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REVIEW ARTICLE: RP-HPLC METHOD FOR THE SIMULTANEOUS DETERMINATION OF TELMISARTAN AND ATORVASTATIN FROM BULK AND PHARMACEUTICAL DOSSAGE FORM

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ABSTRACT

A simple, accurate, precise RP-HPLC method has been developed and for the estimation of telmisartan and atorvastatin in fixed dosage formulation. The separation was achieved on a C-18 reversed phase column (ACE 5, C-18, 150mm x 4.6mm, 5µ) using Acetonitrile: Water: Orthophosphoric acid (95:5:01 v/v) as mobile phase-B & Acetonitrile: Water: Orthophosphoric acid (5:95:01 v/v) as mobile phase-A at a flow rate of 1.5ml/min and temperature of 25^0C. The UV detection was carried out at 254nm. The retention time of Telmisartan and Atorvastatin was found to be 9.08 and 14.68min respectively. The method was quantitatively evaluated in terms of Specificity, Linearity, Accuracy, Precision, and Robustness. The calibration curve for Telmisartan and Atorvastatin were linear from the range of 20.01-120.05µg/ml and 2.5-14.97µg/ml respectively. The main recoveries obtained for Telmisartan and Atorvastatin were 99.9% and 99.2% respectively. The developed method was found to be Specific, Accurate, Precise, Robust and rapid for the simultaneous estimation of Telmisartan and Atorvastatin in Bulk and Tablets 40mg/10mg & 80mg/10mg.

KEYWORDS: Telmisartan and Atorvastatin Tablets, RP-HPLC, Validation and Stability Indicating.

ABBREVATIONS: TEL – Telmisartan, ATR – Atorvastatin, RSD – Relative standard deviation.

INTRODUCTION

Telmisartan is chemically 4-[(1, 4-Dimethyl-2-propyl-[2,6-bi-1H-benzimidazole]-1-yl) methyl]-[1,1-biphenyl]-2-carboxylic acid [Figure 1], is a non peptide angiotensin-II receptor antagonist, atorvastatin is chemically [R-(R*,R*)]-2-(4-fluorophenyl)-β, δ, dihydroxy 5-(1-methyl ethyl)-3-phenyl-4 [(phenyl-amino)-carboxyl]-1 H-pyrrole-1-hepatanoic acid calcium salt [Figure 2] is a second generation synthetic 3-hydroxy-3-methyl glutaryl coenzyme A (HMG CoA) reductase inhibitor, Literature survey reveals several methods for determination of Telmisartan and Atorvastatin individually in biological fluids and formulation like HPLC, TLC-densitometric, and derivative spectrophotometer 3-8HPLC and HPTLC methods were reported for determination of Telmisartan and Atorvastatin in combination. However, so far, no method was reported using only poor solvents range of PH: 2.5±0.05 with RP-HPLC method for simultaneous determination of Telmisartan and Atorvastatin in bulk and pharmaceutical dosage form. The present developed HPLC method is simple, Precise and Accurate for simultaneous determination of both drugs in their pharmaceutical dosage forms as per International Conference on Harmonization (ICH) guidelines.[9]

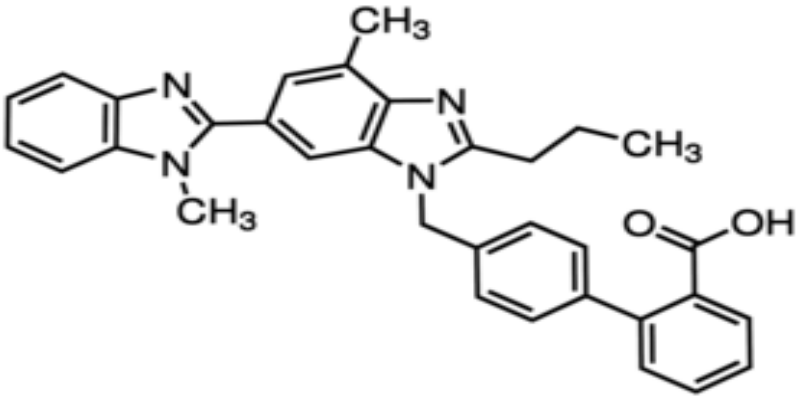

Figure 1: Structure of Telmisartan (TEL).

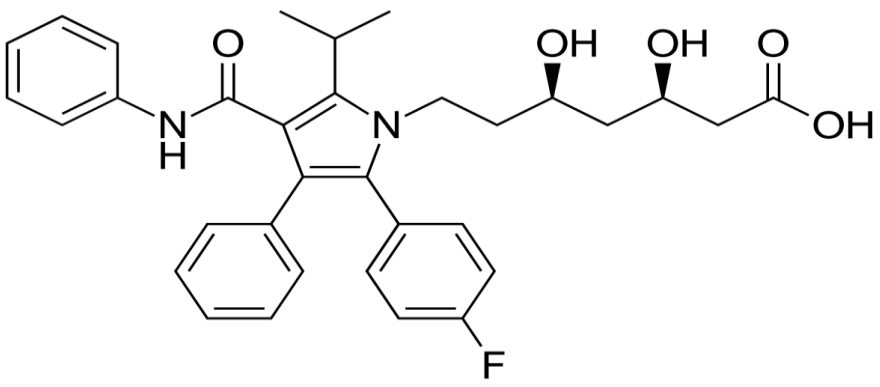

Figure 2: Structure of atorvastatin (ATR).

METHODS AND MATERIALS

Chemicals and Reagents

Telmisartan and Atorvastatin drug substance and impurities generously sponsored by Vendor, India. Commercially available TEL and ATR tablets were procured from the local market. Orthophosphoric acid (88%) were used of Analytical grade. HPLC grade Methanol, Acetonitrile (Merck) was used. Milli-Q water was used for preparation.

Instrumentation

A Chromatographic system, used for method development and method validation system was Waters-alliance HPLC equipped with separation module consisting of binary gradient pump, Auto Sampler, thermostatted column compartment, Photo-diode array detector (Model-2996) Computer with windows based Empower Software.

Chromatographic conditions

Chromatographic conditions with Gradient programme.

Column: ACE 5 C18, (150 X 4.6) mm, 5µm.

Flow Rate: 1.5ml/min.

Wavelength: 254nm

Column Temp: 25^0C

Sampler Temp: 25^0C

Run Time: 20 minutes

Injection Vol: 10µl

Gradient programme

TIME	MOBILE PHASE-A	MOBILE PHASE-B
0.01	95	5
8.0	65	35
12.0	50	50
15.0	5	95
15.1	95	5
20.0	95	5

Preparation of diluent

Methanol: Acetonitrile and Water in this ratio 50:45:5%v/v.

Preparation of standard solution

Accurately weigh and transfer about 80mg of Telmisartan and about 10mg of atorvastatin standards into a 100ml volumetric flask, add 50ml of methanol and sonicate to dissolve and dilute with methanol to volume, and mix well. Further 5ml to 50ml volumetric flask dilute with diluent.

Preparation of sample solution for 40/10mg & 80/10mg strengths

Weigh transfer tablet powder equivalent to one dose into a 100ml volumetric flask. Add 50ml of methanol and sonicate for 45 minutes with intermediate shaking. And add 25ml of diluent and sonicate for 15 minutes with intermediate shaking and dilute to volume with diluent and mix well. Centrifuge a portion of the solution with lid at 5000 RPM about 10 minutes. Pipette out 5 ml of above clear centrifuged solution into a 50 ml volumetric flak, dilute to volume with diluent and mix well.

Validation of proposed HPLC method

Telmisartan and Atorvastatin tablets are available in different strengths such as 40/10mg & 80/10mg tablets. However 80/10mg strength was considered for entire validation experimentation. The developed method was validated for specificity, Precision, Linearity, Accuracy, Solution stability and robustness as per ICH recommendation.

Specificity-Blank and Placebo interference

HPLC chromatograms were recorded for blank and placebo under optimized analytical conditions, compared with that of standard solution. To establish the interference of placebo, study was conducted. Assay was performed on placebo in duplicate equivalent to test concentration. Blank and placebo chromatogram solutions showed no peaks at the retention time of Telmisartan and Atorvastatin peak. This indicates that method is specific. The chromatogram of placebo, and standard shown in Fig 3.

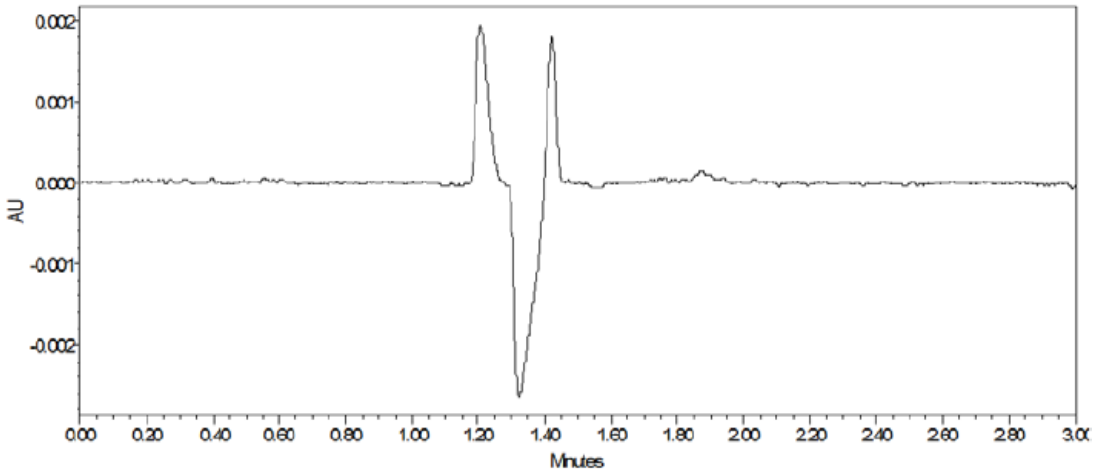

Figure 3: chromatogram of placebo.

Linearity

For HPLC method, the calibration curves for Telmisartan and Atorvastatin. Linearity was studied by plotting a graph of concentration versus response and determining the correlation coefficient. The linearity was found to be linear with a correlation coefficient of 0.999 & 0.999 Telmisartan and Atorvastatin respectively. Shown in Fig 4 & 5.

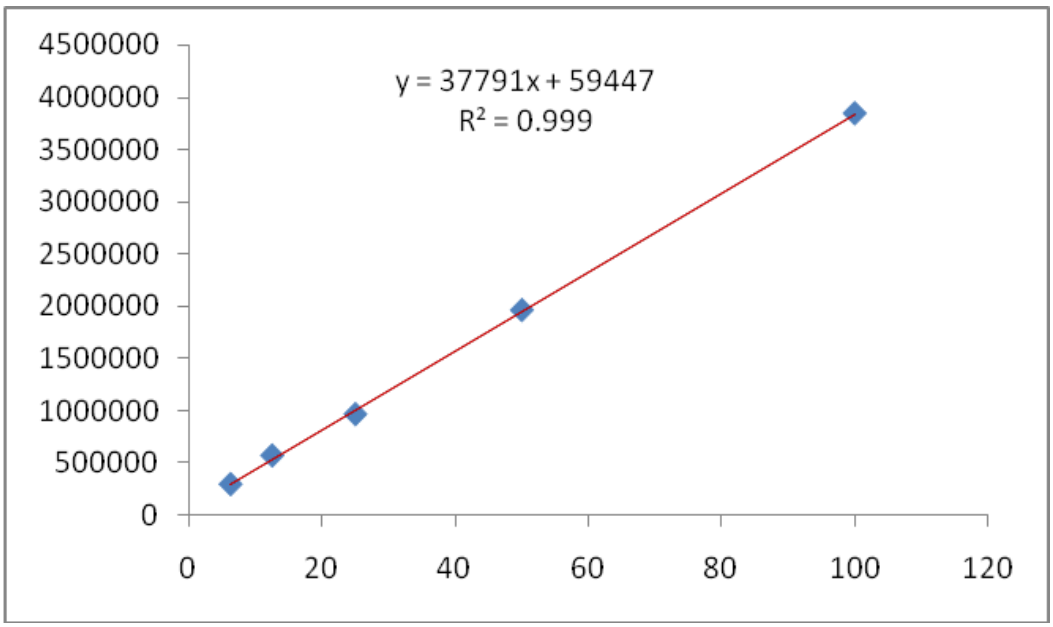

Figure 4: Linearity graph of Telmisartan.

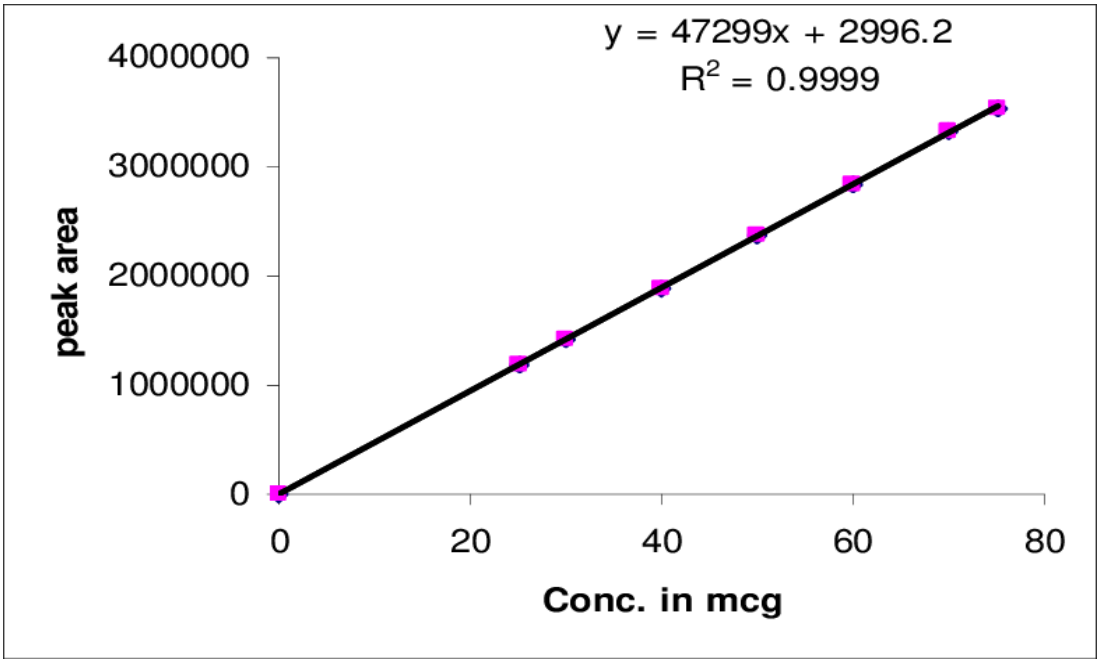

Figure 5: Linearity graph of Atorvastatin.

Method precision

The method precision was established by conducting assay in 6 samples of Telmisartan and Atorvastatin tablets. The average % assays & %RSD of TEL & ATR tablets were found to be 99.9 & 99.6 and 0.72 & 0.61 respectively. Intermediate precision was carried out by analyzing the samples by a different analyst on other instrument. The results was given in table 1.

Table 1: Precision data for TEL and ATR:

Sample No	TEL		ATR	
	% Assay in method precision	% Assay in intermediate precision	% Assay in method precision	% Assay in intermediate precision
1	99.7	100.9	100.6	101.5
2	100.6	98.9	99.5	98.4
3	99.0	100.1	99.1	99.2
4	99.5	99.6	99.1	98.7
5	100.9	99.2	100.1	99.3
6	99.6	99.7	99.3	99.0
Average (n=6)	99.9	99.7	99.6	99.3
%RSD (n=6)	0.72	0.71	0.61	1.11
%RSD (n=12)	0.65		0.91	

Accuracy

A known amount of TEL and ATR drug is added to the placebo at 50% (respect to lower strength), 100% and 150% of the analyte concentration. Sample solutions were prepared in triplicate for each spike level and assay was determined as per proposed method. The observed recovery results were found in the range between 98 to 102% for TEL and 98 to 102% for ATR, demonstrating that the method is accurate with in the desired range. The results were given in table 2 & 3.

Table 2: Accuracy data of telmisartan.

S. No.	% Level	Amount added (mg)	Amount recovered (mg)	% Recovery	% mean recovery	% RSD
1		20.125	20.246	100.6		
2	25	20.145	20.125	99.9	100.2	0.4
3		20.042	20.082	100.2		
1		80.016	79.456	99.3		
2	100	80.115	79.795	99.6	99.6	0.3
3		80.017	79.937	99.9		
1		120.03	120.15	100.1		
2	150	120.19	119.47	99.4	99.8	0.4
3		120.10	119.86	99.80		

Table 3: Accuracy data of atorvastatin.

S. No.	% Level	Amount added (mg)	Amount recovered (mg)	% Recovery	% mean recovery	% RSD
1		5.1254	5.1049	99.6		
2	50	5.1453	5.0630	98.4	99.0	0.6
3		5.0421	4.9917	99.0		
1		10.016	9.826	98.1		
2	100	10.115	10.034	99.2	99.1	1.0
3		10.017	10.017	100.0		
1		15.036	15.05	100.1		
2	150	15.198	15.03	98.9	99.6	0.6
3		15.142	15.11	99.8		

Solution stability

Standard and sample solutions were prepared as per proposed method and analysed initially and at different time intervals by keeping the solutions at room temperature (~25^{0}C) for 96 hours. % Difference between the assays obtained for TEL and ATR, initial and different time interval should not be more than 2.0. From the results it can be concluded that the standard and sample solutions are stable up to 48 hours at room temperature (~25^{0}C).

Robustness

The robustness was studied by evaluating the effect of small but deliberate variations in the chromatographic conditions. The conditions studied were flow rate (altered by ± 0.1ml min-1), wavelength (altered by ± 5nm), variation in mobile phase composition (± 0.2% absolute), column oven temperature (± 5^0C), standard solution was prepared and injected into HPLC system. The system suitability parameters were evaluated. In all the cases, the % RSD obtained was less than 1. From the above study the proposed method was found to be robust.

CONCLUSION

The HPLC method developed is accurate, precise, reproducible, and specific there is allowable variation in flow rate, temperature, pH, and mobile phase composition which indicate that method is robust enough. The low RSD value for percent assay of test preparation revealed that the proposed method is rugged and can be applied for the routine and less cost effective method for bulk and dosage form.

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