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Validated Method Development and Validation for Estimation of Telmisartan as API and in Pharmaceutical Dosage Form by UV-Spectroscopy.

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ABSTRACT

Telmisartan is an angiotensin II receptor blocker (ARB) that has high affinity for the angiotensin II receptor type 1 (AT1). A simple, sensitive method was developed for the estimation and validation of Telmisartan in API and in pharmaceutical dosage form by UV Spectroscopy. The linearity of Telmisartan was found in the range of 2-16µg/ml and it obeys Beer Lamberts Law. The maximum absorbance of Telmisartan was obtained at 295 nm. The polynomial regression data for the calibration plots showed good linear relationship with r2 = 0.9986. The method was validated for precision, accuracy, and recovery. The assay method was done to estimate Telmisartan in pharmaceutical dosage form and mean%Assay±SD was found to be 98.98 ±0.00043. The developed method was validated as per ICH guidelines and was under acceptable range.

Keywords: Telmisartan, UV Spectroscopy, validation, Polynomial regression, ICH Guidelines.

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INTRODUCTION

Telmisartan is an angiotensin II receptor antagonist (angiotensin receptor blocker, ARB) used in the management of hypertension. It 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 shown in figure 1. Telmisartan is official in USP.

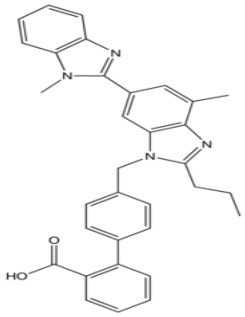

Figure 1: Structure of Telmisartan

Telmisartan is an angiotensin II receptor blocker that shows high affinity for the angiotensin II receptor type 1 (AT_1), with a binding affinity 3000 times greater for AT_1 than AT_2. It has the longest half-life of any ARB (24 hours) and the largest volume of distribution among ARBs (500 liters). The estimation and validated method of Telmisartan done in UV [1] spectrophotometer, HPLC [2-5], TLC [6], UPLC [7,8], LCMS [8] are reported.

EXPERIMENTAL

Chemicals and Reagents

Telmisartan was the gift sample from Alchem International Ltd. The pharmaceutical dosage form containing 40 mg Telmisartan were purchased from local market. Analytical grade of Ethanol procured from local market.

Instrumentation

UV Spectrophotometer (My 13510001) was used to carry out the experiment. To enhance the solubility of the solution of drug sonicator was used. The powder was weighed by using Digital Weighing Balance GR (200).

Preparation of standard solutions

Weigh accurately 25 mg of the drug with the help of digital balance and transferred to 50 ml of volumetric flask. It was dissolved in about 30ml of ethanol and mixed properly and then the volume was made up to the mark. Then 2ml of this solution was pipette out and

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transferred to 10 ml of volumetric flask and diluted up to 10 ml with ethanol. This solution contained 100 µg of drug per ml.

Determination of wavelength of maximum absorbance (λ_{max})

1ml of the standard stock solution was pipette out and transferred to 10 ml of the volumetric flask and diluted up to 10 ml with ethanol. This solution contained 10 µg/ml of the drug. The absorbance of this solution was scanned in the UV range of 200 to 400 nm against water as blank. The maximum absorbance of Telmisartan was obtained at 295 nm as shown in Figure 2.

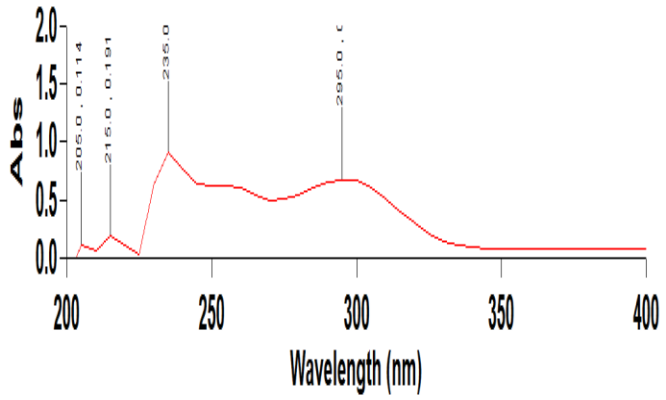

Figure 2: Scan of Telmisartan

Method development

Preparation of calibration curve

1ml, 2ml, 3ml, 4ml, 5ml, 6ml, 7ml and 8ml of the solution from standard stock solution were pipette out into a series of 10 ml volumetric flask. The volumes were made up to the mark with ethanol and mixed to obtain solutions in the concentration range of 2, 4, 6, 8, 10, 12, 14 and 16 µg/ml of the drug.

Table Preparation of calibration curve at 295 nm

Concentration(µg/ml)	Absorbance*
2	0.226
4	0.3239
6	0.4416
8	0.5586
10	0.6862
12	0.826
14	0.9208
16	1.0496

Average of three reading

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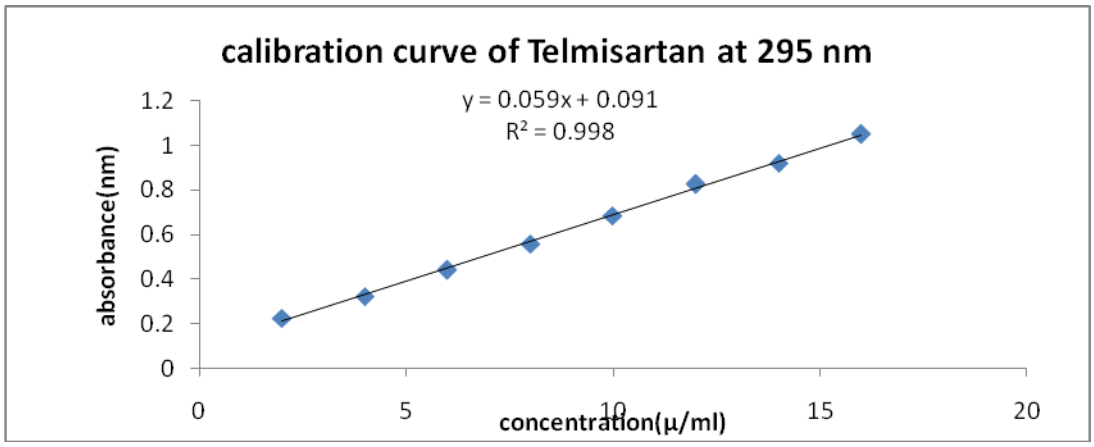

Figure 2: Calibration curve of Telmisartan at 295 nm

The absorbance of these resultant solutions were measured at 295 nm against ethanol as blank and the graph was plotted between absorbance obtained and the concentrations of the solutions. The Beer's Lambert law was obeyed in concentration range of 2-16 µg/ml at 295 nm Result were shown in table 1 and figure 2.

Validation of the Methods

The methods were validated as per ICH guidance .

Specificity

About 2.5 ml of the stock solution was taken in six 20 ml volumetric flasks and volume was made up to the mark with the help of ethanol. The absorbance of these solutions were measured and recorded. For specificity determination 2.5 ml of the stock solution was taken in 6 volumetric flasks and about 2ml of 2 µg/ml solution of each excepient was added to them and the volume was made up to the mark with water. The absorbance's was measured and recorded. The concentration of the solution was determined and % interference was calculated. The results are shown in the table 2.

It can be concluded from the results that developed method is specific and there is no interferences of excepient, since the % interferences was negligible (0.18).

Linearity and Range

A linear relationship was obtained between absorbance and concentration in the range of 7 to 13 µg/ml of the drug in the solution as shown in the Figure 2. A correlation coefficient (r) of 0.9986 was observed as shown in the Table 2.

Accuracy

The accuracy of the developed method was determined by a recovery study carried on Tablet.-6 µg/ml sample solution of extracted Telmisartan was added with solutions of 6, 8 and 10 µg/ml of Telmisartan standard solution. The absorbance's were measured and the % recovery was calculated. The percentage recovery results are shown in table 2.

(Acceptance criteria: The percentage recovery should be in the range 98-102%). The % recovery was found to be 101.52±0.0022 which is acceptable.

Precision

Repeatability

20µg/ml solutions of the drug were made by taking 10ml of the drug solution from the standard stock solution in 50 ml volumetric flask and volume was made up to the mark. Then 1.5 ml of this solution was pipette out in 10 ml volumetric flask to prepare 3µg/ml. The absorbance of this solution was measured six times and recorded. The results are shown in the table 2.The calculated RSD for repeatability study was 0.60417 which is acceptable; this shows good repeatability of method.

Intra-day precision

20µg/ml solutions of the drug were made by taking 10ml of the drug solution from the standard stock solution in 50 ml volumetric flask and volume was made up to the mark. 3ml, 4ml and 5ml of the drug solution was pipette out from this solution and transferred to 10 ml volumetric flask and the volume was made up with ethanol to obtain the concentrations of 6, 8 and 10 µg/ml respectively. The absorbance of these solutions were measured individually thrice within a day and recorded. The results are shown in the Table 2. The calculated mean RSD is 0.28. The readings were taken thrice for each concentration at 0 hr, 3 hr and 6 hr within a day.

Inter-day Precision

20µg/ml solutions of the drug were made by taking 10ml of the drug solution from the standard stock solution in 50 ml volumetric flask and volume was made up to the mark. 3ml, 4ml and 5ml of the drug solution was pipette out from this solution and transferred to 10 ml volumetric flask and the volume was made up with ethanol to obtain the concentrations of 6, 8 and 10 µg/ml respectively. The absorbance of these solutions were measured individually thrice in three days and recorded. The results are shown in the Table 2. These readings were taken thrice at an interval of 0 hr, 24 hr and 48 hr. the calculated RSD was 0.26.

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Table 2: Validation Parameters of Telmisartan.

Parameters	Observation
Linearity (µg/ml)	2-16
Range	7-13
Molar absorptivity ($1\ mole^{-1}\ cm^{-1}$)	$2.48x10^6$
Sandell's sensitivity ($\mu g/cm^2$/0.001 absorbance unit)	$4.8x10^3$
Regression equation (y=a+bc) Slope(b) Intercept(a)	 0.0597 0.0917
Correlation coefficient (r)	0.9986
Accuracy (% recovery)	101.52±0.0022
Specificity (% interference)	0.18
Repeatability (RSD)	0.60417
Precision (RSD) Inter-day precision Intra-day precision	 0.26 0.28

Estimation of Telmisartan in tablet and capsule dosage forms

The Twenty tablets of the same batch number were powdered and mixed. About 126.25 mg powder (equivalent to 25 mg of Telmisartan) was weighed accurately and dissolved in about 50 ml ethanol and shaking was done in sonicator (to enhance solubility) for 10 mins. Filtered through Whatman Filter paper 40 into 50 ml volumetric flask. Then 2ml of this solution was pipette out and transferred to 10 ml of volumetric flask and diluted up to 10 ml with ethanol. This solution contained 100 µg of drug per ml. 1ml of the standard stock solution was pipette out and transferred to 10 ml of the volumetric flask and diluted up to 10 ml with ethanol. This solution contained 10 µg/ml of the drug. The absorbance of this solution was measured in carry win and recorded. The concentration was then determined from the calibration curve. The results are shown in Table 3.

Table 3: Results for estimation of Telmisartan (Temas)

Brand	Label claim(mg/tab)	Theoretical conc.(µg/ml)	Amount found(mg/tab)	% Assay	Mean % Assay ±SD
Temas	10	10	9.78 9.99 9.88 9.98 9.86	97.8 99.9 98.8 99.8 98.6	98.98 ±0.00043

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RESULTS AND DISCUSSION

The validated spectrophotometeric method have been developed for the estimation of Telmisartan in bulk drugs and in pharmaceutical dosage form. This simple Spectrophotometric method for Quantitative recoveries that were obtained from bulk and from pharmaceutical dosage form.

The maximum absorbance of Telmisartan was obtained at 295nm. The linear response obtained was in the concentration range of 2-16 μg/ml with correlation coefficient 0.9986, recovery of the drug was found to be 101.52% and relative standard deviation was found to be less than 2 % for precision studies.

The linearity accuracy, precision and recovery study was done to validate the above method. The accuracy of methods was greater than 98% and RSD not more than 2%. This method was found simple, precise and cost effective, reproducible and reliable for estimation of Telmisartan in bulk, and pharmaceutical dosage form. The methods were stastically validated according to International Conference of Harmonization (ICH).

CONCLUSION

The linearity, accuracy, precision and recovery study was done to validate the above method. The accuracy of methods was greater than 98% and RSD not more than 2%. This method was found simple, precise and cost effective, reproducible and reliable for estimation of Telmisartan in bulk, and pharmaceutical dosage form. The methods were statically validated according to International Conference of Harmonization (ICH)

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