AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

A Validated RP-HPLC Method for the Estimation of Telmisartan in Tablet Dosage forms

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ABSTRACT

An accurate, precise and reproducible high performance liquid chromatographic method was developed for quantitative estimation of telmisartan in bulk drug samples and tablet dosage forms. Chromatographic separation of the drug was achieved on a Kromasil C18 column (150 x 4.6 mm; 5µ) using a mixture of phosphate buffer (pH 4.0) and acetonitrile (40:60 v/v) as the mobile phase at a flow rate of 1.0 mL/min. Under optimized conditions, the retention time of the drug was found to be 2.887 min. Good detecting sensitivity for the analyte was observed at 224 nm. The quantitation calibration curve for the drug was linear over the range of 20-60 µg/mL. The performance of the proposed method was validated as per ICH guidelines. The method was proved to be suitable for the estimation of telmisartan in tablet dosage forms.

Key words: Telmisartan, Estimation, Tablets, HPLC.

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Received 08 January 2013, Accepted 17 January 2013

Please cite this article in press as Rao JVLNS *et al.*, A Validated RP-HPLC Method for the Estimation of Telmisartan in Tablet Dosage forms. American Journal of PharmTech Research 2013.

INTRODUCTION

Telmisartan[1, 2] (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) is an angiotensin II receptor antagonist used in the treatment of hypertension. Generally, angiotensin II receptor blockers bind to the angiotensin II type 1 receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle and ultimately leading to a reduction in arterial blood pressure.

A literature survey revealed that various analytical methods have been reported for the determination of telmisartan in pharmaceutical dosage forms and in biological samples using liquid chromatography [3-9] and spectrophotometry[10-13] techniques. We now propose a new RP-HPLC method with short retention and run times for the determination of telmisartan in tablet dosage forms. The method was duly validated according to the ICH guidelines[14].

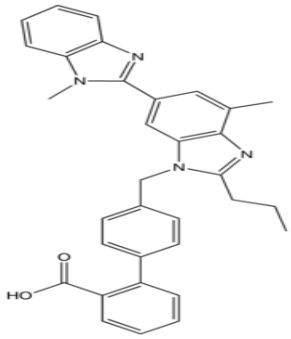

Figure 1: Structure of telmisartan

MATERIALS AND METHODS

Chemicals, solvents and drugs

Disodium hydrogen phosphate and *ortho*- phosphoric acid were purchased from Qualigens Chemicals Limited. HPLC grade acetonitrile was purchased from Merck Limited Mumbai. HPLC grade water was prepared by using Millipore Milli-Q system. The reference sample of telmisartan was obtained from Hetero Labs Ltd. (Hyderabad, India) as a gift sample. The commercial tablet formulation of telmisartan Arbitel (40 mg) manufactured by Micro Labs was used in the study.

Equipment and chromatographic conditions

A Waters Alliance liquid chromatograph (model 2695) fitted with a diode array detector (model 2996) and running on Empower2 software data handling system was employed in the study. A Kromasil C_{18} column (150 x 4.6 mm; 5µm) was used for analyzing the drug. All chromatographic runs were carried out using a mobile phase consisting of phosphate buffer and acetonitrile in isocratic mode at a flow rate of 1.0 mL/min. The injection volume of the samples

was 20 µL. The detector wavelength was set at 224 nm. Under these optimized conditions, the retention time obtained for telmisartan was 2.887 minutes.

Preparation of the Phosphate buffer

The phosphate buffer was prepared by dissolving 2.84 g of disodium hydrogen phosphate in 1000 mL of water and adjusting the pH of the solution to 4.0 using *ortho*- phosphoric acid. It was then filtered through a 0.45µ membrane filter and sonicated.

Preparation of the mobile phase

The mobile phase consisted of a mixture of the above-mentioned phosphate buffer (pH 4.0) and acetonitrile in the ratio of 40:60 v/v. This solution was also used as the diluent for preparing the drug solutions.

Preparation of the working standard solution of telmisartan

100 mg of telmisartan was accurately weighed and transferred into a 100 mL volumetric flask. 70 mL of the diluent was added to the flask and sonicated to dissolve the drug. The volume was then made up with a further quantity of the diluent and mixed well. This was used as the standard stock solution. 2.0 mL of this solution was transferred into a 50 mL volumetric flask, made up to the volume with the diluent and mixed well. This solution containing 40 µg/mL of telmisartan was used as the working standard solution.

Calibration curve

Dilutions of telmisartan were prepared at different concentration levels including the working standard concentration mentioned above. Twenty microlitres of each concentration was injected three times into the HPLC system. The response was read at 224 nm and the corresponding chromatograms were recorded. From these chromatograms, the mean of peak areas obtained for each concentration was calculated. A linearity plot of the mean peak areas over their concentrations was constructed.

Estimation of the drug from the tablet dosage form

Twenty tablets of Arbitel (each claimed to contain 40 mg of telmisartan) were weighed and ground to a fine powder. An amount equivalent to about 100 mg of telmisartan was transferred into a 100 mL volumetric flask. To it, 70 mL of the diluent was added and sonicated for 20 min. Further diluent was added to make up the volume and mixed well. A portion of this solution was filtered through a 0.22 µm membrane filter (discarding the first few mL of the filtrate). 2 mL of this filtrate was transferred into a 50 mL volumetric flask containing 30 mL of the diluent. The volume was made up to 50 mL with the diluent and mixed well. The above solution was then analyzed on the column six times. From the chromatograms obtained, the mean of the peak areas

of the drug was noted and the drug content in the formulation was calculated by using the regression equation of the calibration curve obtained for the reference sample.

RESULTS AND DISCUSSION

During the method optimization studies, various combinations and proportions of the solvents and buffers were examined on the Kromasil C_{18} column for efficient separation of telmisartan. Using a mobile phase consisting of a mixture of phosphate buffer (pH 4.0) and acetonitrile in the ratio of 40:60 v/v a good resolution and baseline separation of the drug peak was obtained. Suitable wavelength for detecting the drug was selected by scanning the standard solution of the drug in the diluent in 200 to 400 nm region. All the chromatographic conditions were optimized after evaluating the column efficiency parameters like theoretical plates and tailing (Table 1). Under these optimized conditions, the retention time obtained for telmisartan was 2.887 min (Figure 2). The proposed method was also found to be applicable to tablet formulations of telmisartan.

Table 1. Optimized chromatographic conditions

Stationary phase	Kromasil C18 (150 x 4.6 mm; 5µm)
Mobile phase	Phosphate buffer - Acetonitrile (40:60 v/v)
Flow rate	1.0 mL/min
Column temperature	26°C
Injection volume	20 µL
Detection wavelength	224 nm
Run time	7 min

Specificity

A good analytical method should be able to measure the analytes accurately in the presence of probable interferences from blank and excipients. Figure 2 shows good chromatographic base-line separation of telmisartan. Figure 3 demonstrates that no interference was found at the retention time of telmisartan in its dosage form due to excipients.

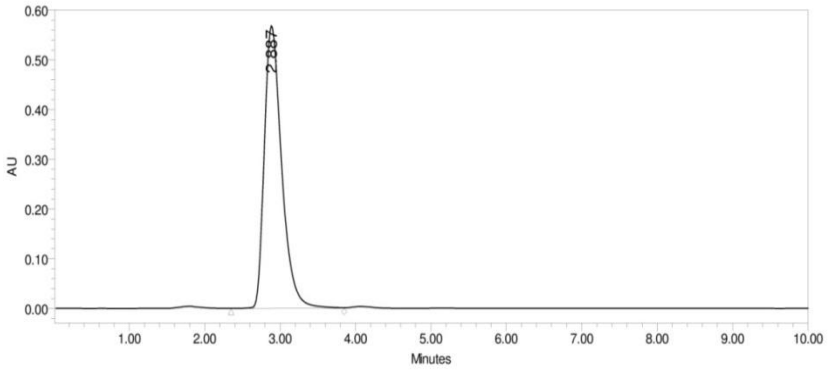

Figure 2: **Typical chromatogram of telmisartan from its standard solution**

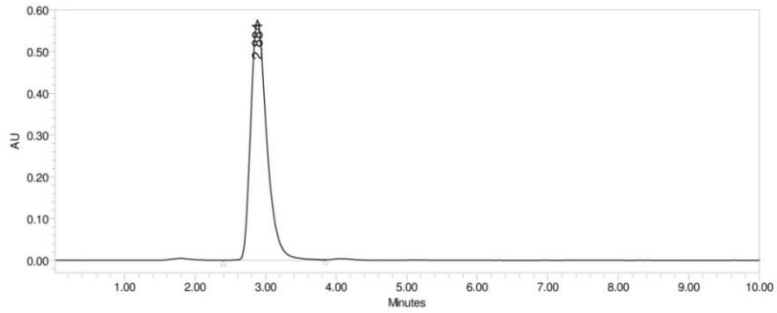

Figure 3: Typical chromatogram of sample of telmisartan formulation

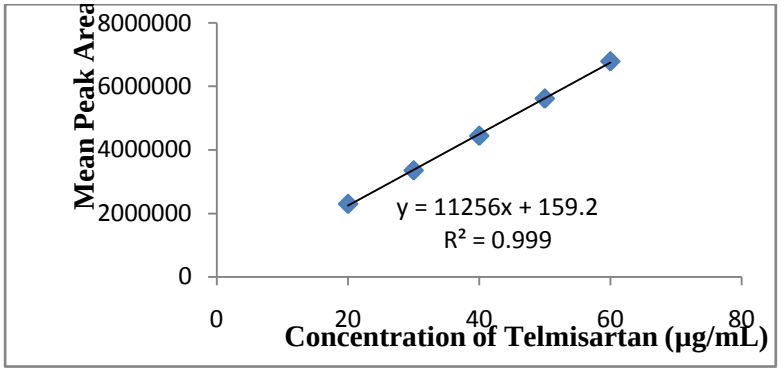

Figure 6: Linearity plot for telmisartan

Linearity

The calibration curve constructed for the drug (Figure 6) was linear over the concentration range of 20-60 µg/mL. The regression of the plot was computed by the least squares method and its correlation coefficient is greater than 0.99. The %RSD for each concentration studied was less than 2.0. The linearity data is shown in Table 2.

Table 2. Linearity data

S.No.	Concentration of Telmisartan (µg/ml)	Mean peak area (n=3)
1	20	2297878
2	30	3355517
3	40	4445756
4	50	5619999
5	60	6793634

Accuracy and precision

The accuracy of the method was determined by recovery experiments. The recovery studies were carried out and the percent recovery and standard deviation of the percent recovery were calculated and presented in Table 3. The high percentage of recovery indicates that the proposed method is highly accurate. The precision of the method was demonstrated by intra-day and inter-day variation studies. Six replicate injections of the sample solution were analyzed and the percentage RSD was calculated (Table 4). From the results obtained, the proposed RP-HPLC

method was found to be precise.

Table 3. Accuracy data of the proposed method

Analyte	Amount of the analyte taken(µg/mL)	Mean recovery (µg/mL) ± SD	% Mean recovery ± SD
Telmisartan	20	20.22 ± 0.12	101.1 ± 0.60
	40	39.86 ± 0.27	99.65 ± 0.68
	60	60.25 ± 0.26	100.42 ± 0.43

Table 4. Precision data for the proposed method

	Intra-day precision (n=6)	Inter-day precision (n=6)
Mean peak area	4437571	4454723
SD	9431.561	64115.97
%RSD	0.21	1.44

System suitability parameters

System suitability parameters were studied with six replicate injections of the standard sample solution. The corresponding values are presented in Table 5.

Table 5. System suitability parameters of the proposed method

Parameter	Value
Tailing factor	1.39
Theoretical plates	3774.5
HETP	6.623×10^{-2}

Method suitability

The commercial tablet formulation Arbitel (40 mg) was analyzed by using the proposed method. The average percent recovery of six replicate samples was found to be 100.05. This confirms the suitability of the method for the estimation of telmisartan in tablet dosage forms.

CONCLUSION

The proposed RP -HPLC method is sensitive, precise and accurate and can be used for the routine quality control analysis of telmisartan in its tablet dosage forms.

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