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DEVELOPMENT OF UV SPECTROPHOTOMETER METHOD AND IT'S VALIDATION FOR ESTIMATION OF TELMISARTAN AS API AND IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT
A simple, sensitive, cost effective, reproducible and specific UV spectrophotometric method was developed for the estimation of Telmisartan in tablet dosage form. The optimum conditions for the analysis of the drug were established with Methanol as solvent. The wavelength maxima (λmax) for Telmisartan were found to be 296 nm. Beer's law was obeyed in the concentration range of 2-22 µg/mL, and was validated with respect to linearity, accuracy (recovery), precision and specificity. The proposed method has been applied successfully for the analysis of the drug as API and in its tablets dosage forms.
Keywords: Telmisartan, UV spectrophotometer, estimation by UV spectrophotometry.

INTRODUCTION

Telmisartan is 2-(4-{[4-methyl-6-(1-methyl-1*H*-1,3-benzodiazol-2-yl)-2-propyl-1*H*-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid (Figure 1), is angiotensin II receptor antagonist (ARB). It is indicated in the treatment of essential hypertension, cardiovascular risk reduction.[1-4]

Analysis is an important component in the formulation development of any drug molecule. A suitable and validated method is required for the analysis of drug(s) in the bulk, in drug delivery systems, from release dissolution studies and in biological samples. If a suitable method, for specific need, is not available then it becomes essential to develop a simple, sensitive, accurate, precise, reproducible method for the estimation of drug samples.[5,6]

The estimation of Telmisartan by potentiometry, high performance liquid chromatography [HPLC], is already reported in literature. Although simultaneous UV spectrophotometric estimation of Telmisartan in combinations had been reported by many analyst, and also single estimation of this drug is reported in bulk and in pharmaceutical formulation with 0.1 N NaOH as solvent. But single estimation of this drug with methanol as solvent has not been reported in bulk and in pharmaceutical formulation, thus the present study was undertaken to develop and validate a simple, sensitive, accurate, precise, and reproducible UV spectrophotometric method for Telmisartan as methanol as solvent. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines.[5,6]

MATERIALS AND METHOD

Instrument and materials

Instrument used were UV-Visible double beam spectrophotometer Shimadzu UV 1800 and 1 cm matched quartz cells. The glasswares used in each procedure were soaked overnight in a mixture of chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven prior to use.

Drug & Reagents

Telmisartan pure drug was obtained from Cipla Ltd. Ahmedabad as gift sample with 99.99% w/w assay value and was used without further purification. All chemicals and reagents used were of analytical grade (AR).

Standard drug solution

A standard stock solution equivalent to 1 mg/mL (1000 µg/ml) of Telmisartan was prepared by dissolving 10 mg of pure drug in methanol and dilute upto 10 mL in calibrated volumetric flask with methanol and was sonicated.

Determination of λ_{max}

For this stock solution 100 µg/ml was prepared by taking 1 ml. of 1000 µg/ml standard stock solution and was diluted with methanol upto 10 ml. Then series of dilution for 2 and 22µg/ml were prepared by taking 0.2 and 2.2 ml of 100 µg/ml in 10 ml. volumetric flask and diluted with methanol upto 10 ml. and scan for λ_{max} was run between 200 to 400 nm, and 296 nm was selected λ_{max} for Telmisartan (Figure 2).

Preparation of calibration curve

Calibration curve was prepared in methanol at λ_{max} 296 nm using Shimadzu 1800 UV-Visible spectrophotometer. For this stock solution of 100 µg/ml was prepared. Then series of dilution 2, 6, 10, 14, 18, 22 µg/ml were prepared and absorbance's at different concentration was taken at λ_{max} 296 nm against the methanol as blank. The standard calibration curve was obtained for data of concentration v/s absorbance; standard calibration curve data reported in (Table 1).

Preparation of sample solution

According to B.P ten tablets were weighed and powdered. The amount of tablet powder equivalent to 10 mg of Telmisartan was weighed accurately and transfer to 10 ml. volumetric flask and volume was made up to 10 ml with methanol and was sonicated for 15 minutes. The solution was then filtered through Whatmann filter paper # 41. This filtrate was diluted suitably with methanol to obtain concentration of 12 µg/ml solution. The absorbance was measured against methanol as blank. The drug content of the preparation was calculated using the standard calibration curve for API. Data for estimation is reported in (Table 3).

RESULT AND DISCUSSION

Precision

Precision of the method was assessed by repeatability, determined by analyzing 12 µg/ml of Telmisartan for six times, the results are reported in (Table 4).

Precision of method was studied as intra-day and interday variations. Intra-day precision was determined by analyzing 9.6, 12 and 14.4 µg/ml of Telmisartan for three times within the day. Inter-day precision was determined by analyzing the same concentration of solutions daily for three days, the results for intraday and interday are reported in (Table 5).

Repeatability study showed a R.S.D of 0.3037 % of Telmisartan. The relative standard deviation (RSD) and assay values of intraday and interday precesion were 0.1669 and 0.1790 respectively which complied with ICH guidelines and data is reported in (Table 5).

Accuracy (Recovery Test)

To assess the accuracy of proposed method, recovery experiment was performed at three different levels that are 80%, 100% and 120%. To the pre-analyzed sample solution, a known amount of standard drug solution was added at three different levels and absorbance's were recorded. The % recovery was then calculated by using the following formula;

% Recovery = [(A-B) / C] x 100

Where,

A= Total amount of drug estimated

B= Amount of drug found on preanalyzed basis

C= Amount of pure drug added

The recovery values for Telmisartan ranged from 99.91± 0.4864 and data is reported in (Table 3).

Linearity

The linearity of the response of the drug was verified at 1 to 30 µg/ml concentrations, but linearity was obtained between 2-22 µg/ml concentrations. The calibration graph was obtained by plotting the absorbance versus the concentration data and were treated by linear regression analysis (Table 2). The equation of the calibration curve for Telmisartan was obtained as Y = 0.052571 X + 0.049143; the calibration curve was found to be linear in the aforementioned concentrations. The correlation coefficient (r^2) of determination was found to be 0.999.

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The LOD and LOQ of Telmisartan were determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines[7]. The LOD and LOQ were 0.10310 and 0.30930 respectively and data is reported in (Table 2.)

Determination of Active Ingredients in Tablets

The validated method was applied to the determination of Telmisartan in tablets. Six tablets were assayed and the results are shown in (Table 6) indicating that the amount of drug was found to be 39.69 mg in 40 mg. tablet samples with %purity 99.22 % which met with B.P. guidelines (98–102% of the label claim).

CONCLUSION

The developed method was found to be simple, sensitive, accurate, precise, reproducible, and can be used for routine quality control analysis of Telmisartan as API and in pharmaceutical formulation in pharmaceutical industry.

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Table 1: Calibration Curve Data at 296 nm.

S.No.	Conc. (µg/ml)	Avg. Abs. ± S.D.	% R.S.D.
1.	2	0.170±.023094	1.3 %
2.	6	0.360±.001527	0.4 %
3.	10	0.560±.001547	0.2 %
4.	14	0.775±.009539	1.2 %
5.	18	1.000±.000577	0.05 %
6.	22	1.215±.000577	0.047 %

Table 2: Validation Parameters

PARAMETER	OBSERVATIONS (Telmisartan)
Specificity	No interference was found w.r.t. excipients
Linearity (Correlation coefficient r)	0.999
Range	2-22 PPM
Accuracy* (% Recovery)	99.91%
Precision RSD** Repeatability (n= 6) Intra-day (n=3) Inter-day (days=3)	0.3033 % 0.1667 % 0.1790 %
LOD(Limit of Detection)	0.10310
LOQ (Limit of Quantitaion)	0. 30930

Table 3: Determination of Accuracy by Percentage Recovery Method

Mixture	Conc.of tablet sol[a] (ppm)	Std. Added (ppm)	Abs.	Amt. Found (mg)	% Recovery	Mean Recovery ± S.D.	% R.S.D.
1	7.922	11.2	.554	9.567	100.06	99.91± 0.4864	0.4868
	8.077	11.2	.554	9.558	99.164		
	8.090	11.2	.558	9.629	99.834		
2	8.056	16	.679	11.930	99.185		
	7.986	16	.683	12.006	100.10		
	7.961	16	.686	12.062	100.68		
3	7.979	20.8	.810	14.429	100.002		
	8.012	20.8	.811	14.448	100.29		
	8.010	20.8	.808	14.398	99.95		

Table 4: Data showing Repeatability of Absorbance's

S. No.	Conc. µg/ml	Wavelength (nm)	ABS.	Mean ± S.D.	% R.S.D.
1	12 µg/ml	296	0.681	0.6825 ± .002073	0.30373 %
2		296	0.680		
3		296	0.682		
4		296	0.685		
5		296	0.682		
6		296	0.685		

Table 5: Results of Intra-day and Inter-day Precision for Telmisartan

Drug	Conc.µg/ml	Intra-day amount found [µg/ml] [n=3]	% R.S.D.	Inter-day amount found [µg/ml] [n=3]	% R.S.D.
Telmisartan	9.6	9.605± .01363	0.1419	9.6116± 0.02392	0.2488
	12	11.9997±.02443	0.2036	12.020 ± 0.0169	0.1405
	14.4	14.408± .02228	0.1546	14.418 ± 0.02133	0.1479
Mean % R.S.D.			**0.1667**		**0.1790**

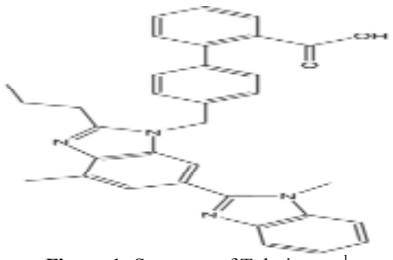

Figure 1: Structure of Telmisartan[1]

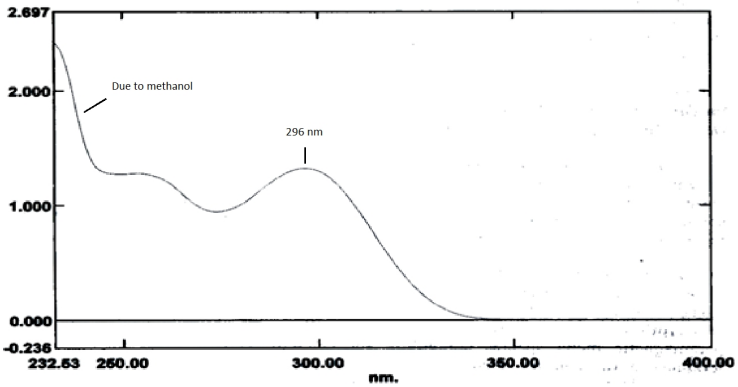

Figure 2: Spectrum of Telmisartan in methanol as solvent

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