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Research Article

UV SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION FOR TELMISARTAN IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

Objective: To develop UV spectrophotometric method for determination of Telmisartan in bulk and tablet dosage form in 0.1 N NaOH by two methods.

Methods: Method A involve Absorption maxima method based on the measurement of absorbance at 295 nm that is the λmax of Telmisartan, while Method B involved Area under the curve based on the measurement of AUC in the range of 275-310 nm. Results: Both methods obey Beer- Lamberts law in concentration range of 2-12 µg/ml. Methods were validated as per ICH guidelines in terms of accuracy, linearity and precision. Conclusion: The proposed methods found to be simple, accurate, precise, reproducible, economic and suitable for routine quality control analysis.

Keywords: Telmisartan (TEM), Absorption Maxima Method, Area under the Curve (AUC) Method.

INTRODUCTION

Telmisartan, is a non-peptide molecule, chemically described as 4'-[(1, 4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1, 1'-biphenyl]-2-carboxylic acid. Its empirical formula is $C_{33}H_{30}N_4O_2$. Its molecular weight is 514.63. It is indicated in the treatment of essential hypertension. The usually effective dose of Telmisartan is 20, 40 and 80 mg once daily. Some patients may benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, Telmisartan dose can be increased to a maximum of 80 mg once daily. Telmisartan is a white to slightly yellowish solid. It is practically insoluble in water and in the pH range of 3 to 9, sparingly soluble in strong acid (except insoluble in hydrochloric acid), and soluble in strong base. Literature survey revealed that there were many methods like Spectrophotometry [1, 6] using first order derivative [5]

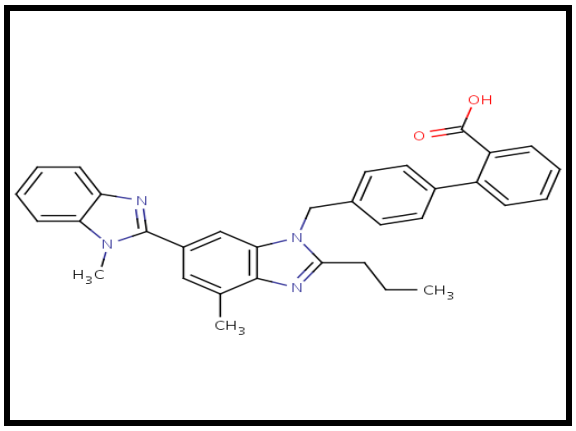

Figure No. 1: It shows chemical structure of Telmisartan

Simultaneous equation, RP-HPLC [7-10] and LC–MS/MS [11, 12] and HPTLC [13, 14] 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 [15]

MATERIALS AND METHODS

Reagents

Telmisartan was obtained as free gift sample from Ranbaxy Laboratories Limited, Gurgaon, India. The pharmaceutical preparation i.e. Telmisartan tablet is procured from local market. Remaining all the reagents and solvents of spectroscopy grade were purchased from Thomas baker, India while double distilled water was used for whole experiment.

Instrumentation

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

Preliminary solubility studies of drugs

25mg of Telmisartan was weighed and solubility was checked in water, methanol, ethanol, 0.1N NaOH. The drug was found to be soluble in 0.1N NaOH.

Preparation of standard stock solution

25 mg of the pure drug was accurately weighed and dissolved in 10 ml 0.1 N NaOH and sonicated for 15 minutes and then volume was made up to 25 ml with 0.1 N NaOH to give standard stock solution 1000 µg/ml. From this, 2.5 ml solution withdrawn and diluted upto 25 ml with 0.1 N NaOH to get 100 µg/ml which used as working stock solution and then further dilutions were made from this stock solution to get concentration in the range of 2-12 µg/ml.

Sample preparation

20 tablets were procured from local market and average weight was determined. The powder equivalent to 50 mg of Telmisartan was weighed accurately and taken in separate 50 ml volumetric flask, it was dissolved in 25 ml 0.1N NaOH by sonication, filtered through Whatmann filter paper no. 41 and volume was made up to 50 ml with 0.1 N NaOH to give 1000 µg/ml stock solution. From this solution, 2.5 ml was withdrawn and diluted to 25 ml with 0.1 N NaOH to get 100 µg/ml solutions and used as working stock solution. From this further dilution was made.

Calibration curve for Telmisartan

From the standard stock solution appropriate dilutions were made to obtain concentration in range of 2, 4, 6, 8, 10 & 12 µg/ml. The

spectra were recorded, absorbances were measured at 295 nm and calibration curve was plotted.

METHOD A: ABSORPTION MAXIMA METHOD

For the selection of analytical wavelength, standard solution of Telmisartan was scanned in the spectrum mode from 200 nm to 400 nm separately. From the spectra of drug, 295 nm was selected as λmax of TEM for the analysis (Figure No.1). Aliquots of standard stock solution were made and calibration curve was plotted.

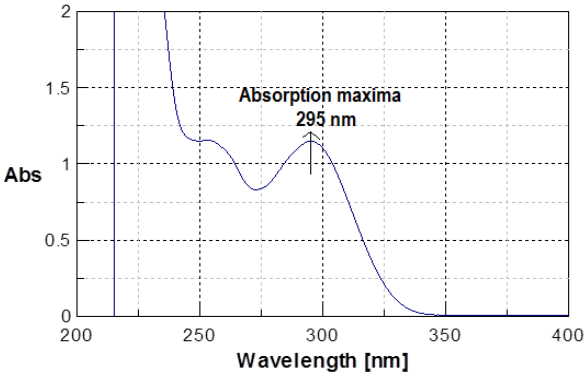

Figure No. 2: It shows Absorption maxima of Telmisartan

METHOD B: AREA UNDER CURVE

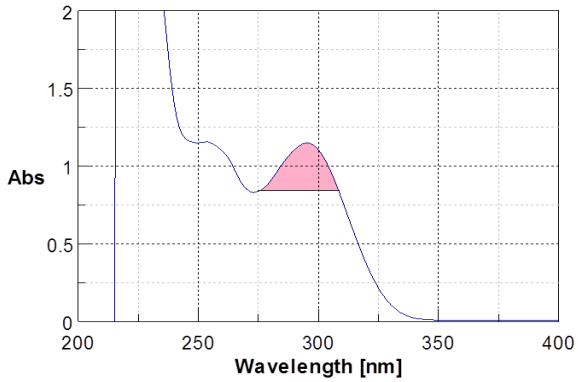

Figure No. 3: It shows Area under the Curve Method

For the determination of Telmisartan using the area under curve (AUC) method, suitable dilutions of the working stock solutions (100 µg/mL) of Telmisartan were prepared in 0.1 N NaOH and scanned in the range of 200 - 400 nm. For Area under curve method, the sampling wavelength ranges from 275-310 nm (Figure No. 2) selected for estimation of Telmisartan and area were integrated between these selected wavelength range, which showed linear response with increasing concentration hence the same wavelength range were used for estimation of tablet formulations.

METHOD VALIDATION

Various method of analysis of TEM in bulk and pharmaceutical formulations (marketed and developed) was carried out as ICH

Table No. 1: It shows Optical Characteristics of Two Methods

Parameters	Method A	Method B
λmax (nm)	295 nm	Area range 275 nm- 310 nm
Beer's range (µg/ml)	2-12 µg/ml	2-12 µg/ml
Correlation coefficient (r^2)	0.999	0.999
Regression equation	Y = 0.12009x + (-0.02858)	Y = 1.423319x + (-0.137431)
Intercept (a)	-0.028587	-0.137431
Slope (b)	0.120096	1.423319

Guidelines Q_2 (R_1)

Linearity and Range

Calibration curve constructed was linear over the selected range of 2-12 µg/ml for Telmisartan at λmax of 295. 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.

Accuracy

Accuracy of the developed method was confirmed by doing recovery study of TEM as per ICH guidelines at three different concentration levels- 80%, 100%, 120% by replicate analysis (n=3). This study was performed by addition of known amounts of pure TEM to a known concentration of the commercial tablets. The amount of standard recovered was calculated in the terms of mean recovery with the percent Relative Standard Deviation (% RSD)

Table No. 2: It shows results of recovery studies

Level of % Recovery	Amount of drug taken from tablet (µg/ml)	Amount of standard drug Added (µg/ml)	% Recovery*	Standard Deviation	% R.S.D.
80	4	3.2	102.48	0.528488	0.52
100	4	4.0	99.72	0.081445	0.08
120	4	4.8	92.44	0.060583	0.07

*** Estimation of three determinations**

Table No. 3: It shows results of LOD and LOQ

Active Ingredient	LOD (µg/ml)	LOQ (µg/ml)
Telmisartan	1.491	4.518

Precision

Precision was determined by studying the repeatability which indicates the precision under the same operating conditions over a short interval time. The experiments were repeated for six times for precision. The developed method was found to be precise for repetability on the basis of % RSD values for TEM.

Table No. 4: It shows results of Precision studies

Sr. No	Label Claim (µg/ml)	Amount found (µg/ml)	% Found of Label Claim
1	4	3.978	99.496
2	4	3.979	99.495
3	4	3.979	99.494
4	4	3.978	99.496
5	4	3.979	99.492
6	4	3.979	99.494
Mean			99.495
Std. Deviation (S.D.)			0.00164
% Relative Std. deviation			0.001648
Standard Error (S.E.)			0.00067

Table No. 5: It shows results of Tablet Assay

Active Ingredients	Label Claim (mg/tab)	Amt. of Drug Estimated (mg/tab)*	% Assay
Telmisartan	100	99.15	99.15

*** Estimation of Six determination**

RESULTS AND DISCUSSION

The present paper describes estimation of TEM in bulk and tablet dosage form by Absorbance maxima method and Area under curve method. Solubility studies indicated that a Telmisartan shows better solubility in 0.1 N NaOH solution as compared to solubility in distilled water. The Beer- Lambert's concentration range was found to be 2-12 µg/ml for Telmisartan at 295 nm and coefficient of correlation were found 0.999. (Table No. 1) for both methods. Precision was determined by studying the repeatability. The values LOD and LOQ were 1.491 µg/ml and 4.518 µg/ml respectively (Table No. 3).The standard deviation and Relative Standard deviation (% RSD) were calculated for Telmisartan. For both the methods % COV were not more than 1.0% which indicates good intermediate precision (Table no. 4). Percentage estimation of TEM in tablet dosage form was 99.15 by the proposed methods. (Table No. 5)

CONCLUSIONS

Telmisartan showed better solubility in 0.1N NaOH as compared to distilled water alone. Both drugs showed good regression values at their respective wavelengths and the results of recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method and low values of LOD and LOQ indicated good sensitivity of proposed methods. Hence proposed methods are new, simple, accurate, sensitive, economic and precise and can be adopted for routine analysis and in tablet dosage form.

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