Original Article

Development and Validation of Stability Indicating UV-Spectrophotometric Method for the Simultaneous Estimation of Telmisartan and Metformin Hydrochloride in Bulk Drugs

Tirodkar Chaitali Uday, Palled Mahesh Shivabasappa*, Shailendra Suryawanshi Sanjay, Majukar Suryamala Maruti

Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi, Karnataka, INDIA.

ABSTRACT

Background: In present work attempt has been made to develop and validate a simple and sensitive UV spectrophotometric method for simultaneous estimation of Telmisartan and Metformin Hydrochloride. **Objectives:** To develop simple, precise, robust, sensitive and accurate UV-Spectrophotometric method for the simultaneous estimation of Telmisartan and Metformin HCl and to formulate the combined tablet dosage formulation of Telmisartan and Metformin HCl respectively. **Methods:** The optimum condition for the analysis of the drug was established with Methanol as solvent. Maximum absorption wavelength were found to be 296nm and 237nm for Telmisartan and Metformin Hydrochloride. It showed linear response between the concentration ranges of 2-12μg/ml and 0.1-0.6 μg/ml for Telmisartan and Metformin Hydrochloide espectively. The linear regression coefficient was found to be 0.999. The method was validated for linearity, Precision, ruggedness, specificity, Sensitivity as per ICH guidelines and all the values of validation was found to be within the acceptance. Hence it can be concluded that method was new, simple, selective, specific, precise for simultaneous estimation of Telmisartan and Metformin Hydrochloride in bulk powder.

Key words: Telmisartan, Metformin HCl, Method validation, ICH guidelines, Stability indicating, UV-Spectrophotometric.

Submission Date: 07-07-2020;
Revision Date: 19-12-2020;
Accepted Date: 23-03-2021

DOI: 10.5530/ijper.55.2.98

Correspondence:
Dr. Mahesh Palled
Professor, Department of Pharmaceutical chemistry, KLE college of Pharmacy, KLE Academy of Higher Education and Research, Belagavi-590010, Karnataka, INDIA.
Phone no: +91 9448634244
Email id: drpalled@gmail.com

INTRODUCTION

Telmisartan

Telmisartan (Figure 1) is the drug of angiotensin receptor blockers (ARBs). Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT1-receptor by binding reversibly and selectively to the vascular smooth muscle and the adrenal gland. Telmisartan chemically designated as 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl]methyl] phenyl]benzoic acid.[1]

Metformin HCl

Metformin (Figure 2) is a biguanide derivative, it decreases the blood glucose levels by decreasing the hepatic glucose production, deceases the intestinal absorption of glucose and increasing insulin sensitivity by increasing peripheral glucose uptake and utilization.[2]

The main advantage of this combination is Telmisartan act as an adjunct to Metformin HCl it helps to prevent ischemic heart diseases in diabetes patient. It also helps in the activation of peroxisome proliferator activated-γ receptor (PPAR- γ) which helps to regulate insulin and glucose metabolism. Metformin also HCl helps in fat metabolism in obese diabetes patients.[3]

Many methods have been reported such as HPLC, HPTLC, GC, UV-Spectroscopy for Telmisartan and Metformin HCl in alone

www.ijper.org

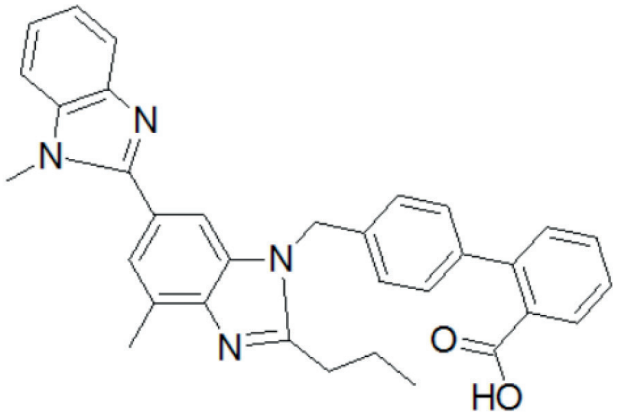


Figure 1: Telmisartan.

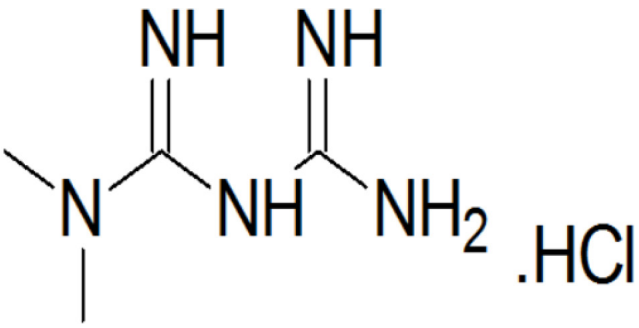


Figure 2: Metformin HCl.

and combination with other drugs.[4,5] Till now there is no UV-Spectrophotometric method has been reported for this combination and no combined formulation is available in the market. Hence in the present research work an attempt has been made to develop and validate simple, rapid, sensitive, precise and accurate UV-Spectrophotometric method determination of Telmisartan and Metformin HCl.[6,7,8]

MATERIALS AND METHODS

Materials

Telmisartan and Metformin hydrochloride with 99.8% purity was obtained as a gift sample from FDC Ltd. Verna-Goa. All the chemicals and reagents used for the experiment were pure and analytical grade and obtained from the store house of KLE College of Pharmacy, Belagavi. Methanol is of Fisher scientific was used.

Instruments and apparatus

UV-Spectrophotometer of Shimadzu make and 1800 model having UV probe software were used for analysis.

Method development

Samples were tested for the solubility by using different solvents such as Methanol, Acetonitrile, 0.1N HCl, 1N NaOH. By looking in to solubility condition Methanol were selected as a solvent. Samples were scanned in UV range between 200-400nm using methanol as a solvent. The maximum absorption for Telmisartan showed at 296nm and Metformin Hydrochloride at 237nm.[9,10,11]

Preparation of standard

10mg of Telmisartan and Metformin Hydrochloride were weighed separately using analytical balance and transferred in to 10ml of volumetric flask and volume was made up to 10ml with a solvent Methanol to give the concentration of 1000 µg/ml of each analyte.1ml of Telmisartan and 0.1 ml of Metformin HCl solution from each flask was pipetted out and transferred in to 10ml volumetric flask individually and volume was made up to 10ml with methanol to get a concentration of 100 µg/ml for Telmisartan and 10 µg/ml for Metformin HCl.

Forced Degradation studies

To evaluate the stability condition of the developed UV-Spectroscopic method samples were stressed in conditions such as acid, base, oxidation, thermal and photolytic degradation. In all study % degradation were calculated. The limit of forced degradation study is 5-20%.

Acid degradation study

Acid degradation were carried out by weighing 10 mg of Telmisartan and Metformin Hydrochloride in different 10ml volumetric flask. Dissolved in methanol to get the concentration of 1000 µg/ml. Secondary stock solution were prepared in the concentration i.e 100µg/ml of Telmisartan and 10 µg/ml Metformin Hydrochloride. From this 4 µg/ml of Telmisartan and 0.4 µg/ml of Metformin Hydrochloride of solution were stressed by using 0.1N HCl on water bath at 80°C for for 2 hr. Samples were scanned in UV range at 200-400nm and spectra were noticed.

Base degradation study

For Base degradation study 4 µg/ml of Telmisartan and 0.4 µg/ml of Metformin Hydrochloride of solution were prepared from primary and secondary stock solution and diluted by using 0.1NaOH. Both the solutions were stressed at 80°C for 2 hr and spectra were scanned.

Oxidation study

Oxidation degradation study 4 µg/ml of Telmisartan and 0.4 µg/ml of Metformin Hydrochloride of solution were prepared from primary and secondary stock solution and diluted by using 30 % Hydrogen peroxide. Both the solutions were stressed at 80°C for 2 hr and spectra were scanned.

Photo degradation study

Photo degradation study were carried out by exposing 10mg of both the drugs in UV light at 254 nm for 24 hr. After that solutions were prepared by using methanol to obtain final concentration of 4 µg/ml of Telmisartan and 0.4 µg/ml of Metformin Hydrochloride and then scanned to get suitable spectra.

Thermal degradation

Thermal degradation were performed by exposing the drugs at 40°C in hot air oven for 4 hr. After that solutions were prepared by using methanol to obtain final concentration of 4 µg/ml of Telmisartan and 0.4 µg/ml of Metformin Hydrochloride and then scanned to get suitable spectra.

Formula to calculate % degradation

$$\% \text{ Degradation} = \frac{(\text{Initial degradation} - \text{Final degradation})}{\text{Initial degradation}} \times 100$$

METHOD VALIDATION

The method was developed and validated according to the ICH guidelines in order to determine Linearity, Specificity and selectivity, Precision, Ruggedness, stability, LOD and LOQ etc. Linearity range were constructed for Telmisartan is 2-4 µg/ml and 0.1-0.6 µg/ml for Metformin Hydrochloride.Calibration curve was plotted by using area versus the concentration. Precision study was performed in System, Intraday and Interday precision and results were expressed in terms % RSD.

Ruggedness were performed by changing the analyst and instrument % RSD were noted. Stability was carried out in bench and freeze by keeping the solution in stable conditions for 72hr. LOD and LOQ were calculated from the linearity slope.

RESULTS AND DISCUSSION

Both the drugs were absorbed at 296nm and 237nm and spectra of both the drugs in Figure 3 and 4 and overlain spectra of different linearity range were showed in Figure 5.

Forced degradation study

The results of forced degradation study using methanol as a solvent were summarised in Table 1.

Acid degradation study

Both the drugs were found extreme acid degradation. 0.1 N HCl heating at 80°C for 2 hr showed more than

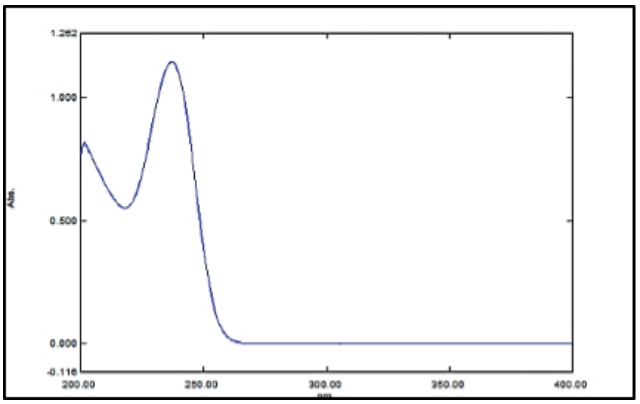


Figure 3: Spectra of Metformin HCl.

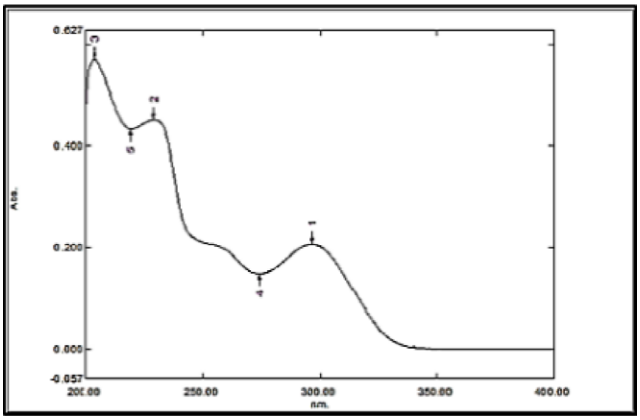


Figure 4: Spectra of Telmisartan.

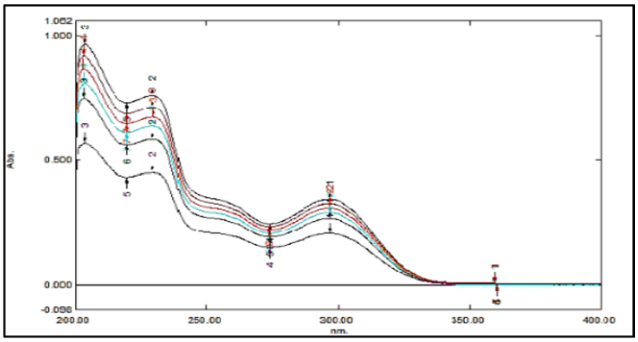


Figure 5: Combine spectra.

Table 1: Data of forced degradation study.

Con	Telmisartan at 296nm			Metformin HCL at 237nm		
	Initial	Final	% deg	Initial	Final	% deg
Acid	0.282	0.248	12.05	0.548	0.487	11.13
Base	0.312	0.271	13.14	0.723	0.628	13.13
Oxidation	0.678	0.603	11.06	0.623	0.568	9.68
Thermal	0.323	0.272	15.78	0692	0.596	13.87
Photolytic	0.280	0.260	7.14	0.486	0.451	7.20

10% degradation and slightly change in spectra were found Figure 6.

Base degradation study

In base degradation heating at 80°C by using 0.1 N NaOH showed 13% gegradation of both the drugs Figure 7.

Oxidation Degradation study

Oxidation degradation by using 30% Hydrogen peroxide showed very less degradation compared to the Telmisartan Figure 8.

Thermal degradation study

Thermal degradation were showed both the drugs were undergone extreme degradation and changes in the spectra were observed Figure 9.

Photolytic degradation study

Photolytic degradation showed very slight changes in the spectra and level of the degradation were very less compared to other degradations Figure 10.

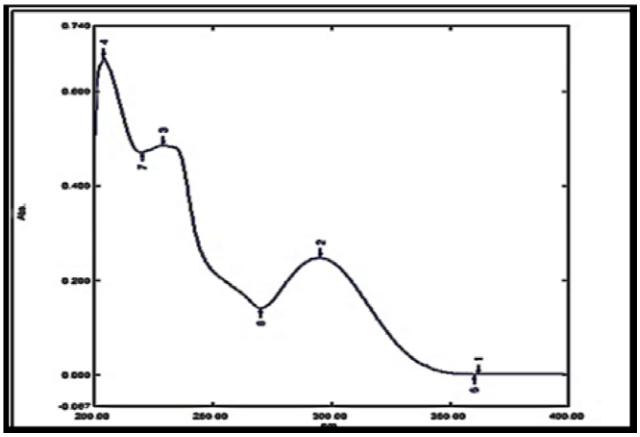


Figure 6: Spectra of Acid.

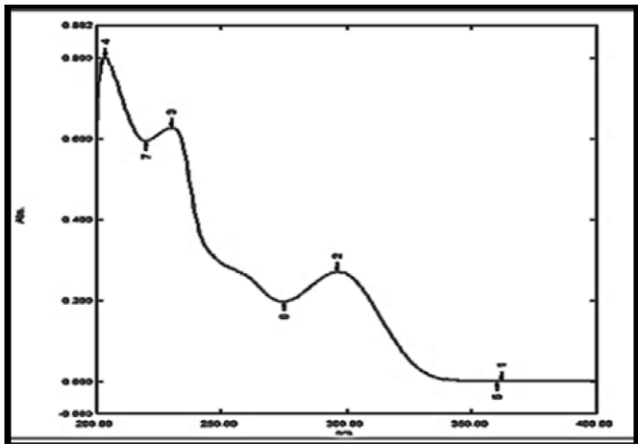


Figure 7: Spectra of Base.

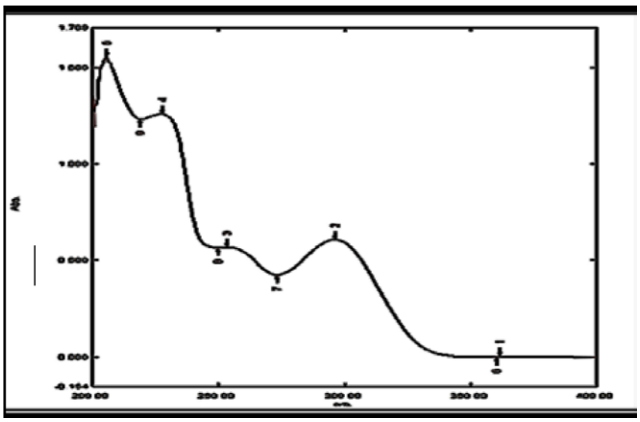


Figure 8: Spectra of Oxidation.

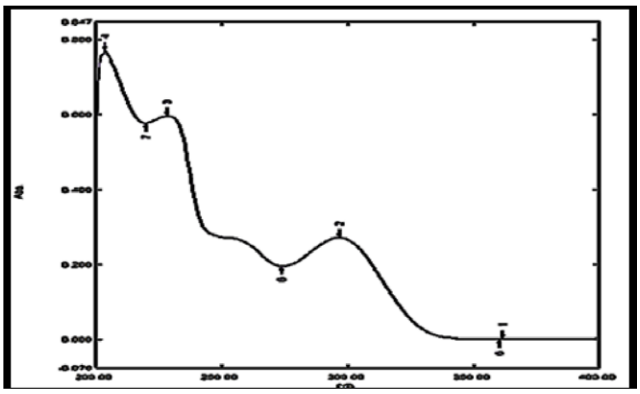


Figure 9: Spectra of Thermal.

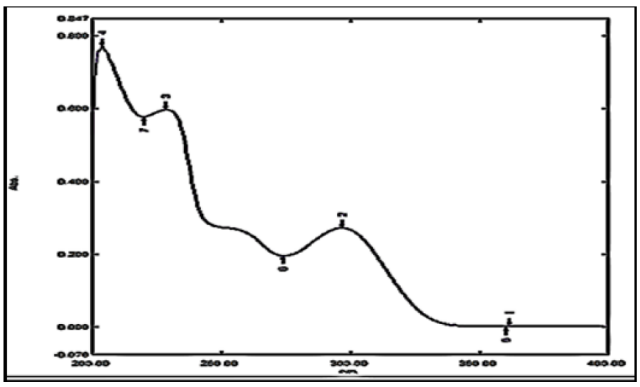


Figure 10: Spectra of Photolytic.

Method Validation

Specificity and Selectivity

The solvent methanol and each drug solutions were scanned and UV spectra were obtained which indicate no interference of solvent Figure 11.

Linearity range Response

Linearity and range for both the drugs was obtained by analysing 2-12 µg/ml for Telmisartan and 0.1-0.6 µg/ml for Metformin HCl solutions in triplicate. Absorbance was obtained and calibration curve was plotted Table 2 and graphs were presented in Figure 12 and Figure 13.

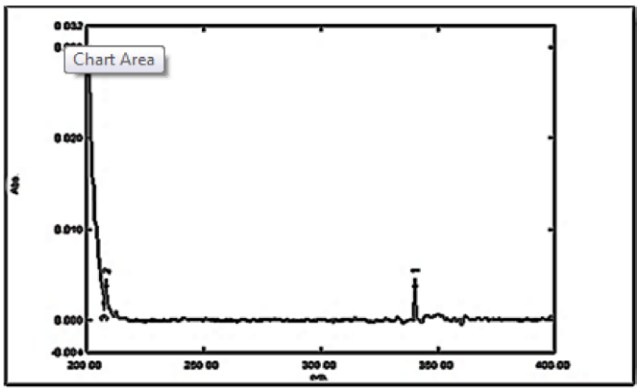


Figure 11: Spectra of solvent.

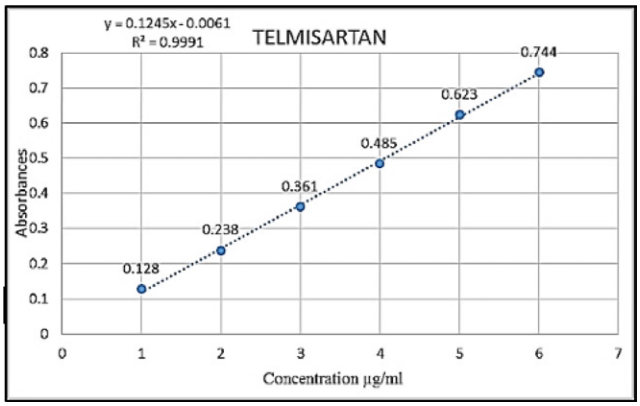


Figure 12: Calibration curve of Telmisartan.

Table 2: Linearity data of Telmisartan and Metformin Hydrochloride.

Sr. No	Concentration (µg/ml) (Telmisartan)	Concentration (µg/ml) Metformin HCl	Absorbance's of Telmisartan at (296 nm)	Absorbance's of Metformin. Hcl at (237 nm)
1	2	0.1	0.128	0.136
2	4	0.2	0.238	0.246
3	6	0.3	0.361	0.383
4	8	0.4	0.485	0.496
5	10	0.5	0.623	0.648
6	12	0.6	0.744	0.772
r^2 0.999			0.998	

Precision

Precision study was carried out by performing System, Intraday and Interday precision. System precision was performed by analysing 6 replicates of each drug solutions. Intraday and interday precision was performed by analysing the each solutions on same day at 3 different intervals and at 3 different days. Absorbance was obtained and % RSD was calculated from the absorbance Table 3-5.

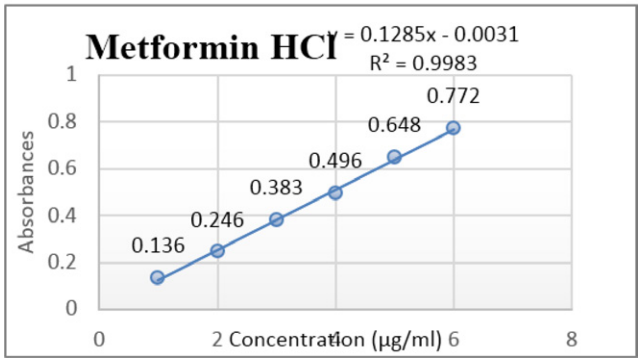


Figure 13: Calibration curve of Metformin HCl.

Table 3: System precision data of Telmisartan and Metformin HCl.

Concentration (µg/ml)		Telmisartan	Metformin HCl
6	0.3	0.364	0.257
6	0.3	0.367	0.254
6	0.3	0.371	0.256
6	0.3	0.374	0.253
6	0.3	0.375	0.252
6	0.3	0.377	0.255
Average		**0.371333**	**0.2545**
Std.Dev		**0.005007**	**0.001871**
%RSD		**1.348293**	**0.7351**

Stability

The stability of solutions were checked by keeping the solution for 72hrs at unstable conditions and stability were checked after the 72hr (Table 6).

Ruggedness

Ruggedness parameter was carried out by changing in an analyst and changing in an instrument and % RSD was calculated (Table 7).

LOD and LOQ

Limit of detection and quantification was calculated by using statistical calculations using formula (Table 8):

$$\text{LOD} = \frac{3.3 \times \text{standard deviation of } y - \text{intercept}}{\text{Slope of the calibration curve}}$$

$$\text{LOQ} = \frac{10 \times \text{standard deviation of } y - \text{intercept}}{\text{Slope of the calibration curve}}$$

CONCLUSION

Statistical analysis proved that the developed method was simple, specific, selective, linear, precise, rugged and reproducible for the simultaneous determination of Telmisartan and Metformin HCl. The developed

Table 4: Intraday precision data of Telmisartan and Metformin HCl.

		Intraday 1		Intraday 2		Intraday 3	
Concentration µg/ml		Telmisartan	Metformin HCl	Telmisartan	Metformin HCl	Telmisartan	Metformin HCl
6	0.3	0.348	0.301	0.343	0.303	0.340	0.314
6	0.3	0.342	0.305	0.342	0.306	0.336	0.310
6	0.3	0.343	0.303	0.341	0.308	0.334	0.311
6	0.3	0.341	0.302	0.347	0306	0.336	0.314
6	0.3	0.344	0.306	0.344	0.303	0.336	0.313
6	0.3	0.345	0.301	0.344	0.304	0.334	0.314
Average		**0.343833**	**0.303**	**0.3435**	**0.305**	**0.336**	**0.312667**
Std.Dev		**0.002483**	**0.002098**	**0.002074**	**0.002**	**0.002191**	**0.001751**
%RSD		**0.722233**	**0.692283**	**0.603681**	**0.655735**	**0.652051**	**0.560082**

Table 5: Interday precision data of Telmisartan and Metformin HCl.

Precision		Interday 1		Interday 2		Interday 3	
Concentration (µg/ml)		Telmisartan	Metformin HCl	Telmisartan	Metformin HCl	Telmisartan	Metformin HCl
6	0.3	0.372	0.316	0.386	0.323	0.394	0.336
6	0.3	0.378	0.318	0.385	0.321	0.392	0.332
6	0.3	0.378	0.314	0.385	0.323	0.391	0.339
6	0.3	0.376	0.316	0.384	0.322	0.393	0.332
6	0.3	0.374	0.318	0.386	0.323	0.393	0.334
6	0.3	0.375	0.315	0.387	0.320	0.391	0.332
Average		**0.3755**	**0.316167**	**0.3855**	**0.322**	**0.392333**	**0.334167**
Std. Dev		**0.002345**	**0.001602**	**0.001049**	**0.001265**	**0.001211**	**0.002858**
%RSD		**0.624556**	**0.506721**	**0.272065**	**0.39283**	**0.308681**	**0.855182**

Table 6: Solution stability data.

Stability Solutions		Telmisartan		Metformin HCl		
Replicates	Conc	Fresh	Old	Conc	Fresh	Old
1	6 µg/ml	0.242	0.248	0.3	0.180	0.183
2	6 µg/ml	0.244	0.246	0.3	0.179	0.186
3	6 µg/ml	0.245	0.245	0.3	0.181	0.185

Table 7: Ruggedness data.

Ruggedness		By change in analyst		By change in Instrument	
Concentration (µg/ml)		Telmisartan	Metformin HCl	Telmisartan	Metformin HCl
6	0.3	0.356	0.302	0.243	0.189
6	0.3	0.359	0.308	0.241	0.187
6	0.3	0.358	0.305	0.245	0.186
6	0.3	0.355	0.309	0.241	0.185
6	0.3	0.357	0.302	0.242	0.187
6	0.3	0.359	0.310	0.243	0.186
Avg		**0.357333**	**0.306**	**0.2425**	**0.186667**
Std. Dev		**0.001633**	**0.003521**	**0.001517**	**0.001366**
%RSD		**0.456994**	**1.150772**	**0.625392**	**0.731925**

Table 8: LOD and LOQ data.		
Analytes	**Telmisartan at 296nm**	**Metformin at 237nm**
LOD	0.212	0.644
LOQ	0.021	0.066

method showed better results with shorter analysis time. Hence it was proved that the method was simple, precise, rugged and reproducible for the analysis of Telmisartan and Metformin HCl in bulk and can be utilised for the daily quality control analysis.

ACKNOWLEDGEMENT

The authors shows sincere thanks to the FDC verna goa for providing the drug samples. Special and sincere thanks to the staff of Dr. Prabhakar Kore Basic Science Research centre (BSRC) for giving permission to carry out the research work. Authors also acknowledge the Principal and Vice-principal KLE College of Pharmacy, Belagavi for their constant support during the work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

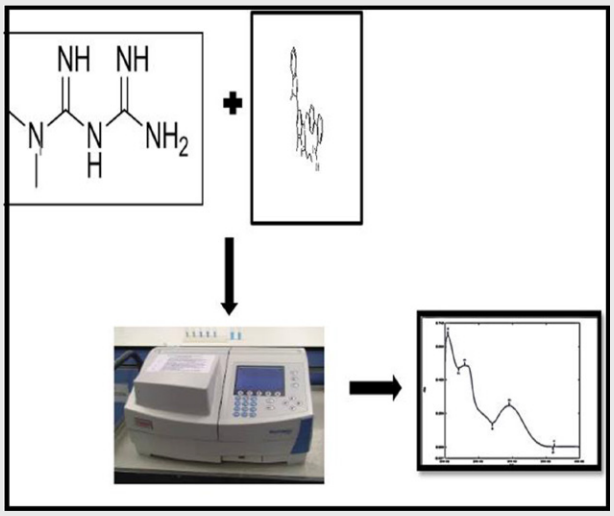
ABBREVIATIONS

UV: Ultra violet; **HPLC:** High performance liquid chromatography; **LOD:** Limit of detection; **LOQ:** Limit of quantification; **RSD:** Relative standard deviation; **SD:** Standard deviation; **ICH:** International conference of harmonization.

REFERENCES

1. www.drugbank.ca/drugs/DB00966.
2. www.drugbank.ca/drugs/DB00331.
3. Dange YD, Honmane SM, Bhinge SD, Salunke VR, Jadge DR. Development and validation of UV-Spectophotometric method for estimation of Metformin in bulk and tablet dosage form. IJPER. 2017;51(4):764-9.
4. Pawar BR, Thorat MB, Pawar NB, Karanjkar MD, Karande TS, Katkar TH. To develop UV-Spectroscopic method for estimation of Metformin hydrochloride in tablet dosage form. WJPPS. 2018;7(5):627-31.
5. Patil VP, Angadi SS, Kale SH, Shelke SD, Kawade ST, Kadam RL. Stability indicating UV-Spectroscopic method for the estimation of Metformin Hydrochloride in bulk and tablet dosage form. IJLSR. 2015;1(1):27-33.
6. 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 form. Pharm Methods. 2011;2(4):253-9.
7. Thakare L, Ahmad S, Shastry VM. Development and validation of UV-Spectrophotometric method for estimation of Clinidipine and Telmisartan in bulk and tablet dosage form. Indo Am J Pharm. 2017;7(4):8552-9.
8. Tambe MB, Patil PM. Development and Validation of Analytical Method for Estimation of Telmisartan in Bulk and Marketed Formulation by UV-Spectrophotometer. Int J Pharm Sci Rev Res. 2016;40(1):121-4.
9. Patil S, Tamboli A, More S, Pawar S. Development and validation of UV Spectrophotometric method for simultaneous estimation of Bisoprolol Fumarate and Telmisartan in tablet dosage form. IJDSR. 2020;5(6):58-63.
10. Sonia K, Nappinai M, Panneerselvam P. Stability indicating method development and Validation of Telmisartan and Ramipril by UV Spectrophotometry. Research J Pharm and Tech. 2018;11(7):3087-90.
11. Kharbade S, Asnani A, Kumar P. Development and Validation of UV Spectrophotometric Method for Simultaneous Estimation of Metformin HCl and Repaglinide in Pharmaceutical Formulation. JDDT. 2019;9(3):344-7.

PICTORIAL ABSTRACT



SUMMARY

The UV-Spectrophotometric method was developed and validated for the simultaneous estimation of Telmisartan and Metformin HCl in bulk drugs. The method was validated according to the ICH Q_2 guidelines. The solvent used for the detection was methanol and detection wavelength were found at 296nm for Telmisartan and 237nm for Metformin HCl. The forced degradation study was carried out in acidic, basic, oxidation, thermal and photolytic condition and all the values within the 5-20%. All the values of validation parameters were found to be within the acceptance limit as per the ICH guidelines. Hence the developed and validated UV-Spectrophotometric method can be used for routine quality control of Telmisartan and Metformin HCl.

About Authors

Miss. Tirodkar Chaitali Uday, has completed her B.pharm from Goa college of Pharmacy Panaji-Goa. She worked as Senior officer in Glenmark pharmaceutical limited Goa. She completed M.Pharm in Pharmaceutical chemistry from KLE College of Pharmacy Belagavi-Karnataka. Her area of interest is development and validation of analytical and chromatographic method.

Dr. M S Palled, has completed his Ph.D in Pharmaceutical Chemistry in 2011 from RGUHS, Bengaluru and M.Pharm in Pharmaceutical Chemistry from KLE College of Pharmacy, Belgaum, KUD University, Dharwad. Karnataka. His area of interest is development and validation of analytical methods and synthetic chemistry. Currently working as Professor in Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi.

Mr. Suryawanshi Shailendra Sanjay, has completed his M.Pharm in Pharmaceutical Chemistry in 2016 from Government College of Pharmacy, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka. He had 9th rank in University, Pharmaceutical Chemistry Department. He worked as Officer Bioanalytical in Bioanalytical Research and Development Department of Lotus Labs Pvt. Ltd. Bengaluru. Also he worked as Research Assistant in Analytical Research and Development unit of Apotex Research Pvt. Ltd. Bengaluru. His area of interest is development and validation of analytical and bioanalytical method which includes spectrophotometric and chromatographic analysis for drugs in bulk and pharmaceutical dosage forms. Currently he is working as Assistant Professor in Department of Pharmaceutical Chemistry, KLE College of Pharmacy, KLE Academy of Higher Education and Research, Belagavi and also he is part time Ph.D Research Scholar of KLE Academy of Higher Education and Research, Belagavi.

Miss. Majukar Surayamala Maruti, has completed B.Pharm from Maratha Mandal College of Pharmacy Belagavi-Karnataka. She also completed M.Pharm in Pharmaceutical Chemistry from KLE college of Pharmacy- Belagavi. Her area of interest is Analytical and chromatographic method development and validation.

Cite this article: Uday TC, Shivabasappa PM, Sanjay SS, Maruti MS. Development and Validation of Stability Indicating UV-Spectrophotometric Method for the Simultaneous Estimation of Telmisartan and Metformin Hydrochloride in Bulk Drugs. Indian J of Pharmaceutical Education and Research. 2021;55(2):590-7.