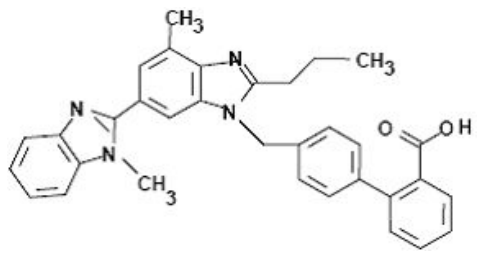

Fig. 1: Chemical structure of Telmisartan

Chemicals and solvents

The reference sample of telmisartan was supplied by Sun Pharmaceutical Industries Ltd., Baroda. HPLC grade water and acetonitrile were purchased from E. Merck (India) Ltd., Mumbai. Potassium dihydrogen phosphate and orthophosphoric acid of AR Grade were obtained from S.D. Fine Chemicals Ltd., Mumbai.

Preparation of phosphate buffer (pH 3.0)

Seven grams of KH_2PO_4 was weighed into a 1000 ml beaker, dissolved and diluted to 1000 ml with HPLC water. 2 ml of Triethyl amine was added and pH adjusted to 3.0 with orthophosporic acid.

Preparation of mobile phase and diluents

400 ml of the phosphate buffer was mixed with 600 ml of acetonitrile. The solution was degassed in an ultrasonic water bath for 5 minutes and filtered through 0.45µ filter under vacuum.

Procedure

A mixture of buffer and acetonitrile in the ratio of 40:60 v/v was found to be the most suitable mobile phase for ideal separation of telmisartan. The solvent mixture was filtered through a 0.45µ membrane filter and sonicated before use. It was pumped through the column at a flow rate of 0.9 ml/min. The column was maintained at ambient temperature. The pump pressure was set at 800 psi. The column was equilibrated by pumping the mobile phase through the column for at least 30 min prior to the injection of the drug solution. The detection of the drug was monitored at 229 nm. The run time was set at 6 min. Under these optimized chromatographic conditions the retention time obtained for the drug was 2.736 min. A typical chromatogram showing the separation of the drug is given in Fig. 2.

Calibration plot

About 25 mg of telmisartan was weighed accurately, transferred into a 100 ml volumetric flask and dissolved in 25 ml of a 40:60 v/v mixture of phosphate buffer and acetonitrile. The solution was sonicated for 15 min and the volume made up to the mark with a further quantity of the diluent to get a 100 µg/ml solution. From this, a working standard solution of the drug (40µg/ml) was prepared by diluting 2 ml of the above solution to 10 ml in a volumetric flask. Further dilutions ranging from 20-60 µg/ml were prepared from the solution in 10 ml volumetric flasks using the above diluent. 20 µl of each dilution was injected six times into the column at a flow rate of 0.9 ml/min and the corresponding chromatograms were obtained. From these chromatograms, the average area under the peak of each dilution was computed. The calibration graph constructed by plotting concentration of the drug against peak area was found to be linear in the concentration range of 20-60 µg/ml of the drug. The relevant data are furnished in Table-1**.** The regression equation of this curve was computed. This regression equation was later used to estimate the amount of telmisartan in tablets dosage forms.

Validation of the proposed method

The specificity, linearity, precision, accuracy, limit of detection, limit of quantification, robustness and system suitability parameters were studied systematically to validate the proposed HPLC method for the determination of telmisartan. Solution containing 40 µg/ml of telmisartan was subjected to the proposed HPLC analysis to check intra-day and inter-day variation of the method and the results are furnished in Table-2. The accuracy of the HPLC method was assessed by analyzing solutions of telmisartan at 50, 100 and 150% concentrated levels by the proposed method. The results are furnished in Table-3. The system suitability parameters are given in Table-4.

Estimation of telmisartan in tablet dosage forms

Two commercial brands of tablets were chosen for testing the suitability of the proposed method to estimate telmisartan in tablet formulations. Twenty tablets were weighed and powdered. An accurately weighed portion of this powder equivalent to 25 mg of telmisartan was transferred into a 100 ml volumetric flask and dissolved in 25 ml of a 40:60 v/v mixture of phosphate buffer and acetonitrile. The contents of the flask were sonicated for 15 min and a further 25 ml of the diluent was added, the flask was shaken continuously for 15 min to ensure complete solubility of the drug. The volume was made up with the diluent and the solution was filtered through a 0.45 µ membrane filter. This solution containing 40 µg/ml of telmisartan was injected into the column six times. The average peak area of the drug was computed from the chromatograms and the amount of the drug present in the tablet dosage form was calculated by using the regression equation obtained for the pure drug. The relevant results are furnished in Table-5.

Table-1: Calibration data of the method

Concentration (µg/ml)	Mean peak area (n=5)
20	2395392
30	3474808
40	4677202
50	5699253
60	6937725

Table-2: Precision of the proposed HPLC method

Concentration of Telmisartan(40µg/ml)	Peak area	
	Intra-day	Inter-day
Injection-1	4700148	4723338
Injection-2	4696685	4722324
Injection-3	4700823	4725118
Injection-4	4699330	4758167
Injection-5	4700718	4755466
Average	4699541	1773220
Standard Deviation	1703.0	18249.7
%RSD	0.04	0.39

Table-3: Accuracy studies

Concentration	Amount added (mg)	Amount found (mg)	% Recovery	% Mean recovery
50%	20.1	20.05	99.75%	
100%	40.0	40.01	100.04%	
150%	59.80	59.55	99.59%	99.79%

Table-4: System suitability parameters

Parameter	Result
Linearity ((µg/ml)	20-60
Correlation coefficient	0.9996
Theoretical plates (N)	2347
Tailing factor	1.2
LOD (µg/ml)	0.01
LOQ (µg/ml)	0.033

Table-5: Assay and recovery studies

Formulation	Label claim(mg)	Amount found (mg)	% Amount found
Formulation 1	40	40.003	100.0
Formulation 2	40	39.992	99.97

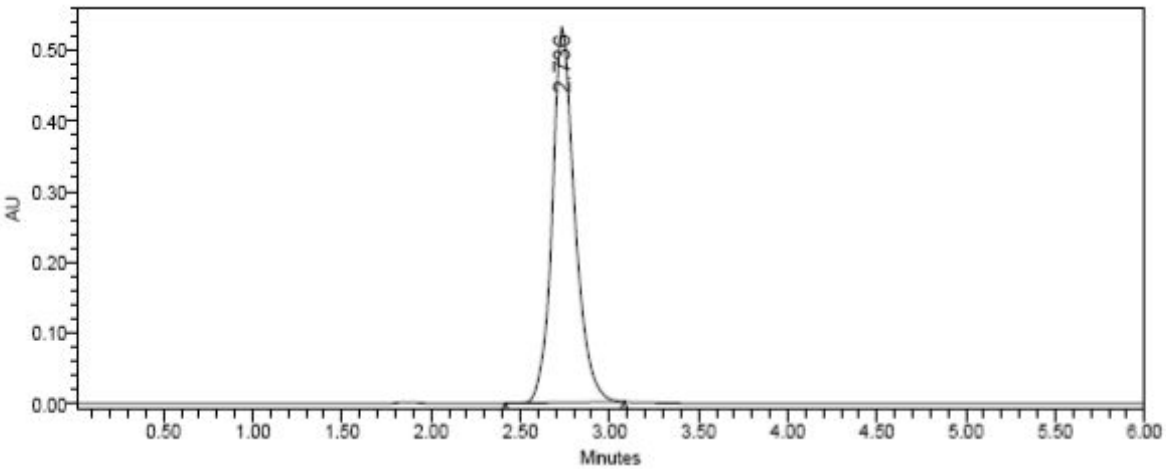

Fig. 2: Typical chromatogram of Telmisartan

Results and Discussion

In the proposed method, the retention time of telmisartan was found to be 2.736 min. Quantification was linear in the concentration range of 20-60 µg/ml. The regression equation of the linearity plot of concentration of telmisartan over its peak area was found to be Y=113231.6+113091.11X (r^2=0.9996), where X is the concentration of telmisartan (µg/ml) and Y is the corresponding peak area. The number of theoretical plates calculated was 2347, which indicates efficient performance of the column. The limit of detection and limit of quantification were found to be 0.01 µg/ml and 0.033 µg/ml respectively, which indicate the sensitivity of the method. The use of phosphate buffer and acetonitrile in the ratio of 40:60 v/v resulted in peak with good shape and resolution. The high percentage of recovery indicates that the proposed method is highly accurate. No interfering peaks were found in the chromatogram of the formulation within the run time indicating that excipients used in tablet formulations did not interfere with the estimation of the drug by the proposed HPLC method.

Conclusion

The proposed HPLC method is rapid, sensitive, precise and accurate for the determination of telmisartan and can be reliably adopted for routine quality control analysis of telmisartan in its tablet dosage forms.

Acknowledgements

The authors are thankful to M/s Sun Pharmaceutical Industries Ltd., Baroda for providing a reference sample of telmisartan.

References

1. www.drugbank.com
2. Bankey S, Tapadiya GG, Saboo SS, Bindaiya S, Jain D and Khadbadi SS. Simultaneous determination of ramipril, hydrochlorothiazide and telmisartan by spectrophotometry. International Journal of Chem Tech Research, 2009;1:183-188.
3. Palled MS, Chatter M, Rajesh PMN, Bhatt AR. Difference spectrophotometric determination of telmisartan in tablet dosage forms. Indian Journal of Pharmaceutical Sciences. 2006;68:685-686.
4. Vijaya Kumar M, Muley PR. Stability indicating RP-HPLC method for determination of telmisartan in solid dosage forms. The Indian Pharmacist. 2005; 36:69-72.
5. Nie J, Zhao Q, Huang J, Xiang B, Feng YQ. Determination of telmisartan in rat tissues by in-tube solid-phase microextraction coupled to high

performance liquid chromatography. Journal of Separation Science. 2006;29:650-655.

6. Shen J, Jiao Z, Li ZD, Shi XJ, Zhong MK. HPLC determination of telmisartan in human plasma and its application to a pharmacokinetic study. Pharmazie. 2005; 60:418-420.
7. Patil KR, Rane VP, Sangshetti JN and Shinde DB. A stability- indicating LC method for the simultaneous determination of telmisartan and ramipril in dosage form. Chromatographia. 2008;67:575-582.
8. Kurade VP, Pai MG and Gude R. Development and validation of a reverse phase liquid chromatographic method for quantitative estimation of telmisartan in human plasma. Indian Journal of Pharmaceutical Sciences. 2009;71:148-151.
9. Shah NJ, Suhagia BN, Shah RR, Shah PB. Development and validation of a HPTLC method for the simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian Journal of Pharmaceutical Sciences. 2007; 69:202-205.
10. Ben-Mei C, Yi-Zeng L, Ya-Li W, Fu-Liang D, Fang-Qiu G, Lan- Fang H. Development and validation of LC-MS method for the determination of telmisartan in human plasma. Analytica Chimica Acta. 2005;540:367-373.

*****