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Research Article

Method development and validation of telmisartan in bulk and pharmaceutical dosage forms by UV spectrophotometric method

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ABSTRACT

This paper describes the analytical method suitable for validation of Telmisartan by UV Spectrophotometric method. The method utilized UV spectroscopy (Shimadzu, model 1700).The solvent system was consists of Methanol: water in the ratio of 90:10 at wave length (λ_{max}) 298 nm. Validation experiments were performed to demonstrate System suitability, Specificity, Precision, Linearity, Accuracy Interday assay, intraday assay, robustness, ruggedness, LOD, &LOQ. The method was linear over the concentration range of 5-45 mg/ml. The method was showed good recoveries (98.04- 101.04%) and the recovery studies were carried out by adding different amounts (80%, 100% & 120%) of bulk samples of Telmisartan. The Proposed method was simple, sensitive &reliable with good Precise, Accurate, and Reproducible and rapid for the determination of Telmisartan. While estimating the commercial formulation without interference of excipients & other additives hence this method can be used for routine determination of Telmisartan in bulk and their pharmaceutical dosage forms.

Keywords: Analytical Method; Telmisartan; UV Spectroscopy; Validation.

INTRODUCTION

2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2- propylbenzimidazol -1-yl] methyl] phenyl] benzoic acid**,** is a novel, potent, highly selective non peptide Angiotensin II type 1 (AT1) receptor blocker which is administered orally as Telmisartan , which is rapidly and completely hydrolyzed to Telmisartan, the active moiety, during absorption from the gastrointestinal tract (PS Blake.,2002) (Moffat C *et al*.,2004) (H Singh *et al*.,2001)**.** Telmisartan has much greater affinity (> 10,000 folds) for the AT1 receptor than for the AT2 receptor blockade of the renin-angiotensin system with ACE inhibitors; it does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation (A Rall *et al.,* 1990) (A Davidson *et al*., 2007). UV spectrophotometry method was developed and validated as per ICH guidelines. Spectrophotometry is generally preferred especially by small-scale industries as the cost of the equipment is less and the maintenance problems are minimal. The method of analysis is based on measuring the absorption of a monochromatic light by colorless compounds in the near ultraviolet path of spectrum (200-380nm). (JK Singh., 2009) (Crouch., 2007) (D hong., 2008).The API is subjected to a number of force of degradation conditions to include acidic, basic, and oxidative conditions. Force of degradation should be one of the activities performed early in the development process to ensure that the method is discriminating before a lot of time, effort and money have been expended. Depending on the API, not every stress agent may effect degradation, but each agent has to be evaluated to determine whether degradation results (Matthews *et al*., 2008).

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MATERIALS AND METHODS

Reagents and chemicals

Extra pure methanol procured from Merck (Mumbai) and distilled water prepared from the department of PA &QA (RCPHS, Berhampur).

Apparatus

Digital balance, Ultra sonicator, a double-beam UV-Visible spectrophotometer, 1700 pharmaspec with spectral band width of 2nm, wavelength accuracy ± 0.5nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solutions.

Preparation of Stock Solutions

Standard stock solution of Telmisartan was prepared by dissolving 10 mg of each drug in 100ml of Methanol: Water (9:1). Shake it properly to dissolve the drug and then adjusted the volume with methanol: water (9:1) to get 100 µg/ml.

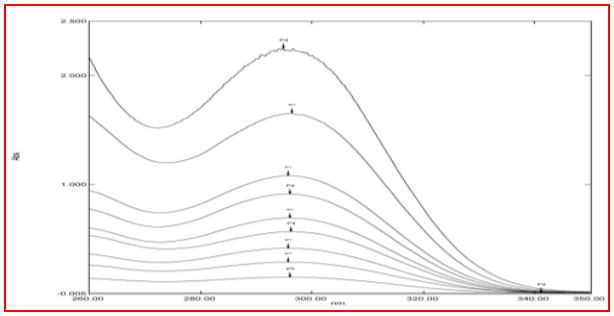

Figure 1: A typical UV Chromatogram Showing Telmisartan at 298 nm

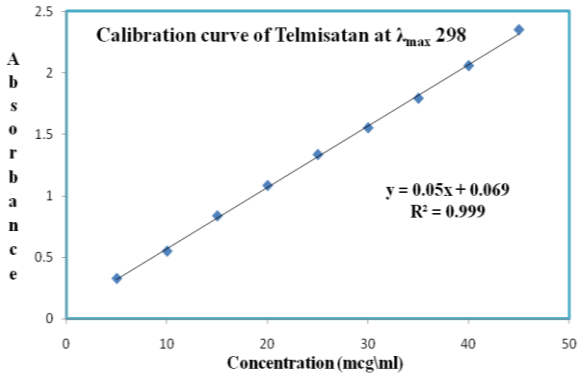

Figure 2: Linearity graph of Telmisartan

Table 1: Linearity table of Telmisartan in methanol: water (90:10)

Sl.no	Concentration (µg/ml)	Absorbance*
1	5	0.326
2	10	0.548
3	15	0.835
4	20	1.082
5	25	1.334
6	30	1.551
7	35	1.791
8	40	2.056
9	45	2.349

*Results are the absorbances of nine different drug concentration

Table 2: Optical characteristics of Telmisartan

Sl.No	Optical Characters*	Values
1	Absorbance Maxima	298nm
2	Beer's Limit	5-45 µg/ml
3	% R.S.D	0.228647
4	Regression equation (Y*)	0.05X+0.069
5	Slope (a)	0.05
6	Intercept (b)	0.069
7	Correlation Coefficient	0.999

*Results are the different optical characteristics of the drug

Preparation of working Standard Solutions

The Prepared stock solution was further diluted with methanol: water (9:1) to get working standard solution of 5ppm, 10ppm, 45ppm to construct Beer's law plot for, Telmisartan. The absorbance of each solution was measured at 298 nm against methanol: water (9:1) as blank. The standard graph for Telmisartan was plotted by taking concentration of drug on X-axis and absorbance on Y-axis

Scanning and determination of maximum wavelength (λ_{max})

In order to ascertain the wavelength of maximum absorbance (λ_{max}) of the pharmacodynamic agents solutions of particular concentrations of drugs 100 mg/ml and 10 mg/ml in methanol: water (9:1) were scanned

Table 3: Precision Results Showing Repetability of Telmisartan

Concentrations (µg/ml)	Absorbance	Calculated Amount	Statistical Analysis
20	1.082	20.26	*Mean=20.28 **St.Dev=0.08 ***%RSD=0.394477
20	1.078	20.18	
20	1.089	20.4	
20	1.08	20.22	
20	1.086	20.34	
20	1.083	20.28	

*Result is the mean calculated amount of drug after repeatability study; **Result is the standard deviation of the drug after repeatability study; *** Result is the % relative standard deviation of the drug after repeatability study

Table 4: Intraday assay of Telmisartan

Conc.(µg/ml)	Absorbance 1*	Absorbance 2**	Absorbance 3***	Statistical Analysis
20	1.084	1.083	1.082	Mean=20.32778 St.Dev=0.013878 %RSD=0.06827
20	1.089	1.083	1.085	
20	1.083	1.089	1.089	
20	1.088	1.088	1.086	
20	1.081	1.082	1.086	
20	1.092	1.084	1.083	
Mean	1.086167	1.084833	1.085167	
Calc.Amt.	20.34333	20.31667	20.32333	

*Results are the absorbance of the drug at fixed concentration in first preparation in same day; ** Results are the absorbance of the drug at fixed concentration in second preparation in same day; *** Results are the absorbance of the drug at fixed concentration in third preparation in same day

Table 5: Inter day assay of Telmisartan

Sl.No.	Concentration	Day 1*	Day 2*	Day 3*	Statistical Analysis
1	20	1.084	1.079	1.082	Mean =20.26111 Std Dev =0.038634 %Rsd =0.190681
2	20	1.087	1.078	1.085	
3	20	1.083	1.08	1.087	
4	20	1.085	1.08	1.08	
5	20	1.081	1.077	1.081	
6	20	1.08	1.085	1.083	
	Mean	1.083333	1.079833	1.083	
	Calc. Amt.	20.28667	20.21667	20.28	

*Results are the absorbance of drug at fixed concentration in day 1; ** Results are the absorbance of drug at fixed concentration in day 2; *** Results are the absorbance of drug at fixed concentration in day 3

within the wavelength range of 200-400nm against a corresponding reagent blank. The resulting spectra were presented in fig 1.The absorption curves showed characteristic absorption maxima at 298 nm for Telmisartan.

RESULTS AND DISCUSSION

Preparation Calibration Curve

The calibration curve was plotted by taking concentration of drug on x-axis and absorbance on y-axis and was shown in Fig:2 the drug has obeyed Beer's law in the concentration range of 5-45 µg/ml, and it was found to be linear with R^2= 0.999.

Linearity

The linear fit of the system was illustrated graphically. Least square regression analysis was carried out for the slope, intercept and correlation coefficient. The linearity range was found to be in between 5-45 µg/ml. The linearity range and linearity graphs were shown in Table 1 & the optical characteristics on table 2

Precision

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed concentration of the drug within the beer's range and finding out the absorbance's by the proposed method. From this absorbance's mean, Standard deviation, %R.S.D was calculated and presented in the table 3.

The precision of the assay was also determined in terms of intra-and inter-day variation in the absorbance for a set of drug solutions on three different days. The intra-and inter-day variation in the absorbance of the standard drug solution was calculated in terms of % RSD and the results are presented in table 3.i, 3.ii.

Table 6: Accuracy readings of Telmisartan

No. of preparations					Statistical Analysis	
	Formulation	Pure Drug	% Recovery*	Mean	SD	%RSD
S1 : 80 %	20	16	100.03			
S2 : 80 %	20	16	99.1	99.39	0.555068	0.558474
S3 : 80 %	20	16	99.04			
S4 : 100 %	20	20	101.04			
S5 : 100 %	20	20	100.04	100.4667	0.515881	0.513485
S6 : 100 %	20	20	100.32			
S7 : 120 %	20	24	98.04			
S8 : 120 %	20	24	99.69	99.26333	1.075469	1.08345
S9 : 120 %	20	24	100.06			

*****Results are the percentage recovery after assay of the formulation

Table 7: Results showing ruggedness of Telmisartan

Analyst-1*				Analyst-2**			
Conc. (µg/ml)	Abs.	Calc. Amt.	Statistical Analysis	Conc. (µg/ml)	Abs.	Calc. Amt.	Statistical Analysis
20	1.082	20.26	Mean= 20.22333 S.D=0.06377 %RSD=0.315331	20	1.081	20.24	Mean=20.2733 S.D =0.074476 %RSD=0.36735
20	1.085	20.32		20	1.079	20.2	
20	1.081	20.24		20	1.089	20.4	
20	1.078	20.18		20	1.085	20.32	
20	1.076	20.14		20	1.082	20.26	
20	1.079	20.2		20	1.08	20.22	

*Results are the calculated amount of the drug at fixed concentration by analyst 1

** Results are the calculated amount of the drug at fixed concentration by analyst 2

Table 8: Results showing robustness of Telmisartan at different solvent composition

(92:08)*				(88:12)**			
Conc. (µg/ml)	Abs.	Calc. Amt.	Statistical Analysis	Conc. (µg/ml)	Abs.	Calc. Amt.	Statistical Analysis
20	1.085	20.32	Mean=20.25 S.D=0.04858 %RSD=0.2399	20	1.084	20.3	Mean=20.2666 S.D=0.05164 %RSD=0.25480
20	1.082	20.26		20	1.08	20.22	
20	1.08	20.22		20	1.079	20.2	
20	1.078	20.18		20	1.083	20.28	
20	1.081	20.24		20	1.082	20.26	
20	1.083	20.28		20	1.086	20.34	

*Results are the calculated amount of drug after changing solvent system composition to 92ml of methanol & 8ml of distilled water

**Results are the calculated amount of drug after changing solvent system composition to 88ml of methanol & 12ml of distilled water

Sl.No	Parameters	S.D*	b**	Formula***	Calculation
1	LOD	0.002515	0.05	3.3(S.D/b)	0.16599
2	LOQ	0.002515	0.05	10(S.D/b)	0.5030

*Results are the standard deviation of the drug obtain from the linearity table

** Results are the slope drug obtains from the calibration curve.

***Formula for calculation of limit of detection and limit of quantification

Accuracy

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of bulk samples of Telmisartan along with internal standard (I.S) within the linearity range were taken and added to the pre-analyzed formulation of concentration 20 µg/ml. From that percentage recovery values were calculated. The results were shown in table 4.

Analysis of formulations

For analysis of commercial formulations, 2 tablets were weighed and powdered and powder equivalent to 10mg of Telmisartan were transferred into 100ml volumetric flasks and dissolved in methanol: water (9:1) to get 100 µg/ml solutions. Then the solution was sonicated for 15 min and filtered and further dilutions were made with methanol: water (9:1) to get the concentrations within the linearity range of respective drugs and measured the absorbance at 298 nm for solution against methanol: water (9:1). Here 3ml was taken and made up to 10ml. The drug content in each tablet was estimated by using the standard graph.

Ruggedness (Intermediate Precision)

To determine the ruggedness the same procedure was carried by another analyst and the results was compared with the same previous procedure and the results were shown in Table 5.

Robustness

This procedure was carried out by changing the solvent system composition in different ratio (8: 2, 7: 3). Then results were compared. And the results were shown in Table 6.

Limit of detection and Limit of Quantification

Limit of detection (LOD) and Limit of quantification (LOQ) of Telmisartan was calculated by using equation given in the ICH guidelines. The result of the same is shown in the table 7.

CONCLUSION

The proposed method is simple, sensitive and reliable with good precision and accuracy and also method is specific while estimating the commercial formulation without interference of excipients and the other additives. Hence, this method can be used for routine determination of Telmisartan in bulk sample and pharmaceutical formulation. The proposed UV-Spectrophotometric method is evaluated over the linearity, accuracy, precision, specificity, LOD and LOQ and proved to be convenient and effective for the quality control of Telmisartan.

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