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VISIBLE SPECTROPHOTOMETRIC DETERMINATION OF TELMISARTAN FROM URINE

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ABSTRACT

The proposed method is new, simple, sensitive, reproducible, economical, accurate and precise and can be successfully applied in estimation of Telmisartan (Telmi) from urine. This method can find applications in clinical studies and therapeutic drug monitoring. This method of colorimetric estimation of telmisartan from urine is based on the formation of yellow colored chromogen when it is reacted with alizarin in presence of thionyl chloride. The concentration of telmisartan over a range of 10-60 µg/ml was found to obey Beer's law in the stated range. The yellow colored complex has absorption maxima at 427 nm with molar absorptivity and sandell's sensitivity 2.2387 × 10^4 lit $mol^{-1}cm^{-1}$ and 0.0154 µg/cm^2/0.001 absorbance units, respectively. The proposed method is highly sensitive, reproducible, specific, and the reagent was not found to react with the soluble matters of the body fluids. The results of analysis were validated as per ICH Q2B guidelines.

INTRODUCTION: Telmisartan or (4-((2-*n*-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-yl) methyl)-biphenyl-2-carboxylic acid is an angiotensin II receptor (type AT1) antagonist [1, 2] (**fig. 1**). It acts by blocking the vasoconstrictor and aldosterone secreting effect of angiotensin II by selective blocking the binding of angiotensin II to AT1 receptor found in vascular smooth muscles [3]. It is not official in any pharmacopoeia. It is an effective agent for the treatment of hypertension and renal impairment. It has a lower incidence of cough than ACE inhibitors. It is white to off-white crystalline powder that is insoluble in water, freely soluble in methanol and acetonitrile [4].

Literature survey reveals that difference in spectrophotometry [5], spectrophotometry in combination with other drugs [6-10], colorimetry [11-12], immunoassay development [13], liquid chromatography-tandem mass spectrometry [14-18], HPLC [19-25], micellar electrokinetic chromatographic method [26], linear sweep polarography [27], determination of pKa [28], capillary zone electrophoresis [29], HPTLC [30-33], voltametry [34] are reported for estimation of telmisartan.

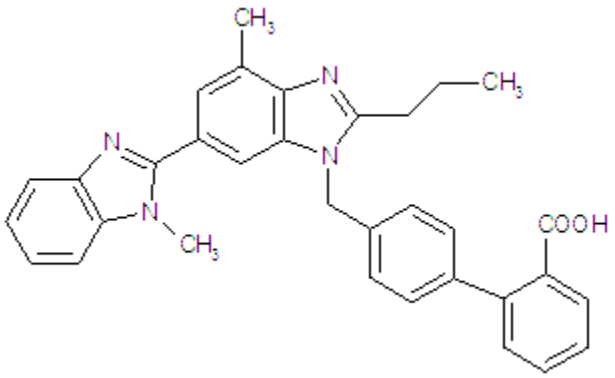

FIG. 1: STRUCTURE OF TELMISARTAN

MATERIALS & METHOD:

Instruments:

1. A PC based Jasco V-530 recording spectrophotometer with spectral bandwidth (resolution) of 2 nm and wavelength accuracy ±0.3 nm (with automatic wavelength correction) was employed for all measurements using a matched pair of 10 mm quartz cells.
2. Shimadzu AY 120 analytical balance was used for weighing.

Reagents:

1) Six concentrations of standard drug (Sun Pharma.) extracted from urine reconstituted in methanol (Standard solutions-01 to 06): 10mg of drug was added into 100 ml of collected urine sample. Protein precipitation was carried out by the addition of acetic acid and then filtered.
2) Thionyl chloride (E. Merck)
3) Alizarin reagent (Loba Chem): 10 mg alizarin was dissolved in 100ml of methanol.

Procedure for plotting calibration curve: In to a series of 10 ml volumetric flasks, 1 ml of standard solution was pipetted out separately and to each flask 1ml of thionyl chloride was added. To this, 1ml of alizarin reagent was added and the solution was heated for 10 min on water bath. The flasks were cooled and final volume was made up to 10 ml with methanol. The absorbance of yellow color complex developed was measured against the reagent blank. The colored complex showed absorbance maxima at 427 nm and obeyed Beer's law in the concentration range of 10-60 µg/ml.

The overlain spectra for the above stated concentration range is given in **figure 2**. The absorbance readings were used for plotting the calibration curve and are given in **figure 3**. Using quantitative modes of the instruments, slope, intercept and correlation coefficient values for calibration curve were obtained. The results are given in **table 1 & 2**. The concentration of telmisartan in sample solution was calculated by using formula Abs = A + B* C. The calibration curve for the above stated concentration range is given in **figure 3**.

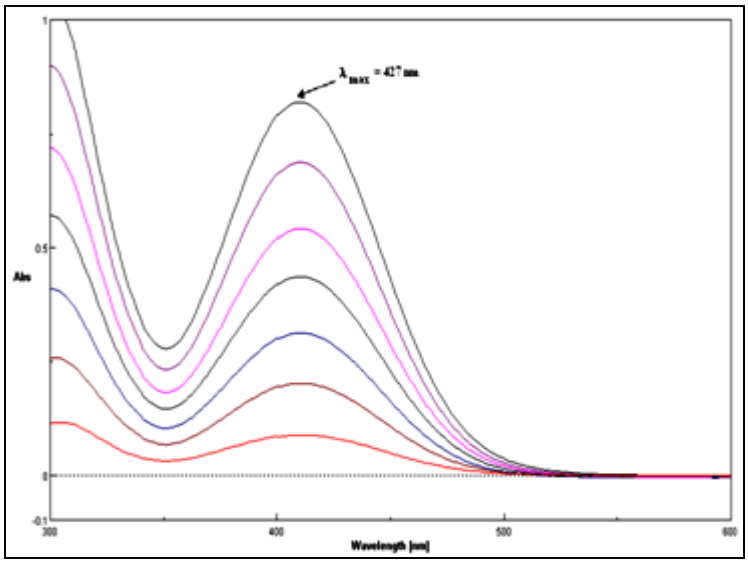

FIG. 2: OVERLAIN SPECTRA OF COMPLEX OF TELMISARTAN WITH ALIZARIN

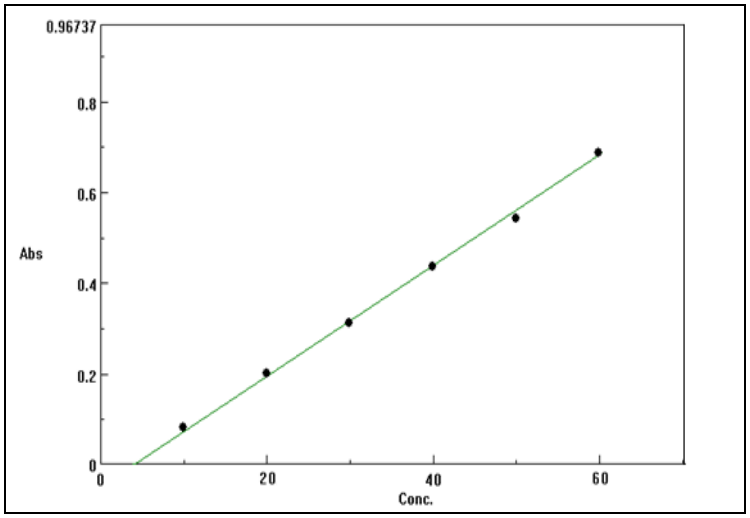

FIG. 3: CALIBRATION CURVE FOR TELMISARTAN AT 427 NM

TABLE 1: OPTICAL CHARACTERISTICS

Parameters	Values for AB
λ_{max}	427 nm
Beer's law limit (µg ml^{-1})	10-60 µg/ml
Correlation coefficient	0.9991
Regression equation (Y*)	
Slope (B)	1.2201
Intercept (A)	-0.0482

Y= A + B*C, where C is the concentration in µg ml^{-1} and Y is absorbance unit

TABLE 2: RESULTS OF ANALYSIS OF LABORATORY SAMPLE FROM URINE

Analyte	% Concentration Estimated* (Mean ± S.D.)	% R.S.D
Telmi	101.17 ± 2.00	1.20

*Average of nine determinations

Method Validation: The proposed method was validated according to ICH Q2B guidelines for validation of analytical procedures [35]. The reagent was not found to react with the soluble matters of the body fluids as shown in **Table 3**. So, there was no interference in the results of analysis due to body fluid. The validation parameters determined are precision, accuracy, specificity, linearity, LOD & LOQ. The results are given in **table 3 & 4**.

TABLE 3: RESULTS OF SPECIFICITY

Analyte (1 ml)	Absorbance at 427 nm	% R.S.D
Plasma	-0.00672*	0.45
Urine	0.00031*	0.78
Telmi	0.40375*	0.69

*Average of six determinations

Table 4: Method Validation Parameters

Parameters	Telmisartan
Linearity range	10-60 µg/ml.
Correlation coefficient (r^2)	0.9991
Precision (n = 9) (%CV)	0.54
Specificity	No interference from any of the body fluid components.
Limit of detection (LOD)	8.362 µg/ml
Limit of quantitation (LOQ)	9.21 µg/ml

RESULTS AND DISCUSSION: In the proposed method the color intensity of chromogen was intensified with 1ml of Alizarin reagent and the yellow colored complex showed a peak maximum at 427nm. Stability of the colored complex was studied and the chromogen was found to be stable for more than 48 hrs. Beer's law was obeyed in the concentration range of 10-60 µg/ml.

The equation of straight line was found to be Abs = 1.2201+0.0482 C with a correlation coefficient of 0.9991. The values for LOD and LOQ were found to be 8.362 and 9.21 respectively. The proposed method is new, simple, sensitive, accurate and precise and can be successfully applied for estimation of Telmisartan from urine.

CONCLUSION: The proposed bioanalytical method provides a sensitive and simple, approach to the determination of telmisartan in urine. Being a spectrophotometric method, the specificity is high as compared to chromatographic method. This method can find applications in clinical studies and therapeutic drug monitoring.

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REFERENCES:

1. Ebner T, Heinzel G, Prox A, Beschke K and Wachsmuth H: Disposition and chemical stability of telmisartan 1-O-acylglucuronide. Drug Metab. Dispos. 1999; 27: 11-43.
2. Stangier J, Schmid J, Turck D, Switek H, Verhagen A, Peeters, PA, Marle SP, Tamminga WJ, Sollie FA and Jonkman JH: Absorption, metabolism, and excretion of intravenously and orally administered telmisartan in healthy volunteers. J. Clin. Pharmacol. 2000; 40: 1312.
3. Patel, VA, Patel PG, Chaudhary BG, Rajgor NB and Rathi SG: Development and Validation of HPTLC Method for the Simultaneous Estimation of Telmisartan and Ramipril in combined Dosage Form. Int J Pharm Bio Res. 2010; 1(1): 18-24.
4. Gupta Y and Shrivastava A: Isocratic RP-HPLC-UV Method Development and Validation for The Simultaneous Estmation of Ramipril and Telmisartan in Tablet Dosage Form. Asian J Pharm Clin Res. 2009; 2(4): 104-111.
5. Palled MS: Difference spectrophotometric determination of telmisartan in tablet dosage forms. Indian J Pharm Sci. 2006; 68(5): 685-686.
6. Bebawy LI., Abbas SS, Fattah LA and 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(10): 859-867.
7. Bankey S, Tapadiya GG, Saboo SS, Bindaiya S, Jain D and Khadbadi SS. Simultaneous Determination of Ramipril Hydrochlorothizide and Telmisartan by Spectrophotometry. Int J ChemTech Res. 2009; 1(2): 183-188.
8. Patil UP, Gandhi SV, Sengar MR and Rajmane VS: Simultaneous determination of atorvastatin calcium and telmisartan in tablet dosage form by spectrophotometry. Int J ChemTech Res. 2009; 1(4): 970-973.
9. Thomas AB, Jagdale SN, Dighe SB and Nanda RK: Simultaneous Spectrophotometric Estimation of Amlodipine Besylate and Telmisartan in Tablet. Dosage Form. Int J ChemTech Res. 2010; 2(2): 1334-1341.
10. Mohite PB, Pandhare RB and Bhaskar VH: Simultaneous Estimation of Ramipril and Telmisartan in Tablet Dosage Form by Spectrophotometry. Eur J Ana Chem. 2010; 5 (1).
11. Zonghui Q, Weifen N and Rongn T: Spectrophotometric method for the determination of telmisartan with congo red. J Ana Chem.2009; 64(5): 449-454.
12. Kalyankar TM, Khan M, Rangari and Kakde RB: A rapid colorimetric method for the estimation of ammonia in Telmisartan in bulk and solid dosage form. International J Pharma World Res. 2010, 1(2).
13. Hempen C et al: Determination of telmisartan in human blood plasma Part I: Immunoassay development. Analytica Chimica Acta. 2006; 560: 35-40.
14. Chen BM et al: Development and validation of liquid chromatography–mass spectrometry method for the determination of telmisartan in human plasma. Analytica Chimica Acta. 2005; 540: 367-373.
15. Hempen C et al: Determination of Telmisartan in human blood plasma Part II: Liquid chromatography-tandem mass spectrometry method development, comparison to immunoassay and pharmacokinetic study. Analytica Chimica Acta. 2006; 560: 41-49.
16. Nozomu KN et al: Development and validation of a method for quantitative determination of telmisartan in human plasma by liquid chromatography-tandem mass spectrometry. J Pharm Biomed Analysis. 2007; 1:1769-1774.
17. Pengfie L et al: Determination of Telmisartan in human blood plasma Part II: Liquid chromatography-tandem mass spectrometry method development, comparison to immunoassay and pharmacokinetic study. J Chromatography B. 2005; 828: 126-129.
18. Jemal M: High-throughput quantitative bioanalysis by LC/MS/MS. Biomed. Chromatogr. 2000; 14: 422.
19. Daneshtalab N. et al: High-performance liquid chromatographic analysis of angiotensin II receptor antagonist telmisartan using a liquid extraction method. J Chromatography B. 2002; 766: 345-349.
20. Palled MS et al: RP-HPLC determination of telmisartan in tablet dosage forms. Indian J Pharm Sci. 2005; 67(1): 108-110.
21. Torrealday N et al. Experimental design approach for the optimisation of a HPLC-fluorimetric method for the quantitation of the angiotensin II receptor antagonist telmisartan in urine, J Pharm Biomed Analysis. 2003, 32, 847-857.
22. Wankhede SB: Tajne MR, Gupta KR and Wadodkar SG: RP-HPLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian J Pharm Sci., 2007; 69(2): 298-300.

23. Bhat LR, Godge RK, Vora AT and Damle MC: Validated RP-HPLC Method for Simultaneous Determination of Telmisartan and Hydrochlorothiazide in Pharmaceutical Formulation. J Liquid Chromatography & Related Technologies. 2007; 30(20): 3059-3067.
24. Kurade, VP, Pai MG and Gude R: RP-HPLC Estimation of Ramipril and Telmisartan in Tablets. Indian J. Pharm Sci. 2009; 71(2): 148-151.
25. Rane VP, Sangshetti JN and Shinde DB: Simultaneous High-Performance Liquid Chromatographic Determination of Telmisartan and Hydrochlorothiazide in Pharmaceutical Preparation. J Chromatographic Sci 2008; 46 (9): 887-891.
26. Hillaert H et al: Optimization and validation of a micellar electrokinetic chromatographic method for the analysis of several angiotensin-II-receptor antagonists. J Chromatography A. 2003; 984: 135-140.
27. Maotian X et al: Rapid determination of telmisartan in pharmaceutical preparations and serum by linear sweep polarography. J Pharm Biomed Analysis. 2004; 34: 681-687.
28. Cagigal E et al: p*K*a determination of angiotensin II receptor antagonists (ARA II) by spectrofluorimetry. J Pharm Biomed Analysis. 2001; 26: 477-486.
29. Hillaret S and Bossche VD: Optimization and validation of a capillary zone electrophoretic method for the analysis of several angiotensin-II-receptor antagonists. J. Chromatography A. 2002; 979: 323-333.
30. Prabhu C, Subramanian GS, Karthik A, Kini S, Mallayasamy SR and Udupa N: Determination of Telmisartan by HPTLC – A Stability Indicating Assay. J Planar Chromatography 2007; 20 (6): 477–481.
31. Potale LV, Damle MC, Khodke AS and Bothara KG: A validated stability indicating HPTLC method for simultaneous estimation of ramipril and telmisartan. Int. J. Comprehensive Pharm. 2010; 2 (2): 15-19.
32. Shah NJ, Suhagia BN, Shah RR and Shah PB: Development and validation of a HPTLC method for the simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian J Pharm Sci 2007; 69(2): 202-205.
33. Vekariya NR, Patel MB, Patel GF and Dholakiya RB: Development and validation of TLC-densitometry method for simultaneous determination of telmisartan and amlodipine besylate in bulk and tablets. Journal of young pharmacists. 2009; 1(3): 259-263.
34. Tasdemir IH, Akay MA, Erk N, Kılıc E. Voltammetric Behavior of Telmisartan and Cathodic Adsorptive Stripping Voltammetric Method for Its Assay in Pharmaceutical Dosage Forms and Biological Fluids, Electroanalysis, 2010; 22: 101–2109.
35. ICH Q2B, Validation of Analytical Procedures: Methodology, International Conference on Harmonization, ICH Harmonized Tripartite Guideline, Geneva, Fed. Regist, 1997; 62:27463.

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