Research Article

Development and Validation of Analytical Method for Estimation of Telmisartan in Bulk and Marketed Formulation by UV-Spectrophotometer.

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ABSTRACT

We done work on development and validation of analytical method for estimation of telmisartan in bulk and marketed formulation by UV-spectrophotometer. In this simple, rapid, accurate, reproducible and economical methods have been described for telmisartan by using first and second order derivative method by UV visible spectrophotometer. For first order λmax of 313 and for second order λ max of 330. The concentration range over which the drugs obeyed Beer- Lambert's law was found to be 2-12 µg/ml for Telmisartan. The developed UV spectroscopic methods were found suitable for determination of Telmisartan as bulk drug and in marketed solid dosage formulation without any interference from the excipients. It can therefore be concluded that use of these methods can save much time and money and it can be used in small laboratories with accuracy.

Keywords: Telmisartan, Method development, First and Second derivative spectroscopy.

INTRODUCTION

Telmisartan chemically is 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. It is anangiotensin II receptor antagonist, effective in the treatment of hypertension.[1] It is also effective when used alone or in combination with other drugs for the treatment of high blood pressure.[2] The pharmacokinetic properties of Telmisartan have been investigated in healthy volunteers after oral administration of the sample.[3] Telmisartan and Hydrochlorothiazide we determined in tablets simultaneously by HPTLC and HPLC method.[4-10] No validated UV spectrophotometric studies on Telmisartan individually in pharmaceutical preparations have been found in the literature.

RP-HPLC[11-13] and LC–MS/MS[14,15] and HPTLC[16,17] for determination of Telmisartan with alone and with other drugs in combination have been reported. As the analysis is an important component in the formulation development of any drug molecule. Hence there is a need to develop a simple, sensitive, accurate, precise, reproducible method for the estimation of drug samples. Our main concern is development and validation of UV spectrophotometric method as per ICH guidelines.[18]

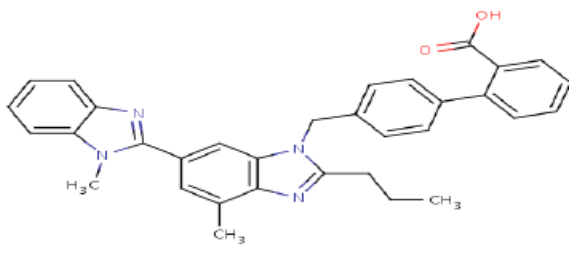

Figure 1: Chemical Structure of Telmisartan

MATERIALS AND METHODS

A JASCO double beam UV–visible spectrophotometer, model: v-630, with a fixed band width (2 nm) and a pair of 1-cm quartz cell was used for spectral and absorbance measurements. Gift sample of Telmisartan was obtained from UMEDICA R &D Centre D-25/4, TTC Industrial Area, MIDC, Navi Mumbai. All chemicals and reagents were used of analytical grade and purchased from fine chemicals, Mumbai, India. Marketed formulation Telmisar tablet containing Telmisartan 20mg was used as sample; purchased from local pharmacy Pune. Calibration glassware's were used throughout the work.

Preparation of Standard Stock Solution

Weigh accurately 10 mg of Telmisartan was transferred to 100 ml volumetric flask separately, dissolved in 40 ml Methanol by sonicater, sonicate up to 10 minute. The volume was adjusted with the same up to the mark to give final strength i.e. 100 µg/ml.

Selection of Wavelength for Analysis

Method A

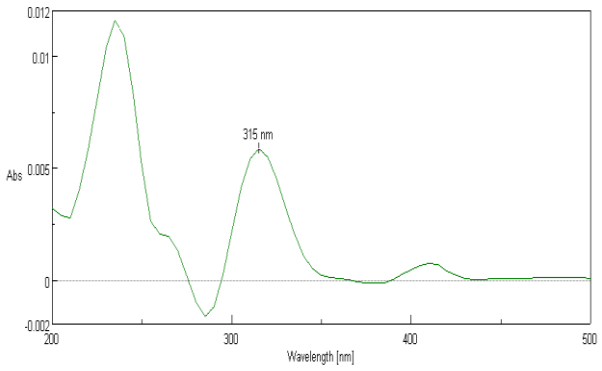

Figure 2: First Order Derivative Spectra

By appropriate dilutions with methanol were prepared for each drug from the standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm and their spectra were overlaid. For first order derivative & second order derivative spectra at N=1, selected wavelength were 315nm and 330nm, which were selected for quantitation of Telmisartan respectively. Telmisartan shows zero crossing point at 315nm for first order.

Method B

By appropriate dilutions with methanol were prepared for each drug from the standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm and their spectra were overlaid.

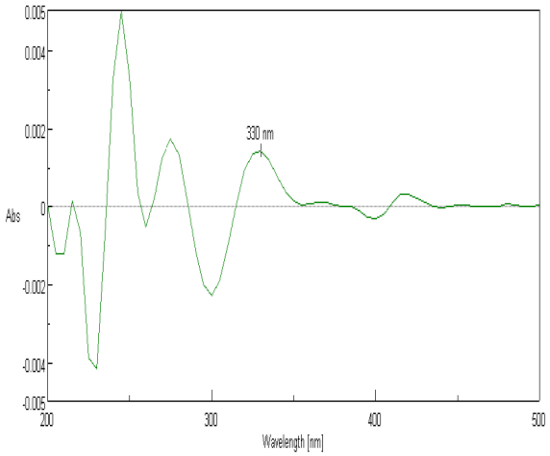

Figure 3: Second Order Derivative Spectra

Linearity

Calibration curve constructed was linear over the selected range of 2-12 µg/ml for Telmisartan at λmax of 295. For first order λmax of 313 and for second order λmax of 330. Each concentration was repeated three times. The assays were performed according to experimental conditions and the linearity of the calibration graphs were validated by the high value of the correlation coefficient and the intercept value. The concentration range over which the drugs obeyed Beer- Lambert's law was found to be 2-12 µg/ml for Telmisartan shown in Fig 4 & 5.

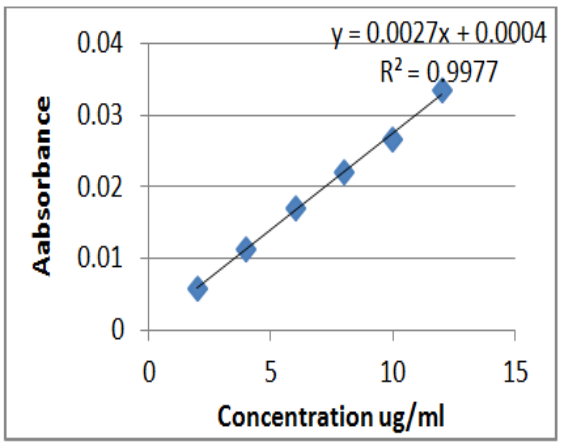

Figure 4: Calibration Curve of First Order Derivative

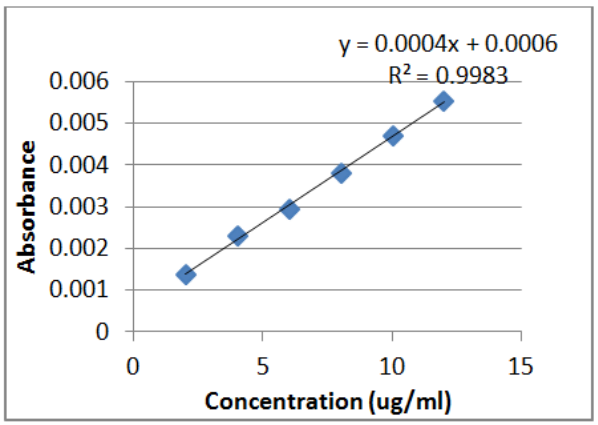

Figure 5: Calibration Curve of Second Order Derivative

Validation of the Method

Marketed tablets containing 20mg Telmisartan were used. Ten tablets were weighed and average weight was calculated. The tablets were triturated to a fine powder. An accurately weighed quantity of powder equivalent to 10mg Telmisartan were transferred to 100 ml volumetric flask and dissolved in 40 ml of methanol solution by sonicating for 10 mins and volume was then adjusted up to 60 ml with methanol. The solution was filtered through Whatmann filter paper no. 41.

Sensitivity

The sensitivity of measurements of Telmisartan by the use of the proposed method was estimated in terms of the limit of quantification (LOQ) and limit of detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 x n/b and LOQ = 10 x n/b, where, 'n' is standard deviation of the peak areas of the drugs (n = 3), taken as a measure of noise, and 'b' is the slope of the corresponding calibration curve.

Repeatability

Repeatability was determined by analyzing 10µg/ml concentration Telmisartan solution for to the preanalysed sample solutions, a known amount of standard stock solution was six times.

Accuracy

Added at different levels 80%, 100% and 120%. The solutions were reanalyzed by proposed method.

Precision

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 10µg/ml of Telmisartan solutions. For three times in the same day. Inter-day precision was determined by analyzing the 8µg/ml of Telmisartan solutions daily for three days over the period of week.

RESULTS AND DISCUSSION

Method Validation

The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as

per the earlier adopted procedure given in the experiment.

Linearity Studies

The linear regression data for the calibration curves showed good linear relationship over the concentration range 2-12 mg/ml for Telmisartan. The result is expressed in Table 1.

Sensitivity

The LOD and LOQ for Telmisartan for method A and B; shown in Table 2.

Repeatability

Repeatability was determined by analyzing 10µg/ml concentration of Telmisartan. For six times and the % amount with % R.S.D.

Accuracy

The solutions were reanalyzed by proposed method; results of recovery studies are reported in Table 3.

Precision

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These result shows reproducibility of the assay.

The % R.S.D. values found to be less than 2, so that indicate this method precise for the determination of both the drugs in formulation shown in Table 2 and Table 4.

Table 1: Optical Characteristics of Telmisartan

Parameters	Telmisartan (295nm) Zero Order	Telmisartan (315 Nm) First Order	Telmisartan (330nm) Second Order
Slope*	0.872	0.0027	0.0004
Intercept*	0.018	0.0004	0.0006
Correlation coefficient	0.995	0.997	0.998
Linearity Range µg/ml)	2-12	2-12	2-12

*Average of Six Determinations

Table 2: Summary of Validation Parameter

S. No.	Parameter	Method A (First Order Derivative)	Method B (Second Order Derivative)
1	Linearity (R^2)	0.997	0.998
2	Accuracy (% Recovery ± *SD)	99.77 ± 0.3700	99.59 ± 0.1135
3	Range (µg/ml)	2-12	2-12
4	Repeatability (% Mean ± *SD)	100 ± 0.00021	99.5 ± 0.00040
5.	Reproducibility (% Mean±)	98.13 ± 0.00021	100.3 ± 0.00012
5	*LOD	0.2566	3.31
6	*LOQ	0.7777	10.12

*Average of Six Determinations

Table 3: Determination of Accuracy by Percentage Recovery Method for Telmisartan

Method	Tablet Amount (µg/ml)	Amount Added (µg/ml)	Level Of Addition	Percentage Recovery (%)	Average (% Recovery *S.D.)
First Order	10	8	80%	99.58	99.77 ± 0.3700
	10	10	100%	100.2	
	10	12	120%	99.54	
Second Order	10	8	80%	99.64	99.59 ± 0.1135
	10	10	100%	99.46	
	10	12	120%	99.67	

*Average of Six Determinations

Table 4: Inter-day and Intra-day Precision

Method	Inter-Day			Intra-Day		
	Mean	*S.D.	*%R.S.D.	Mean	*S.D.	*%R.S.D.
First Order	98.13	0.00021	0.0079	98.91	0.00015	0.00584
Second Order	100.3	0.00012	0.0254	99.78	0.00001	0.00213

*Average of Six Determinations

CONCLUSION

The results of our study indicate that the proposed UV spectroscopic methods are simple, rapid, precise and accurate.

The developed UV spectroscopic methods were found suitable for determination of Telmisartan as bulk drug and in marketed solid dosage formulation without any interference from the excipients.

Statistical analysis proves that, these methods are repeatable and selective for the analysis of Telmisartan.

It can therefore be concluded that use of these methods can save much time and money and it can be used in small laboratories with accuracy.

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