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Method development and validation for telmisartan in bulk and tablet dosage form by uv-spectrophotometric method

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ABSTRACT

The main objective was to develop and validate the UV- spectrophotometric method for the estimation of telmisartan in bulk and pharmaceutical formulations as per ICH guidelines. A simple, rapid, accurate, and economical UV-spectrophotometric method has been developed for the estimation of telmisartan from bulk and pharmaceutical formulation. The λmax of telmisartan in methanol was found to be 298 nm. The drug follows linearity in the concentration range 2–10 µg/ml with a correlation coefficient value of 0.9956. The proposed method was applied to pharmaceutical formulation and % amount of drug estimated was 99.19% and was found to be in good agreement with the label claim. The accuracy of the method was checked by recovery experiment performed at three different levels, i.e., 50%, 100%, and 150%. The % recovery was found to be in the range of 98.54 – 99.98%. The low values of % RSD are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intraday; interday variations. The % RSD value < 2 indicates that the method is precise.

Keywords: Telmisartan, Methanol, UV- Spectrometer, ICH Validations

INTRODUCTION

Ultra Violet Spectroscopy

Ultraviolet spectroscopy is concerned with the study of absorption of UV radiation which ranges from 200 nm to 400 nm. Compounds which are coloured, absorb radiation from 400-800nm. But compounds which are colorless absorb radiation in the UV region. In both UV as well as visible spectroscopy, only the valence electrons absorb the energy, thereby the molecule undergoes transition from ground state to excited state. This absorption is characteristic and depends on the nature of electrons present. The intensity of absorption depends on the nature of electrons present. The intensity of absorption depends on the concentration and pathlength as given in Beer-Lambert's law.

The types of electrons present in any molecule may be conveniently classified as:

1. **σ electrons:** These are the ones present in the saturated compounds. Such electrons do not absorb near UV, but absorb vacuum UV radiation [<200nm].
2. **π electrons:** These electrons are present in unsaturated compounds [eg] double or triple bonds [eg] >C=C<, -C=C-
3. n electrons: These are non bonded electrons which are not involved in any bonding [eg] lone pair of electrons like in S, O, N and halogens [X].

The analytical procedure refers to the way of performing the analysis. It should describe in detail the steps necessary to perform each analytical test. This may include but is not limited to: the sample, the reference standard and the reagents preparations, use of the apparatus, generation of the calibration curve, use of the formulae for the calculation, etc.

Specificity

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc.

Lack of specificity of an individual analytical procedure may be compensated by other supporting analytical procedure(s).

This definition has the following implications:

Identification: To ensure the identity of an analyte.

Purity Tests: To ensure that all the analytical procedures performed allow an accurate statement of the content of impurities of an analyte, i.e. related substances test, heavy metals, residual solvents content, etc.

Assay (content or potency): To provide an exact result which allows an accurate statement on the content or potency of the analyte in a sample.

Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness.

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility. Precision should be investigated using homogeneous, authentic samples. However, if it is not possible to obtain a homogeneous sample it may be investigated using artificially prepared samples or a sample solution. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements.

Repeatability

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision.

Intermediate precision

Intermediate precision expresses within-laboratories variations:

different days, different analysts, different equipment, etc.

Reproducibility

Reproducibility expresses the precision between laboratories (collaborative studies, usually applied to standardization of methodology).

Detection limit

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantified as an exact value.

Quantitation limit

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample. Which can be quantitatively determined with suitable precision and accuracy. The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices, and is used particularly for the determination of impurities and/or degradation products.

Linearity

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample.

Range

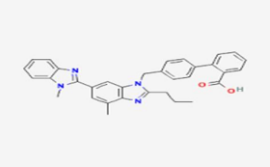
The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.

Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage[3].

Telmisartan, sold under the brand name Micardis among others, is a medication used to treat high blood pressure, heart failure, and diabetic kidney disease. It is a reasonable initial treatment for high blood pressure. It is taken by mouth.

Structure of Telmisartan



IUPAC NAME:
2-[4-[[4-methyl-6-(1-methyl benzimidazol-2-yl) - 2-propyl benzimidazole-1-yl]methyl]phenyl] benzoic acid
MOLECULAR WEIGHT: 514.62
MOLECULAR FORMULA: C33H30N4O2
DRUG CATEGORY: Anti-Hypertensive.
DRUG CLASS: Angiotensin II Receptor Antagonist

MATERIALS AND METHODS

Materials

Instruments and glassware

	Instruments And	
1.		LAB INDIA analytical UV3000^{+}
2.	Weighing machine	Contech
3.	Digital ultra sonicator	Nano Enterprise
4.	Beaker	Borosilicate
5.	Measuring cylinder	Borosilicate
6.	Volumetric flask	Borosilicate

Chemicals used

S.No.	Chemicals	Company Name
1.	Telmisartan	Evertogen Life Sciences
2.	Telmisartan Tablet 40mg	Mankind pharma
3.	Methanol	Research lab

METHODOLOGY

Solvent selection

In start of method development for this drug, different solvents were used such as water, methanol, dicholoroethanol and 0.1 NaoH. In order to select suitable solvent for determination of Telmisartan, various solvents were selected for solubility studies and it was than Telmisartan was freely soluble in methanol and 0.1 NaoH. In the present investigation, methanol was used for all the dilutions since it is economical and easily available than other organic solvents. Due to greater solubility and reproducible readings of maximum absorbance, methanol was taken under consideration for further work.

Selection of wavelength for analysis of Telmisartan

Appropriate volume 1 ml of standard stock 2 solution of Telmisartan was transferred into a 10 ml volumetric flask, make upto a mark with methanol to give concentration of 10µg/ml.

Preparation of standard solutions

Preparation of primary standard (stock-1) solution

Accurately weighed 10 mg of Telmisartan was transferred to a 10 ml volumetric flask, dissolved in 10 ml methanol by shaking manually for 10 min. The volume was adjusted with the same up to the mark to give the final strength, i.e. 1000 µg/ml.

Preparation of secondary standard (stock-2) solution

Take 1ml of stock 1 solution was transferred to a 10 ml volumetric flask, dissolved in 10 ml methanol by shaking manually for 10 min. The volume was adjusted with the same up to the mark to give the final strength, i.e. 100µg/ml.

Preparation of working standards (stock-3) solution

Take 1ml of stock 2 solution was transferred to a 10 ml volumetric flask, dissolved in 10 ml methanol by shaking manually for 10 min. The volume was adjusted with the same up to the mark to give the final strength, i.e. 10µg/ml.

Preparation of Test solution

Take 10 tablets of telmisartan and crushed it well to a powered form and take equivalent weight 50mg and transferred into a 10ml volumetric flask containing 10 ml methanol, and the volume was made up to the mark using the same. Appropriate volume 1ml of this solution was transferred to a 10 ml volumetric flask, and the volume was adjusted to the mark using metanol. The resulting solution was scanned on a spectrophotometer in the UV Visible range 200–400 nm.

VALIDATION OF THE METHOD

The method was validated in terms of Linearity, Accuracy and precision

Linearity study

Different aliquots of telmisartan in the range 2-10 ml were transferred into series of 10 ml volumetric flasks, and the volume was made up to the mark with methanol to get concentrations 2,4,6,8 and 10 µg/ml, respectively. The solutions were scanned on a spectrophotometer in the UV Visible range 200–400 nm. The spectrum was recorded at 298 nm. The calibration plot was constructed as concentration vs absorbance.

Accuracy

To the preanalysed sample solutions, a known amount of standard stock solution was added at different levels, i.e. 50%, 100%, and 150%. The solutions were reanalyzed by the proposed method.

Precision

Precision of the method was studied as intraday and interday variations. Intraday precision was determined

by analyzing the 1,1,1,1,1 and 1µg/ml of telmisartan solutions for three times in the same day. Interday precision was determined by analyzing the 1,1,1,1,1 and 1µg/ml of telmisartan solutions daily for 2 days over the period of week.

RESULT AND DISSCUSSION

Selection of wavelength for analysis of Telmisartan

Appropriate volume 1 ml of standard stock 2 solution of Telmisartan was transferred into a 10 ml volumetric flask, make upto a mark with methanol to give concentration of 10µg/ml. The resulting solution was scanned in the UV range (200–400 nm). In spectrum Telmisartan showed absorbance maximum at 298 nm Fig 1.

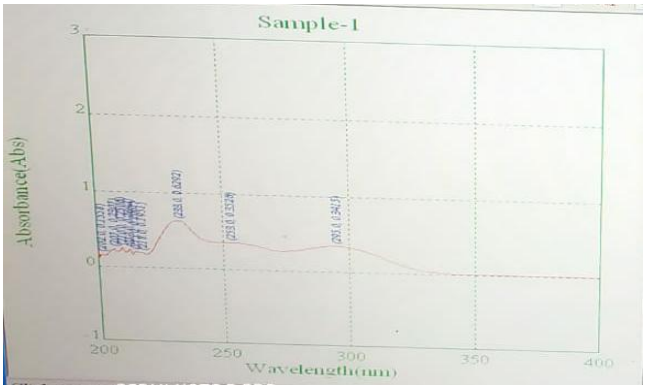


Fig 1: Selection of wavelength for analysis of Telmisartan

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 2–10 µg/ml for Telmisartan Fig.1 Linear regression equation was found to be $Y = 0.0482X + 0.0063$ ($r^2 = 0.9956$). The result is expressed in Table 1.

Table 1: Absorbance of various concentrations of drug solutions

1.	0	0
2.	2	0.1237
3.	4	0.1854
4.	6	0.2915
5.	8	0.3901
6.	10	0.4943

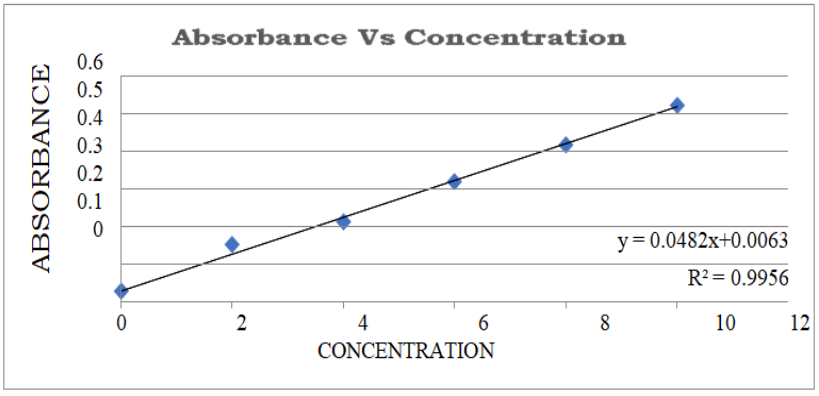


Fig 2: Absorbance of various concentrations of drug solutions and its linearity

Accuracy

The solutions were reanalyzed by the proposed method; results of recovery studies are reported that the % amount found was between 98.9% and 99.7% with %RSD> 2.

Precision

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These results show reproducibility of the assay. The % RSD values found to be less than 2 that indicate this method precise for the determination of both the drugs in formulation

Assay

Table 2: Absorbance of standard and test drugs

S.No.	Sample	Absorbance
1.	Standard	0.955
2.	Test-I	0.943
3.	Test-II	0.947
4.	Average	98.94

The individual % assay of telmisartan should not be less than 98.0% and not more than 102.0%.

Determination of Test solution

The concentrations of the drug were calculated from linear regression equations $Y = 0.0482X + 0.0063$ ($r^2 = 0.9956$). The % amount found was between 99.12% and 100.43%.

Optical Characteristics

Table 3: Optical characteristics results

S.NO.	Parameter	Results
1.	Absorption maximum(nm)	298 nm
2.	Linearity Range(µg/ml)	2-10µg/ml
3.	Standard regression equation	y=0.0482*X* + 0.0063
4.	Slope	0.0482
5.	Intercept	0.0063
6.	Correlation coefficient	0.9956
7.	Accuracy(%Recovery)	98.9% - 99.7%
8.	Precision (Intra-Day)%RSD	0.634

SUMMARY

Simultaneous estimation of Telmisartan was carried out by the selection of wavelength. The selected drug was diluted with methanol and it detected at wave length 298nm. The proposed method was validated as per ICH guidelines Q2(R1). The linearity results show that the Telmisartan were sensitive to the detector in the range 0.9956. Accuracy of the method was established by recovery studies using 50%, 100% and 150% solutions. The percentage recovery was found to be 98.9%, 99.3% and 99.7% respectively for Telmisartan. The precision of the method was performed. The %RSD of peak area was found to be within the acceptance limit (NMT 2%).

CONCLUSION

The above method was a rapid tool for routine analysis of telmisartan in the bulk and in the pharmaceutical dosage form. This UV-spectrophotometric technique is quite simple, accurate, precise, reproducible and sensitive. The UV method has been developed for quantification of telmisartan in tablet formulation. The validation procedure confirms that this is an appropriate method for their quantification in the formulation. It is also used in routine quality control of the formulations containing this entire compound.

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