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SIMULTANEOUS DETERMINATION OF TELMISARTAN AND ATORVASTATIN BY RP-HPLC METHOD IN TABLET DOSAGE FORM

[1]Mohammed Anwar Ahmed[*], [2]**Shaik Harun Rasheed**

[1]Department of Pharmaceutical Analysis, MRM College of pharmacy, Chintapalliguda, Ibrahimpatnam, Hyderabad-501510
[2]Department of pharmaceutics MRM College of pharmacy, Chintapalliguda, Ibrahimpatnam, Hyderabad-501510

ABSTRACT

Estimation of Telmesartan and Atrovastatin was done by RP-HPLC. The Phosphate buffer was p^H 4.5 and the mobile phase was optimized with consists of Acetonitrile: Phosphate buffer mixed in the ratio of 75:25 % v/ v. A Xbridge C18,column was used. The detection was carried out using PDA detector at 220 nm. Telmesartan and Atrovastatin Linear regression coefficient was not more than 0.999. The values of % RSD are less than 2% indicating accuracy and precision of the method.

Key words: Telmesartan, Atrovastatin, RP-HPLC.

Author for correspondence:
Mohammed Anwar Ahmed,
Department of Pharmaceutical Analysis, MRM college of pharmacy, Chintapalliguda, Ibrahimpatnam, Hyderabad-*501510*

Email: md.anwar1601@gmail.com

INTRODUCTION

Telmisartan medoxomil(Fig-1), a prodrug, is hydrolyzed to Telmisartan during absorption from the gastrointestinal tract. Telmisartan is a selective AT1 subtype angiotensin II receptor antagonist.

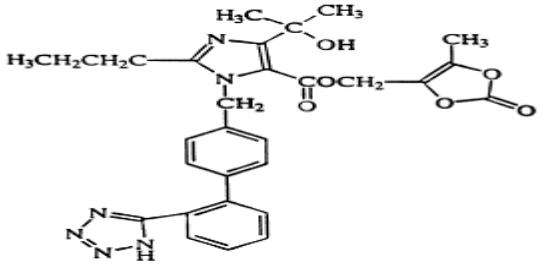
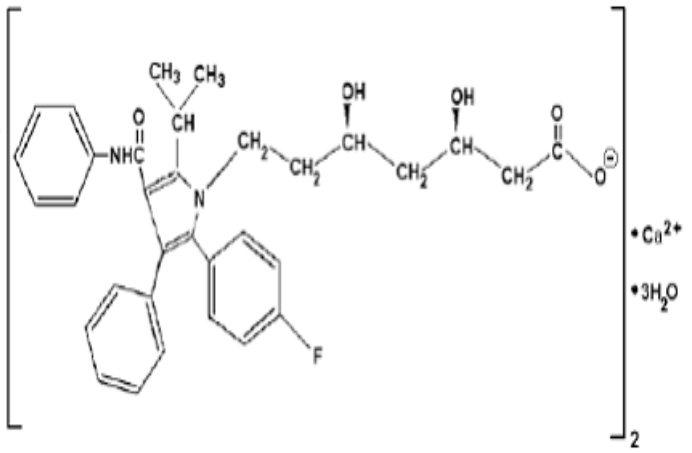


Figure-1 Structure of Telmisartan

Atorvastatin (Fig-2) is a synthetic lipid-lowering agent. Atorvastatin is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step in cholesterol biosynthesis.

Figure-2 Structure of Atorvastatin calcium



A literature survey was carried out for the simultaneous estimation of Telmisartan and Atrovastatin in marketed dosage forms. It was found that a few methods have been reported for these drugs individually or in combination with other drugs (1-5). Therefore an attempt was made to develop and validate a simple and economical RP-HPLC method as per ICH guidelines for the simulataneous estimation Telmisartan and Atrovastatin in pharmaceutical dosage forms.

MATERIALS AND METHODS

Equipment

HPLC with PDA detector (Waters), Sonicator (Ultrasonic sonicator), P^H meter (Thermo scientific), Micro balance (Sartorius) and Vacuum filter pump

Chemicals

Methanol HPLC Grade (RANKEM), Acetonitrile HPLC Grade (RANKEM), HPLC grade Water (RANKEM), Orthophosphoric acid (RANKEM).The standard samples of Telmisartan and Atrovastatin were obtained from Hetero labs, Hyderabad . The tablet dosage form TELTOR-AV is obtained from Hetero Pharmacy (Label claim: 20 mg of Telmisartan , 10 mg of Atrovastatin).

Sample Preparation

5 tablets were weighed and caluculate the average weight of each tablet then the weight equivalent to 20 tablets was transferred into a 100 mL volumetric flask, 70mL of diluent added and sonicated for 25 min, further the volume made up with diluent and filtered. From the filtered solution 1ml was pipeted out into a 10 ml volumetric flask and made upto 10ml with diluent.

Assay Methodology

Assay of the marketed formulation was carried out by injecting sample corresponding to equivalent weight into HPLC system. And percent purity was found out by following formulae.

Calculate the percentage purity of Zidovudine present in tablet using the formula:

Calculation:

$$\text{Assay} = \frac{\text{Spl area}}{\text{Std area}} \times \frac{\text{Std. Dil. Fac}}{\text{Spl. Dil. Fac}} \times \frac{\text{Avg. Wt of Tab}}{\text{L.C}} \times \text{Potency of Std}$$

Validation of developed HPLC Method

A HPLC method has been developed for simultaneous estimation of Telmisartan and Atrovastatin using Xbridge C18 (150 x 4.6 mm, 5µ.), mobile phase Buffer and Acetonitrile(Gradient), detection wavelength at 240 nm, at flow rate of 1 ml/min at retention time 2.6min for Telmisartan, 5.20 min for Atrovastatin. Since the HPLC method has been developed, validation of method by using various parameters such as System suitability, Specificity, LOD (Limit of Detection), LOQ (Limit of Quantification), Linearity and Range, Precision, Accuracy and Robustness was performed to ensure that the performance characteristic of the method meets the requirements for the intended analytical applications (6-10).

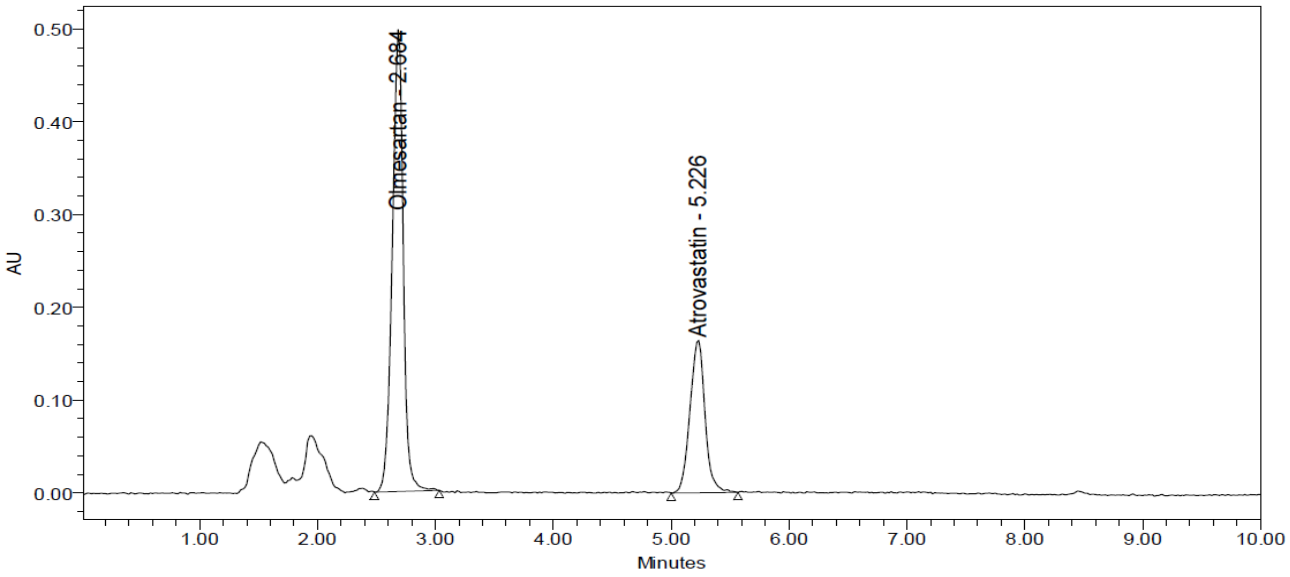
RESULTS AND DISCUSSION

Optimized Chromatographic Conditions were given in table-1.

Table -1 Optimized Chromatographic Conditions

Flow rate	**1**ml/min
Column	Xbridge C18, 150 x 4.6 mm, 5µ.
Detector wave length	240nm
Column temperature	30°C
Injection volume	10µL
Run time	10 min
Diluent	Acetonitrile
Mobile phase	Buffer : Acetonitrile(Gradient)

Figure-3 shows optimised chromatogram of Telmesartan and Atrovastatin with above tableted parameters



	Peak Name	RT	Area	% Area	USP Plate Count	USP Tailing
1	Olmesartan	2.684	3222238	68.90	4213	0.96
2	Atrovastatin	5.226	1454354	31.10	8474	1.04

Figure-3 optimised chromatogram of Telmesartan and Atrovastatin

The retention time for Telmesartan was found to 2.684min, the retention time for Atrovastatin was found to be 5.226min.

Precision was carried out with six samples. Six Sample solutions were prepared individually from Ziprasidone stock solution,as per methodology and injected each solution into HPLC. % RSD Should not is more than 2.0% (Table-2 and 3).

Table -2 precision study

Sample No	Sample (OLME)	%Assay	Sample(ATRO	%Assay
1.	3449188	99.85	1242482	99.19
2.	3473890	100.56	1244990	99.39
3	3451168	99.90	1252525	99.99
4	3449696	99.86	1264376	100.94
5	3427875	99.23	1259931	100.58
6	3455993	100.04	1246329	99.50
AVG	3451302	99.91	1251772	99.93
STANDARD DEVIATION	14752.04	0.427	88086	0.7032
% RSD	0.43	0.4	0.70	0.70

Table -3 system precission

System Precission	Telmesartan Areas	Atrovastatin Areas
1	3431461	1242391
2	3470803	1247949
3	3455555	1243855
4	3459457	1241631
5	3457275	1260268
6	3411000	1264802
AVG	3447592	1250149
SD	22072	9942.85
%RSD	0.64	0.80

The system suitability parameters were determined for Atrovastatin and Telmesartan and were found to be within the acceptance criteria. LOD for Atrovastatin and Telmesartan were found to be 0.76µg/ml and 2.6µg/ml respectively. Limit of quantification of Atrovastatin and Telmesartan were found to be 2.31µg/ml and 7.9µg/ml respectively.

The proposed method is found to be linear at concentration of 100-300 µg/ml for telmisartan and 50-150 µg/ml for Atrovastatin. The correlation coefficient and % curve fitting for Olmeasartan and Atrovastatin were found to be 0.999, 99.9% and 0.999, 99.9% respectively which is well within the acceptance criteria limits.

The mean percentage recovery for Atrovastatin and Telmesartan was found to be between 98.95-102.3%, 98.94-102.66 % and 98.98-101.66 % respectively, which are well within the limit and hence the method was found to be accurate.

The RSD values of intraday precision for replicate injections of Atrovastatin and Telmesartan were found to be between 1.883 and 0.882 respectively which are well within the acceptance criteria limit(RSD $\leq$ 2).

Robustness was carried out check the ability of the system to give unaffected results for small deliberate changes in system parameters and method parameters (Table-4 and 5

Table -4 Change in flow rate

Change in flow rate (±0.1)		Flow rate 1.1ml/min	Flow rate 1ml/min	Flow rate 0.9ml/min	Mean ±SD	%RSD
SYSTEM SUITABILITY PARAMETERS						
Peak area	**Telmesartan**	1138949	1103501	1102054	1114835	1.87
	Atrovastatin	3174175	3133765	3126618	3144853	0.81
Retention time	**Telmesartan**	2.38	2.35	2.34	2.35 ± 0.02	
	Atrovastatin	5.97	5.81	5.87	5.88 ± 0.08	
Tailing factor	**Telmesartan**	1.11	1.19	1.17	1.15 ± 0.04	
	Atrovastatin	0.98	1.04	0.99	1.0 ± 0.03	
Theoritical Plates	**Telmesartan**	2457	2513	2449	247 ± 34	
	Atrovastatin	6932	6534	6575	6680 ± 218	

Table -5 changes in mobile phase concentration

Change in mobile phase Buffer:methanol		60:40v/v	55:45v/v	55:45v/v	Mean ± SD	%RSD
SYSTEM SUITABILITY PARAMETERS						
Peak area	**Telmesartan**	1115364	1103501	110608	110824	0.56
	Atrovastatin	3205021	3133765	324981	3196226	1.83
Retention time	**Telmesartan**	2.36	2.35	2.31	2.34 ± 0.026	
	Atrovastatin	5.94	5.81	5.48	5.74 ± 0.237	
Tailing factor	**Telmesartan**	1.16	1.19	1.14	1.16 ± 0.025	
	Atrovastatin	1.01	1.04	1.00	1.01 ± 0.020	
Theoritical plates	**Telmesartan**	2551	2513	2651	2571 ± 71	
	Atrovastatin	6071	6534	5619	6074 ± 457	

From the above observation, it can be concluded that, the method is robust with respect to change in mobile phase, temperature and organic phase ratio.

CONCLUSION

High performance liquid chromatography is at present one of the most sophisticated tool of the analysis. The estimation of Telmesartan and Atrovastatin was done by RP-HPLC. The Phosphate buffer was p^H 4.5 and the mobile phase was optimized with consists of Acetonitrile: Phosphate buffer mixed in the ratio of 75:25 % v/ v. A Xbridge C18,column was used. The detection was carried out using PDA detector at 220 nm. The solutions were chromatographed at a constant flow rate of 1ml/min. the linearity range of Telmesartan and Atrovastatin were found to be rom 10-50 µg/ml.of Telmesartan and Atrovastatin Linear regression coefficient was not more than 0.999. The values of % RSD are less than 2% indicating accuracy and precision of the method. Telmesartan and Atrovastatin LOD and LOQ were found to be within limit. The results obtained on the validation parameters met ICH and USP requirements .it inferred the method found to be simple, accurate, precise and linear. The method was found to be having suitable application in routine laboratory analysis with high degree of accuracy and precision.

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