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REVERSE PHASE HPLC METHOD FOR THE ANALYSIS OF TELMISARTAN IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

A rapid and sensitive high performance liquid chromatographic method was developed for the estimation of Telmisartan in pharmaceutical dosage forms. Telmisartan was chromatographed on a reverse phase C_{18} column in a mobile phase consisting of methanol: acetonitrile: buffer pH 2.8 in the ratio of 30: 60: 10 v/v. The mobile phase was pumped at flow rate of 1 mL / min and the eluents were monitored at 290 nm. The calibration curve was linear in the range of 10 – 100 µg / mL. The intra – and inter – day variation was found to be less than 2% showing high precision of the assay method. The mean recovery of the drug from the solution containing 20 µg/mL was 96.6 ± 1.13% indicating high accuracy of the proposed HPLC method. Due to its simplicity, rapidness, high precision and accuracy, the proposed HPLC method may be used for determining Telmisartan in bulk drug samples and pharmaceutical dosage forms.

Key words: Telmisartan, Reversed phase HPLC, Dosage forms.

INTRODUCTION

Telmisartan (TMS) is nonpeptide angiotensin II receptor antagonist, used in hypertension[1]. TMS is 4 – [(1, 4′ – dimethyl–2′ –propyl [2,6′ – bi–1 H–benzimidazole]– 1′ – yl) methyl]–[1, 1′ – biphenyl]–2–carboxylic acid. A few analytical methods like Polarography[2], Electrophoresis[3, 4] and HPLC[5] have been reported for the estimation of Telmisartan. All the methods considered tedious. The HPLC methods using the most commonly available columns and detectors like UV are preferred. The present study describes the determination of Telmisartan in bulk drug samples and pharmaceutical dosage forms by using RP – C_{18} column with UV detector. Owing to the wide spread use of HPLC in routine analysis, it is important that well validated HPLC methods are to be developed for estimating Telmisartan. The aim of this study is to develop a simple, precise, rapid and accurate reversed phase HPLC method for the determination of Telmisartan in bulk drug samples or in pharmaceutical dosage forms.

EXPERIMENTAL

Telmisartan was gift sample from Aristo Pharmaceuticals Ltd., Bhopal, India.

Methanol, acetonitrile and water were of HPLC grade (Qualigens). All other reagents were of AR grade.

An isocratic HPLC (Waters India, USA) with a single waters 510 pump, waters 486 tunable absorbance detector and RP–C_{18} column (Bondapak, 5 µm particle size) was used. The HPLC system was equipped with software Millennium 32.

Chromatographic conditions

The contents of the mobile phase, methanol, acetonitrile and buffer pH 2.8 in the ratio of 30: 60: 10 v/v were filtered before use through a 0.4 µm membrane filter and degassed for 30 min.

The components of the mobile phase were pumped from the solvent reservoir to the column at a flow rate of 1 mL / min that yielded column back pressure 140 – 150 kg/ cm^2. The column temperature was maintained at 40°C. The eluents were monitored at 290 nm. Prior to the injection of the drug solutions, the column was calibrated for atleast 30 min with the mobile phase flowing through the systems.

Procedure

The solutions were prepared on a weight basis and volumetric flasks were used to minimize solvent evaporation. Stock solution of a drug was prepared by dissolving 100 mg of Telmisartan in 100 mL volumetric flask containing 70 mL of methanol, sonicated for about 20 min and then made up to volume with methanol. Working standard solution of Telmisartan was prepared by suitable dilution of the stock solution with methanol.

Five sets of the Telmisartan were prepared in methanol at concentrations of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 µm / mL. Each of these samples (20 µL) was injected five times into the column and the peak area of the drug was recorded.

Assay of Telmisartan in capsules

Twenty capsules[6] were weighed, finally powdered and an accurately weighed sample of powdered capsules equivalent to 100 mg of Telmisartan was placed in a 100 mL volumetric flask. 70 mL of methanol was added, shaken well and the flasks allowed to stand for 4 hours with intermittent sonication to ensure complete solubility of drug. The mixture was then made up to volume with methanol, thoroughly mixed and then filtered through a 0.4 µm membrane filter. An aliquot of the filtrate was transferred to a volumetric flask and made up to volume with methanol to give an expected concentration of 20 µm / mL of Telmisartan. All determinations were conducted in triplicate.

Precision

The precision of the assay was determined in terms of intra – and inter – day variation in the peak area for a set of drug solution on three different days (n = 5). The intra – and inter – day

variation in the peak area of drug solution (10 or 20 µg/mL) was calculated in terms of coefficient of variation (CV) obtained by multiplying the ratio of standard deviation to the mean with 100 [CV = ± s.d / mean X 100]

Accuracy

The accuracy of the HPLC assay method was assessed by adding known amount (10 or 20 µg) of the drug to a drug solution of known concentration (20 µg / mL) and subjecting the samples to the proposed HPLC method. Also, known amount of drug solution (10 or 20 µg / mL) was added to the volumetric flask containing the powder sample of the tablet formulation with known amount of drug. The drug was estimated as the procedure described above for the estimation of Telmisartan in the tablet formulations. In both the cases, the recovery studies were replicated five times. The accuracy was expressed in terms of the recovery and calculated by multiplying the ratio of measured drug concentration to the expected drug concentration with 100, so as to give the per cent recovery.

RESULTS AND DISCUSSION

The run time of the method was set at 8 min and Telmisartan appeared on the chromatogram at 3.97 min (Fig. 1). When the same drug solution was injected 5 times, the retention time of the drugs was same. The peak areas of Telmisartan was calculated and the average of five such determinations are given in Table 1. When the concentration of Telmisartan and its respective peak were subjected regression analysis by least square method, a high correlation coefficient was observed (r = 0.9994) in the range of 10 – 100 µg / mL only. The regression of Telmisartan

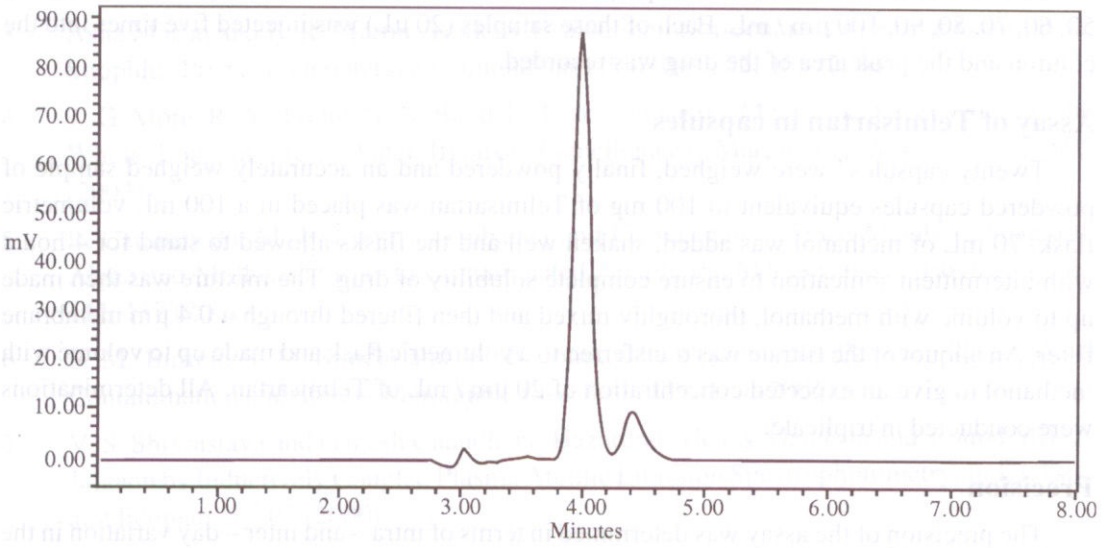

Figure 1 : Typical chromatogram of Telmisartan

concentration over its peak area was found to be Y = 12.693 + 370.02 X, where 'Y' is the peak area and 'X' is the concentration of Telmisartan. This regression was used to estimate the amount of Telmisartan either in tablet formulation or in validation study.

Table 1. Calibration of the HPLC method for the estimation of Telmisartan

Concentration of telmisartan (μg / mL)	Peak area	CV (%)
10	3728.53	1.01
20	7398.31	1.23
30	10932.21	0.98
40	14914.12	1.32
50	17895.23	0.73
60	23086.21	1.28
70	25976.34	1.09
80	29823.61	1.31
90	32946.82	0.87
100	36934.32	0.59

Regression equation (from 10 to 100 μg / mL): Y = 12.693 + 370.02 X (r = 0.9994)

Table 2. Precision of the proposed HPLC method

Telmisartan concentration (μg / mL)	Concentration of Telmisartan (μg / mL) found on			
	Intra – day		Inter – day	
	Mean (n = 5)	CV (%)	Mean (n = 5)	CV (%)
10	9.42	0.81	10.21	0.93
20	20.81	1.41	19.38	1.23

Table 3. Recovery of Telmisartan

Amount of drug added (μg)	Mean (± s.d) amount (μg) recovered (n = 5)	Mean (± s.d) % of Recovery (n = 5)
10	9.62 ± 0.32	96.2 ± 1.08
20	19.32 ± 0.82	96.6 ± 1.13

Table 4. Mean (± s.d) amount of Telmisartan in tablet dosage forms by proposed HPLC method

Brand of the tablet	Labeled amount (mg)	Observed amount (mg)	Purity (%)
AAA	40	38.92 ± 0.07	97.3 ± 10.9
BBB	40	39.21 ± 0.12	98.02 ± 0.82

Proposed HPLC methods were also validated for intra – and inter – day variation. When the solutions containing 10 or 20 µg / mL of Telmisartan were repeatedly injected on the same day, the coefficient of variation (CV) in the peak area of the drug for five replicate injection was found to be less than 2%. Also, the inter – day variation (3 days and five injections) was found to be less than 2% (Table 2). Thus the results have shown that the proposed HPLC method is highly reproducible. When a known amount of drug solution (10 or 20 µg) was added to a known concentration of drug solution (20µg / mL), this was a high recovery (96.6 ± 1.13%) of Telmisartan (Table 3) indicating that the proposed method is highly accurate.

The HPLC method, developed in the present study has also been used to quantify Telmisartan in tablet dosage forms. Telmisartan capsules (containing 40 mg of the drug) were analyzed as per the procedure described above. The average drug content was found to be 98% of the labeled amount (Table 4). No interfering peaks were found in the chromatogram indicating that excipients used in the tablet formulations did not interfere with the estimation of drug by the proposed HPLC method.

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