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Original Article

Development and validation of HPTLC method for determination of Telmisartan in API and pharmaceutical dosage form

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ABSTRACT

The aim of present work was to develop a simple and sensitive, HPTLC for the quantitative estimation of Telmisartan in its single component tablet formulations (40 mg). Telmisartan was chromatographed on silica Gel 60 F254 TLC plate using Toluene:Methanol (7:3 *v/v/v*) as mobile phase. Telmisartan in methanol scanned by Camag TLC scanner 4 with UV visible detector over wavelength range 200 to 400 *nm*, showed R_f *value* of 0.46 at wavelength of 299 *nm* and selected for further studies. The method was validated in terms of linearity (1-3 ng/ml), precision (intra-day variation 1.61, inter-day variation 2.73), accuracy (81.55 to 87.51%) and specificity. The limit of detection and limit of quantification for Telmisartan were found to be 0.25 ng/spot and 0.7 ng/spot, respectively. It can be concluded from the results that the proposed method was accurate, precise and consistent the determination of Telmisartan in Tablet dosage form. This method was validated as per ICH guideline Q2 (R1). Results suggest that this method can be used for routine estimation of Telmisartan in bulk and pharmaceutical dosage forms.

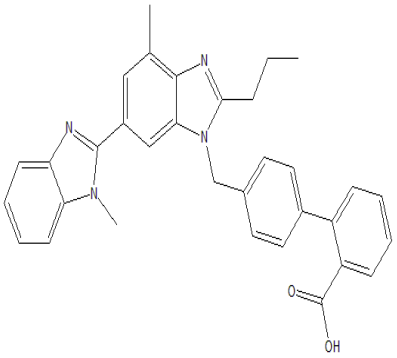
Key Words: Telmisartan, Toluene, Methanol, HPTLC.

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. Telmisartan is official in Indian Pharmacopoeia. Literature survey reveals that some methods have been developed for their determination by HPLC, HPTLC or spectrophotometry. Either alone or in combination. However, overall cost of analysis of reported HPTLC method is more. In this view, an economical HPTLC method has been developed for estimation of Telmisartan in pharmaceutical dosage form.

MATERIALS AND METHODS

Telmisartan standard was provided by Aarati pharmaceuticals, Mumbai, India. "Tazloc 40 mg" Tablet were procured from local market. AR grade of solvents used for this study were purchased from Merck Pvt. Ltd, Mumbai.



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

Fig. 1: Chemical Structure of Telmisartan

Preparation of standard solution: A standard stock solution of Telmisartan was prepared by dissolving 10 mg of standard API in 10 ml of Methanol to get concentration of 1000 µg/ml. This solution was further diluted to get 100 µg/ml solution of Telmisartan as working standard.

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Selection of wavelength for Detection

The working standard of Telmisartan in Methanol was scanned by Camag TLC scanner 4 with UV-Visible detector over wavelength range 200 to 400 nm. Wavelength 299 nm was selected for further studies. (Figure 2).

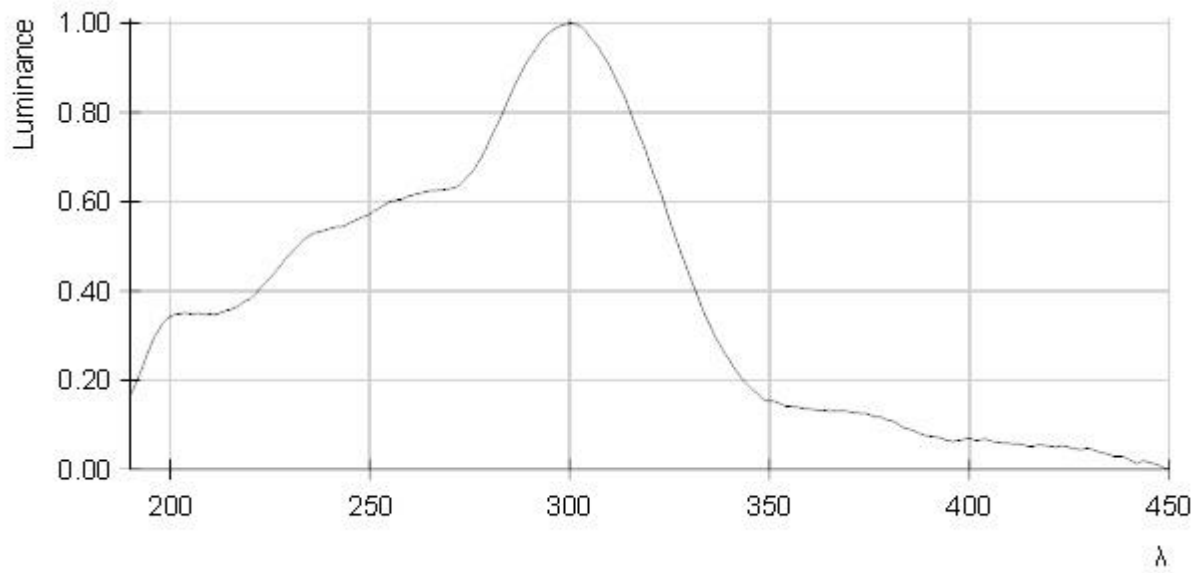

Fig. 2: The overlain UV spectra of 1000 ng/ml Telmisartan (API and sample) between 200- 400 nm

Chromatographic Conditions: This analysis was performed on Camag HPTLC system (Switzerland). It is equipped with a Linomat-5 applicator, 100 µl sample syringe (Hamilton, Switzerland) and Camag TLC scanner4.On the basis of trial and error method using different solvent system, following chromatographic conditions were chosen for analysis. Pre-coated silica gel 60 F254 TLC (E-Merck, Germany) plates (10x10 cm) were used as stationary phase. TLC plates were pre-washed with Methanol and activated at 110°C for 10 min prior to application. The standard samples of Telmisartan were spotted on pre-coated TLC plates in the form of bands of length 4 mm using 100 μl sample syringe with a Linomat-5 applicator. The chromatographic development was carried using Toluene:Methanol (7:3 v/v/v/) as mobile phase with chamber saturation time of 20 minutes and the migration distance of 70 mm. Densitometric scanning was performed using Camag TLC scanner at 299 nm, operated by win CATS Software (Version 1.4.3, Camag).

Preparation of Calibration Curve: Different concentrations of the working standard solution were applied on the TLC plate, corresponding peak areas were recorded and linear regression was done between the absorbance *vs* concentration. Finally, 100-300 ng/spot range was selected for preparation of calibration curve and linear regression equation was obtained in this range (Figure 3).

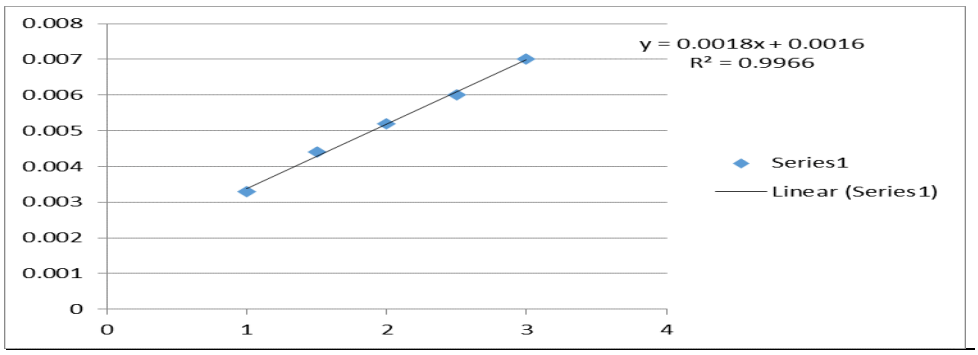

Fig 3. Calibration Curve of Telmisartan

METHOD VALIDATION

The objective of validation of an analytical procedure is to demonstrate whether the procedure is suitable for its intended purpose. The proposed method was validated for various parameters such as Linearity & Range, Precision, Limit of Detection (LOD) & Limit of Quantitation (LOQ) and Accuracy according to ICH Q2 (R1) guidelines.

Linearity and Range: The linearity was determined by using working standard solutions between 100-300 ng/spot. The spectra of these solutions were recorded at wavelength 299 *nm*. Calibration curve of peak area *v/s* concentration was plotted after suitable calculation and simple linear regression was performed. Regression equation and correlation coefficient were obtained. The range of solution has been decided according to statistical parameters of generated equation (Table 2).

Table 2. Linearity and Range of Telmisartan

Concentration ng/spot	Absorbance
100	0.0033
150	0.0044
200	0.0052
250	0.0060
300	0.0070

Precision

Repeatability: The precision of the method was checked by repeatedly injecting (n= 6) standard solutions of Telmisartan (200 ng/spot). Absorption of these solution was measured at 299 *nm*. Relative standard deviation (%RSD) was calculated (Table 3).

Reproducibility: The intra-day and inter-day precision of the proposed method was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days of same concentrations of 200 ng/spot of Telmisartan. The results have been reported in terms of percentage relative standard deviation (%RSD). The results were tabulated in (Table 4).

Limit of Detection (LOD) and Limit of Quantitation (LOQ): Nine sets of known concentrations (0.001-0.009 µg/spot) were prepared. Calibration curves were plotted for each set. LOD and LOQ were calculated using the regression equation (Table 5) and following formulae as

LOD = 3.3 SD/S

LOQ = 10 SD/S

Where,

SD is standard deviation of y-intercept of the calibration curve; S is mean slope of five calibration curve.

Table 3. Repeatability study of Telmisartan

Concentration (ng/spot)	**Absorbance**	**Mean absorbance**	**%RSD**
200	0.00616	0.00612	0.8014
200	0.00619		
200	0.0061		
200	0.00614		
200	0.00606		
200	0.00606		

***n=6, % RSD = % Relative Standard Deviation.**

Table 4. Intraday and Interday Precision study of Telmisartan

Drug	**Concentration (ng/spot)**	**% RSD**	
		Intraday	**Interday**
Telmisartan	200	1.76	1.32
	200	1.81	1.41
	200	1.68	1.38

***n=3**

Table 5. LOD and LOQ of Telmisartan

Drug	**LOD**	**LOQ**
Telmisartan	0.25	0.75

Accuracy

Concentration taken in ng/spot (A)	Standard addition in ng/spot (B)	Total drug Concentration (ng/spot) (A+B)	Area	Average	% Recovery
100	80	180	5462	5495.333	87.51
			5458		
			5566		
100	100	200	5903	5834	84.17
			5826		
			5773		
100	120	220	6224	6232.667	81.55
			6244		
			6230		

Specificity: The specificity of the method was ascertained by analyzing standard drug and sample. The spot for drug in sample was confirmed by comparing the R_f and spectra of the spot with that of standard drug spot. The specificity of the method was also ascertained by peak purity profiling studies by analyzing the spectrum at peak start, middle and at peak end.

RESULTS AND DISCUSSION

The Calibration curve was of Telmisartan was plotted as absorbance v/s Concentration. The generated regression equation was y = 0.001x + 0.001 (R^2= 0.996).The R^2 value as 0.996 indicates that developed method was linear. The calibration curve was obtained in the range of 1-3ng/spot. The proposed method was found to be precise as % R.S.D values for intraday as well interday precision were satisfactory. The drug at each of the 80%, 100% and 120% levels 87.51%, 84.17%, 81.55% showed good recoveries. Hence, it can be said that this method was accurate. The LOD and LOQ were calculated as 0.25 ng/spot and 2.75 ng/spot respectively. The result of the analysis of pharmaceutical formulation by the developed method was consistent with the label claim, highly reproducible and reliable. The method can be used for the routine analysis of the Telmisartan in formulation.

CONCLUSION

It can be concluded from the results that the proposed method was accurate, precise and consistent the determination of Telmisartan in formulation. This method was validated as per ICH guideline Q2 (R1). Results suggest that this method can be used for routine estimation of Telmisartan in bulk and pharmaceutical dosage forms.

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