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spectrophotometry please check Spelling???

Original Article

Stress degradation studies on Telmisartan and development of a validated method by UV spectrophotometry in bulk and pharmaceutical dosage forms

Abstract

Aim and Background: To develop and validate a simple, precise, accurate, and stability indicating a UV-method for estimation of Telmisartan (TELM). UV, HPLC, HPTLC, and many more experiments were carried out by taking single drug and also by combining with other drugs. However, Such type of studies was not reported. **Materials and Methods:** In both methods, TELM has the absorbance maxima at 296 nm. Method A involves method development and validation and Method B involves forced degradation study. In these methods, methanol was used as a solvent. Linearity was observed in the concentration range of 4–16 μg/ml. Validation experiments were performed to demonstrate system suitability, specificity, precision, linearity, accuracy, robustness, LOD, and LOQ as per International Conference on Harmonization guidelines. Furthermore stability studies of TELM were carried out under acidic, alkali, neutral, oxidation, photolytic, and thermal degradation as per stability indicating assay methods. **Results:** The results of analysis have been validated, and recovery studies were carried out using a standard addition method by adding specific drug amount (80%, 100%, and 120%) and show recovery studies in the range (99.26–101.26)%. **Conclusion:** The proposed method can be successfully applied for method development, validation, and stability study of TELM.

Key words: Spectrophotometric, stress degradation, Telmisartan

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Access this article online
Website: www.phmethods.org
DOI: 10.4103/2229-4708.93396
Quick response code

INTRODUCTION

Telmisartan (TELM) is chemically known as 4′-[(1,4′-dimethyl-2-propyl [2,6′-bi-1*H*-benzimidazol]-1′-yl) methyl] [1,1′-biphenyl]-2-carboxylic acid.[1-3] TELM is an antihypertensive drug (angiotensin-II receptor antagonist) and prevents binding of Angiotensin-II to the AT1 receptor. This is used for treatment of hypertension and diabetic nephropathy with an elevated serum creatinine and proteinuria (>300 mg/day) in patients with type-2 diabetes and hypertension.[4,5]

The UV spectrophotometric method was developed and validated as per International Conference on Harmonization (ICH) guidelines.[6] 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 (200–380 nm). TELM is official in British Pharmacopoeia (2009) and Indian Pharmacopoeia (2010), which recommends UV spectrophotometry for its analysis. The active pharmaceutical ingredient is subjected to a number of forced degradation conditions to include acidic, basic, and oxidative conditions. Forced 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 TELM not every stress agent may effect a degradation, but each agent has to be evaluated to determine whether degradation results.[7]

Literature review show that there are developed methods including UV,[8-14] visible spectrophotometric,[15] HPTLC,[16,17] HPLC,[18] and UPLC[19] methods for estimation of TELM, with many drugs combined other than the single drug with stability study. However, no method has been reported till date for the method validation and stability study of TELM using the UV spectrophotometric method. This work deals with the method development, validation, and stability study of TELM by various UV spectrophotometric methods.

MATERIALS AND METHODS

Apparatus

- Digital balance: Acculab (ALC 210.4)
- Sonicator: Eneritech (Ultra Sonicator)
- Photo stability chamber: Thermolab
- Hot air oven: Hicon
- A double beam UV-Visible spectrophotometer (Shimadzu-1800) with UV probe 2.31 software.

Material

Pure samples: TELM was kindly supplied by Zydus Cadila Healthcare Ltd., Ahmedabad, Gujarat, India.

Marketed formulation

TELSAR™ 40 (Emcure^{R} Pharmaceutical Ltd., Hinjwadi, India) was purchased from an open market for this study which contains TELM IP 40 mg.

Reagent and chemical

Methanol was used as a solvent which was procured from Finar Chemicals Ltd., Ahmadabad, India. HCl, NaOH, and H_2O_2 are of analytical grade. Double distilled water was used throughout the analysis.

Stock solution

Accurately weighed 10 mg of TELM was transferred to a 100 ml volumetric flask, 50 ml of methanol was added and allowed to sonicate for 15 min and finally volume was made up to the mark by methanol. Standard stock solution of TELM (100 µg/ml) was prepared.

Absorption maxima method

For the selection of analytical wavelength, 10 µg/ml solution of TELM was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 to 200 nm. From the spectra of drug [Figure 1], λ_{max} of TELM 296 nm was selected for the analysis.

Preparation of working standard solutions

From the stock solution of 100 µg/ml, working standard solutions of drug was prepared by appropriate dilution and were scanned in the entire UV range to determine the λ_{max}. Standard solutions were prepared having concentration of 4, 6, 8, 10, 12, 14, and 16 µg/ml of TELM to construct Beer's law plot for TELM. The absorbance of each solution was measured at 296 nm against methanol as a blank [Table 1 and Figure 1].

Preparation of calibration curve

The standard graph/calibration curve for TELM was plotted by taking concentration of drug on the *X*-axis and absorbance on the *Y*-axis [Figure 2].

Preparation of sample solution

The proposed method was applied to analyze commercially available TELM tablet. Ten tablets were weighed and powdered. The amount of tablet powder equivalent to 10 mg of TELM was weighed accurately and transferred to a 100 ml volumetric flask. Then 50 ml of methanol was added and allowed to sonicate for 15–20 min and the volume was made up to mark with methanol. The solution was then filtered through a Whattman filter paper. This filtrate was diluted suitably with a solvent to get the solution of 10 µg/ml concentration. The absorbance was measured against

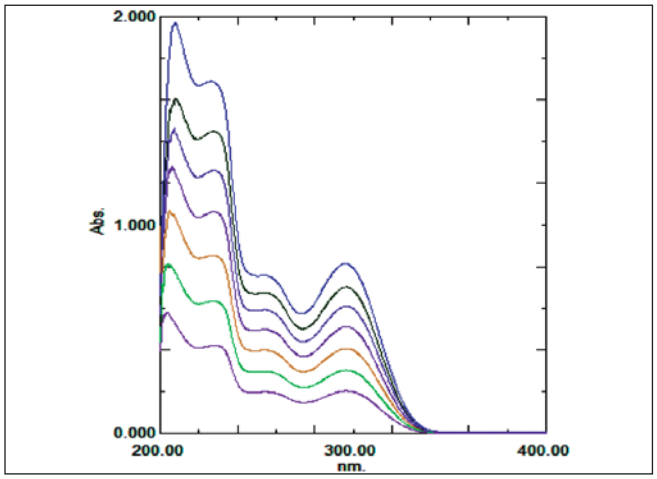

Figure 1: UV spectrum showing Telmisartan at 296 nm.

Table 1: Linearity

Concentration (µg/ml)	Abs at 296 nm
4	0.202
6	0.302
8	0.406
10	0.501
12	0.608
14	0.701
16	0.805

blank solution. The drug content in each tablet was estimated by using the standard graph.

METHOD A: METHOD VALIDATION

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of TELM. Beer–Lambert's concentration range was found to be 4–16 µg/ml for below methods [Table 2].

Specificity

Specificity is a procedure to detect quantitatively the analyte in presence of component that may be expected to be present in the sample matrix. Commonly used excipients in tablet preparation were spiked in a pre weight quantity of drug and then absorbance was measured and calculation done to determine quantity of drugs [Figure 3].

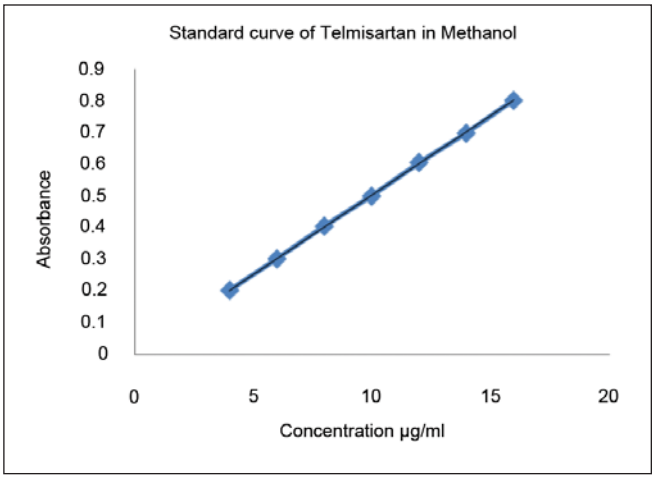

Figure 2: Linearity graph of Telmisartan

Table 2: Optical characteristics

Optical characters	Values
Absorbance maxima	296 nm
Beer's limit	4–16 µg/ml
%RSD	0.519
Regression equation (*Y**)	0.050*x* + 0.002
Slope (*a*)	0.050
Intercept (*b*)	0.002
Correlation coefficient (R^2)	0.999

Accuracy

To ascertain the accuracy of the proposed methods, recovery studies were carried out by the standard addition method at three different levels (80%, 100%, and 120%) of the bulk sample of TELM to the previously analyzed solution of formulation of concentration of 40 µg/ml. The percentage recovery for TELM by all the methods was found to be in the range of (99.26–101.26)% as shown in Table 3.

Precision

The precision of the method was achieved by replicate (n = 6) analysis of tablet preparations [Table 4]. The precision was also studied in terms of intra-day changes in absorbance of drug solution on the same day and inter-day changes on three different days over a period of 1 week. The intra-day and inter-day variations were calculated in terms of percentage

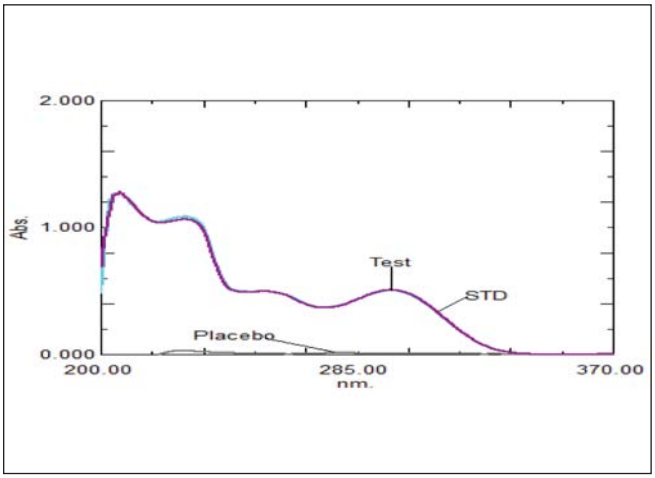

Figure 3: UV spectrum showing Telmisartan standard, test sample, and placebo

Table 3: Accuracy

Levels (%)	Formulation (µg/ml)	Added pure drug (µg/ml)	Amount recovered (µg/ml)	% Recovery	Statistical analysis		
					Mean	SD	% RSD
80	10	8	17.960	99.600	99.267	0.306	0.308
80	10	8	17.920	99.200			
80	10	8	17.900	99.000			
100	10	10	19.920	99.200	100.067	1.332	1.331
100	10	10	20.160	101.600			
100	10	10	19.940	99.400			
120	10	12	22.140	101.400	101.267	0.231	0.228
120	10	12	22.100	101.000			
120	10	12	22.140	101.400			

relative standard deviation and the results are given in Table 4 (a and b).

Robustness

This procedure was carried out by changing the λ_{max} ± 5%. Then, the results are given in Table 5.

METHOD B: METHOD FORCED DEGRADATION STUDY

Acid degradation

First 0.1 N HCl was taken in a 10 ml volumetric flask and then accurately weighed 10 mg bulk drug was dissolved in it. To make soluble the drug, few drops of methanol was added and then the volume is made by 0.1 N HCl. Then, this solution was refluxed for 5 h at 70 °C in water bath. Initially at 0 h take 0.1 ml of this solution and the volume was made up to 10 ml with methanol and then, withdrawing the specific amount of solution in every hour. After this, the absorbance was measured by scanning the prepared solution of required concentration in a UV spectrophotometer [Table 6 and Figure 4].

Table 4: Precision

Concentration (µg/ml)	Abs. at 296 nm	Calculated amount	Statistical analysis
10	0.499	9.94	Mean = 9.913
10	0.496	9.88	
10	0.496	9.88	SD= 0.033
10	0.498	9.92	
10	0.497	9.9	%RSD = 0.329
10	0.500	9.96	
(a) Intra-day precision			
Concentration (µg/ml)	**Abs at 296 nm (*n* = 3)**	**Calculated amount**	**Statistical analysis**
10	0.495	9.86	Mean = 9.903
10	0.499	9.94	
10	0.496	9.88	S.D = 0.034
10	0.498	9.92	
10	0.499	9.94	%RSD = 0.348
10	0.496	9.88	
(b) Inter-day precision			
Concentration (µg/ml)	**Day-1**	**Day-2**	**Day-3**	**Statistical analysis**
10	0.497	0.496	0.492	Mean = 9.839
10	0.499	0.493	0.495	
10	0.495	0.495	0.492	
10	0.497	0.478	0.493	SD = 0.057
10	0.496	0.497	0.495	
10	0.498	0.493	0.494	
Mean	0.497	0.494	0.494	%RSD = 0.579
Amt Found	9.9	9.787	9.83	

Alkali degradation

First 0.1 N NaOH solution was prepared. Accurately weighed 10 mg bulk drug was taken in a 10 ml volumetric flask. Then, the volume was made with 0.1 N NaOH. Then this solution was refluxed for 5 h at 70 °C in a water bath. Initially at 0 h take 0.1 ml of this solution and the volume was made up to 10 ml with methanol. The absorbance was measured in every hour by withdrawing the required amount of the sample. Then, scanning was performed with a UV spectrophotometer [Table 7 and Figure 5].

Neutral degradation

Accurately weighed 10 mg of bulk drug was taken in a 10 ml volumetric flask. Then, little amount of methanol was added to dissolve the drug. The volume was adjusted up to the mark with double distilled water. Then, that solution was refluxed for 5 h at 70 °C in a water bath. Initially at 0 h take 0.1 ml of this solution and the volume was made up to 10 ml

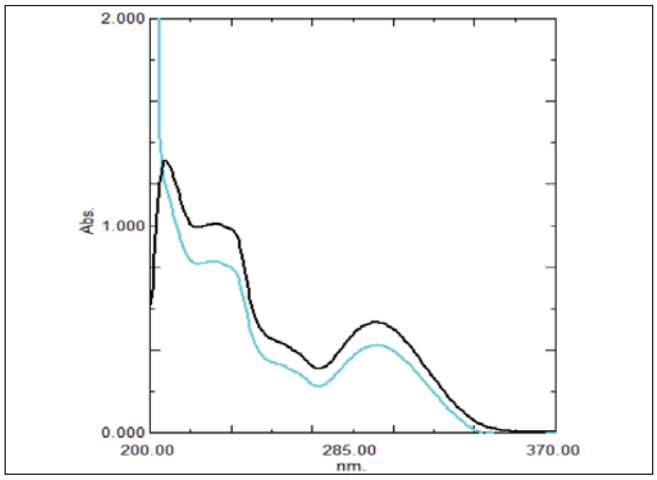

Figure 4: Acid degradation spectrum at 0 h and after 5 h

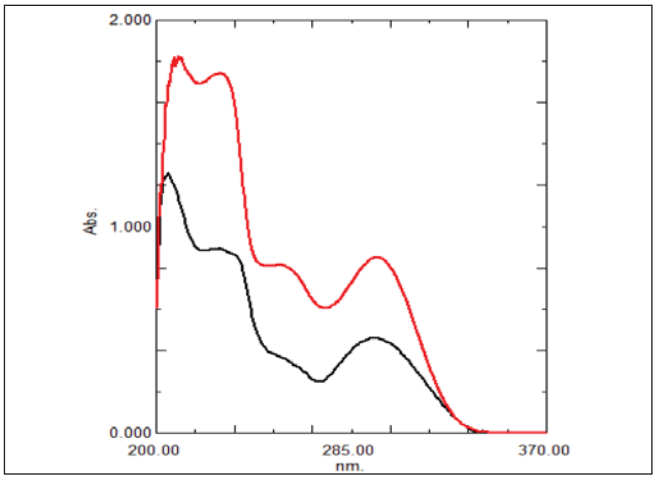

Figure 5: Alkali degradation spectrum at 0 h and after 5 h

Table 5: Robustness

Concentration (µg/ml)	Absorbance at 291 nm	Amt. found	Statistical analysis	Concentration (µg/ml)	Absorbance at 301 nm	Amt. found	Statistical analysis
10	0.456	9.08	Mean = 9.093	10	0.459	9.140	Mean = 9.157
10	0.453	9.02		10	0.456	9.080	
10	0.455	9.06	SD = 0.052	10	0.458	9.120	SD = 0.053
10	0.459	9.14		10	0.462	9.200	
10	0.457	9.10		10	0.461	9.180	
10	0.460	9.16	%RSD = 0.568	10	0.463	9.220	% RSD = 0.577

Table 6: Acid degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.533	10.00	0.0
Analyte at 1 h	0.526	9.87	1.31
Analyte at 2 h	0.476	8.93	10.69
Analyte at 3 h	0.458	8.59	14.07
Analyte at 4 h	0.442	8.29	17.07
Analyte at 5 h	0.421	7.90	21.01

Table 7: Alkali degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.845	10.00	0.00
Analyte at 1 h	0.770	9.11	8.88
Analyte at 2 h	0.766	9.07	9.35
Analyte at 3 h	0.750	8.88	11.24
Analyte at 4 h	0.539	6.38	36.21
Analyte at 5 h	0.459	5.43	45.68

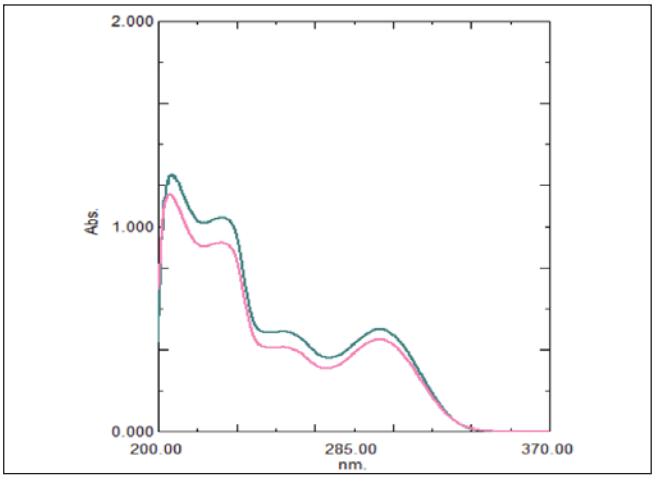

Figure 6: Neutral degradation spectrum at 0 h and after 5 h

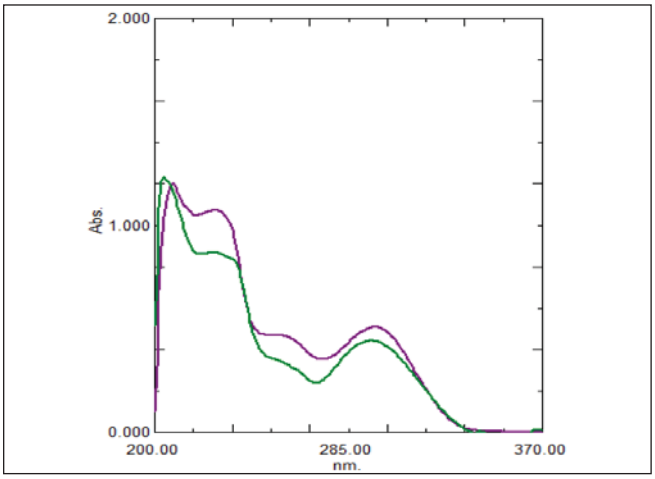

Figure 7: Thermolytic degradation spectrum at 0 h and after 5 h

with methanol. The absorbance was measured at one-hour interval by withdrawing the required amount of sample solution. Then, scanning was performed with a UV-spectrophotometer [Table 8 and Figure 6].

Thermal degradation

A specific amount of bulk drug was taken in a cleaned Petridis and dried, then the Petridis along with bulk drug was placed into the oven at 70 °C for 5 h, at every hour 10 mg of bulk drug was taken from the Petridis, and 1000 ppm solution with methanol was prepared. After this, the required concentration was made and the absorbance measured in the UV spectrophotometer and percentage of degradation was calculated [Table 9 and Figure 7].

Photolytic degradation

Accurately weighed 10 mg of bulk drug was taken in a 10 ml volumetric flask. The volume was adjusted up to the mark with methanol. Then, that solution was placed into the photostability chamber for 5 h Initially at 0 h take 0.1 ml of this solution and the volume was made up to 10 ml with methanol. The absorbance was measured at one-hour interval by withdrawing the required amount of sample solution. Then, scanning was performed with a UV-spectrophotometer [Table 10 and Figure 8].

Oxidation with H_2O_2

Ten milligrams of bulk drug was weighed accurately, 2–3 drops of methanol were added to make the drug soluble. Then the volume was made up by 3% H_2O_2 and placed it in a cupboard for 5 h. At one-hour interval specified amount the sample was taken and the required concentration was prepared. It was scanned in a UV spectrophotometer [Table 11 and Figure 9].

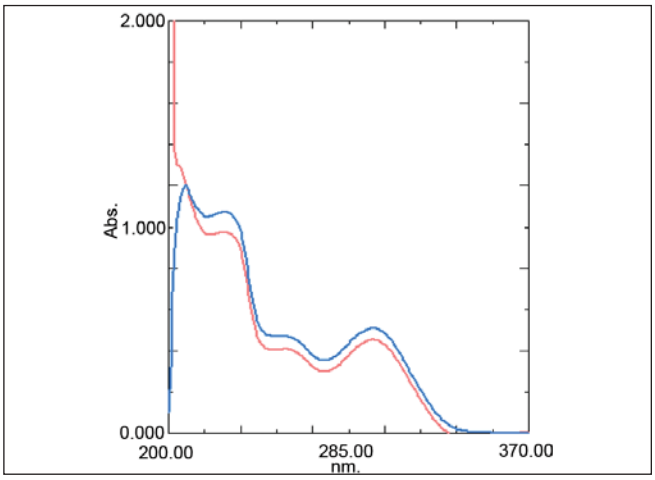

Figure 8: Photolytic degradation spectrum at 0 h and after 5 h

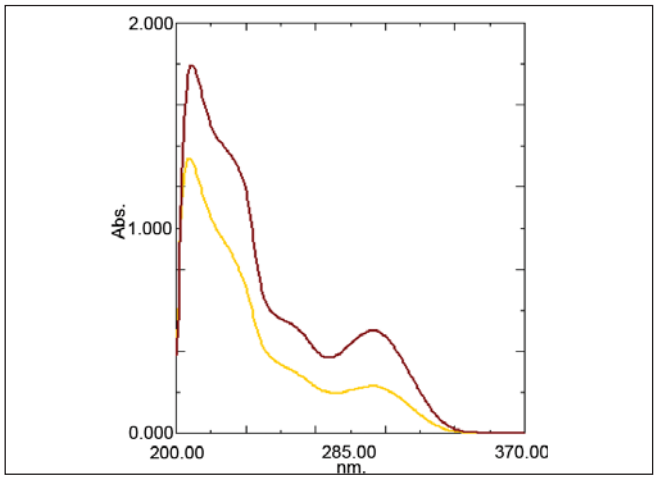

Figure 9: Oxidative degradation spectrum at 0 h and after 5 h

Table 8: Neutral degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.500	10.00	0.00
Analyte at 1 h	0.494	9.88	1.20
Analyte at 2 h	0.491	9.82	1.80
Analyte at 3 h	0.476	9.52	4.80
Analyte at 4 h	0.452	9.04	9.60
Analyte at 5 h	0.450	9.00	10.00

Table 9: Thermal degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.509	10.00	0.0
Analyte at 1 h	0.476	9.35	6.48
Analyte at 2 h	0.474	9.31	6.88
Analyte at 3 h	0.465	9.14	8.64
Analyte at 4 h	0.450	8.84	11.59
Analyte at 5 h	0.442	8.68	13.16

Table 10: Photolytic degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.509	10.00	0.00
Analyte at 1 h	0.491	9.65	3.54
Analyte at 2 h	0.480	9.43	5.70
Analyte at 3 h	0.474	9.31	6.88
Analyte at 4 h	0.459	9.02	9.82
Analyte at 5 h	0.452	8.88	11.20

Table 11: Oxidative degradation

Name	Absorbance	Concentration	%Degradation
Analyte at 0 h	0.500	10.00	0.00
Analyte at 1 h	0.377	7.54	24.60
Analyte at 2 h	0.298	5.96	40.40
Analyte at 3 h	0.252	5.04	49.60
Analyte at 4 h	0.250	5.00	50.00
Analyte at 5 h	0.229	4.58	54.20

RESULTS AND DISCUSSION

The main objective of this work was to develop and validate the stability indicating a UV method for TELM in the pharmaceutical dosage form. The absorbance maxima of TELM at 296 nm and linearity were observed in the concentration range of 4–16 μg/ml for all validated methods. A percent assay for TELM by above validated methods was found in the range of 98.8–99.60%. Standard deviation was found to be less than ±2.0 and the coefficient of variance was found to be less than ±1.0 indicating the precision of the methods. Accuracy of proposed methods was ascertained by recovery studies, and the results were expressed as % recovery. Percent recovery for TELM was found in the range of 99.26–101.26%. Values of standard deviation and coefficient of variation were satisfactorily low indicating the accuracy of all the methods.

For forced degradation studies, the absorbances in all stressed conditions were decreased for repeated times and percent degradation was found out. Two overly spectra indicate that the degradation shows at initial 0 h and total degradation after 5 h. Therefore, the drug TELM undergoes degradation in all stressed conditions. TELM gives more absorbance with alkali medium as compared to other medium, alkali degradation, chances of generating degradation with 0.1 N sodium hydroxide solution drug is degraded in specific time interval as compared to original drug. Based on the results obtained, it is found that the proposed methods are accurate, precise, reproducible, and economical and can be employed for routine quality control of TELM in its pharmaceutical dosage form [Table 12].

CONCLUSION

The proposed method is specific in estimating the commercial formulation without interference of excipients and the other additives. Hence, this method can be used for routine determination of TELM in the

Table 12: Forced degradation study results for Telmisartan after 5 h

Conditions	% Degradation
0.1 N HCl	21.01
0.1 N NaOH	45.68
H_2O	10
Thermal degradation, 65° C	13.2
UV light, 200 lux h	11.2
3% H_2O_2	54.2

bulk sample and pharmaceutical formulation. The proposed method for stability study shows that there is appreciable degradation of TELM found in stress conditions. A new simple analytical method has been developed to apply for the evaluation of the stability of TELM to quantify TELM and its degradation products in a solid premix dosage forms.

REFERENCES

1. Budavari S, editor. In: The Merck Index. 13th ed. White House Station, NJ: Merck and Co. Inc.; 2001. p. 1628.
2. Indian Pharmacopoeia. Government of India Ministry of Health and Family Welfare. Vol. 3. New Delhi: The Indian Pharmacopoeia Commission; 2010. p. 2186-7.
3. British pharmacopoeia. Vol. 2. London: Her Majesty's stationary Office; 2009. p. 5872-7.
4. Ean CS, Martindale. The Complete Drug Reference. 36th ed. London: The Pharmaceutical Press; 2009. p. 1409.
5. Anon. Pharmacy and Theraputics Review-Telmisartan. The Formulary, Jan 1999. p. 13.
6. ICH Q2 (R1), Harmonizazed Tripatite Guidline, Validation of Analytical Procedure: Text and Methodology, 2005.
7. Patro1 DR, Pradhan1 K, Mishra1 D, Sahu KC. Stress degradation studies on olmesartan and development of a validated method by UV spectrophotometric in bulk and pharmaceutical dosage form. Inventi Rapid: Pharm Anal Qual Assur 2011;3:1-5.
8. Palled MS, Chatter M, Rajesh PM, Bhat AR. Difference spectrophotometric determination of telmisartan in tablet dosage forms. Indian J Pharm Sci 2006;68:685-6.
9. Tatane S. Glenmark Pharmaceuticals Limited, Sinnar Nashik. Development of UV spectrophotometric method of telmisartan in tablet formulation. J Adv Pharm Healthc Res 2011;1:23-6.
10. Bebawy LI, Abbas SS, Fattah LA, Refaat HH. Application of first-derivative, ratio derivative spectrophotometry, TLC-densitometry and spectrofluorimetry for the simultaneous, determination of telmisartan and hydrochlorothiazide in pharmaceutical dosage forms and plasma. Farmaco 2005;60:859-67.
11. Kondawar MS, Kamble KG, Raut KS, Maharshi KH. UV spectrophotometric estimation of amlodipine besylate and telmisartan in bulk drug and dosage form by multiwavelength analysis. Int J ChemTech Res 2011;3:1274-8.
12. Gangola R, Singh N, Gaurav A, Maithani M, Singh R. Spectrophotometric simultaneous determination of hydrochlorothiazide and telmisartan in combined dosage form by dual wavelength method. Int J Comprehens Pharm 2011;2:1-3.
13. Ilingo K, Shiji Kumar PS. Simultaneous estimation of telmisartan and hydrochlorothiazide in pharmaceutical dosage form. Asian J Pharm Health Sci 2011;1:12-5.
14. Thomas AB, Jagdale SN, Dighe SB, Nanda RK. Simultaneous spectrophotometric estimation of amlodipine besylate and telmisartan in tablet dosage form. Int J ChemTech Res 2010;2:1334-41.
15. Kumbhar ST, Chougule GK, Gajeli GB, Tegeli VS, Thorat YS, Shivsharan US. Visible spectrophotometric determination of telmisartan from urine. Int J Pharm Sci Res 2011;2:1254-8.
16. Prabhu C, Subramanian GS, Karthik A, Kini S, Rajan MS, Udupa N. Determination of telmisartan by HPTLC – a stability indicating assay. J Planar Chromatogr 2007;20:477-81.
17. Chabukswar AR, Jagdale SC, Kumbhar SV, Kadam VJ, Patil VD, Kuchekar BS, *et al*. Simultaneous HPTLC estimation of telmisartan and amlodipine besylate in tablet dosage form. Scholars Research Library. Arch Appl Sci Res 2010;2:94-100.
18. Palled MS, Chatter M, Rajesh PM, Bhat AR. RP-HPLC Determination of telmisartan in tablet dosage forms. Indian J Pharm Sci 2005;67:108-9.
19. Nalwade S, Reddy VR, Rao DD, Rao IK. Rapid simultaneous determination of telmisartan, amlodipine besylate and hydrochlorothiazide in a combined poly pill dosage form by stability-indicating ultra performance liquid chromatography. Sci Pharm 2011;79:69-84.

How to cite this article: Patel K, Dhudasia K, Patel A, Dave J, Patel C. Stress degradation studies on Telmisartan and development of a validated method by UV spectrophotometry in bulk and pharmaceutical dosage forms. Pharm Methods 2011;2:253-9.
Source of Support: Nil **Conflict of Interest:** None declared.