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Simultaneous estimation of telmisartan and atorvastatin calcium in API and tablet dosage form

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ABSTRACT

A new method has been established for the simultaneous estimation of Telmisartan and Atorvastatin calcium by RP-HPLC method. The chromatographic conditions were successfully developed for the separation of Telmisartan and Atorvastatin calcium by using boston ODS C18 column, flow rate was 1.0ml/min, mobile Phase consists of methanol:Acetonitrile:buffer in ratio of 35:25:40. Detection wave length was 235nm.The instrument used was SHIMADZU HPLC auto sampler. The retention time of Atorvastatin calcium and Telmisartan was found to be 2.350 and 3.490 minutes respectively. The analytical method was validated according to ICH guidelines (ICH Q2b). The correlation coefficient (r^2) was found to be 0.997 and 0.999 for Telmisartan and Atorvastatin calcium respectively. % mean recovery was found to be 100.943% and 100.576% for Telmisartan and Atorvastatin calcium respectively. %RSD for precision on replicate injection was 0.46 and 0.70 for Telmisartan and Atorvastatin calcium respectively. The validation study was found to be precise, robust, and repeatable.

Keywords: Telmisartan, Atorvastatin calcium, ICH guidelines, Validation.

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INTRODUCTION

Telmisartan

Telmisartan is an orally active non peptide Angiotensin II antagonist that acts on the AT_1 receptor subtype. Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT_1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of aldosterone, blockage of its effects results in decreases in systemic vascular resistance. Telmisartan does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels[1-3].

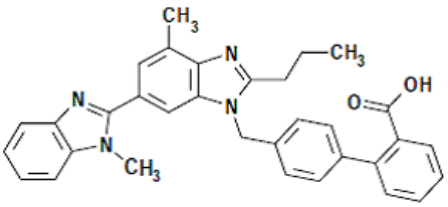


Figure 1: Chemical Structure of Telmisartan

Atorvastatin calcium

Atorvastatin calcium (ATV), (βR,dR)-2-(4fluorophenyl)-β,d-dihydroxy-5-(1-methylethyl)-3-phenyl4-[(phenylamino) carbonyl]-lH-pyrrole-1-heptanoic acid, calcium salt, is a synthetic cholesterol-lowering agent1. Atorvastatin calcium selectively and competitively inhibits the hepatic Hydroxy methyl glutaryl-coenyme A (HMG-CoA) reductase, the rate-determining enzyme located in hepatic tissue that produces mevalonate, a small molecule used in the synthesis of cholesterol and other mevalonate derivatives. This lowers the amount of cholesterol produced which in turn lowers the total amount of LDL cholesterol.[4-6]

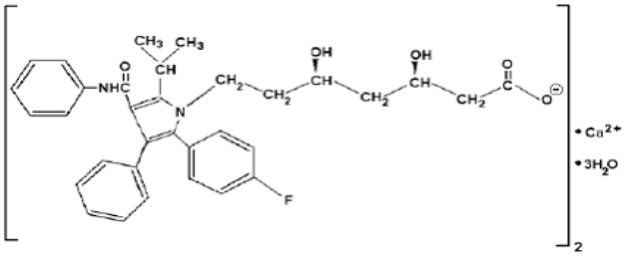


Figure 2: Chemical Structure of Atorvastatin calcium

METHODS & MATERIALS

Chemicals and reagents Analytically pure Telmisartan and Atorvastatin calcium were obtained as gift samples from Sun Pharmaceutical Pvt. Ltd., Baroda, India. AR grade acetonitrile, methanol, Triethylamine, Potassium Dihydrogen phosphate, Sodium Dihydrogen phosphate were obtained from E. Merck Ltd., Mumbai, India. Tablet formulation Telmisartan and Atorvastatin calcium tablets were purchased from local market.

Method development of telmisartan and atorvastatin calcium by RP-HPLC[7-12]:

The detection wavelength was selected by dissolving Telmisartan and Atorvastatin calcium in diluent to get concentration of the 10µg/ml. The resulting solution was scanned in U.V range from 200-400nm. The absorbance maximum was found to be 235nm. The chromatographic method development for the estimation of Telmisartan and Atorvastatin calcium were optimized by several trials for various parameters as different column, flow rate and mobile phase, finally the following chromatographic method was selected for the separation and quantification of Telmisartan and Atorvastatin calcium in API and pharmaceutical dosage form by RP-HPLC.

Preparation of solutions for optimized conditions of method validation[8-10]:

Buffer Preparation:

1.3609 gm of Potassium di-hydrogen phosphate was added in sufficient water to produce 1000ml, pH adjusted to 4.5 with orthophosphoric acid.

Solvent mixture:

Prepare mixture of methanol, acetonitrile and buffer in ratio of 35:25:40v/v respectively.

Mobile phase:

Prepare a filtered (0.45µ) and degassed mixture of methanol, acetonitrile and buffer preparation in ratio of 35:25:40v/v respectively.

Chromatographic conditions:

Parameter	Condition
Column	Boston ODS C18 column
Mobile phase	methanol:Acetonitrile:buffer 35:25:40
Column Temperature	25^{0}C
Wavelength	235nm
Flow rate	1.0 ml/min
Auto sampler temperature	Ambient
Injection volume	0.2ml
Run time	8 minutes

RESULTS AND DISCUSSION

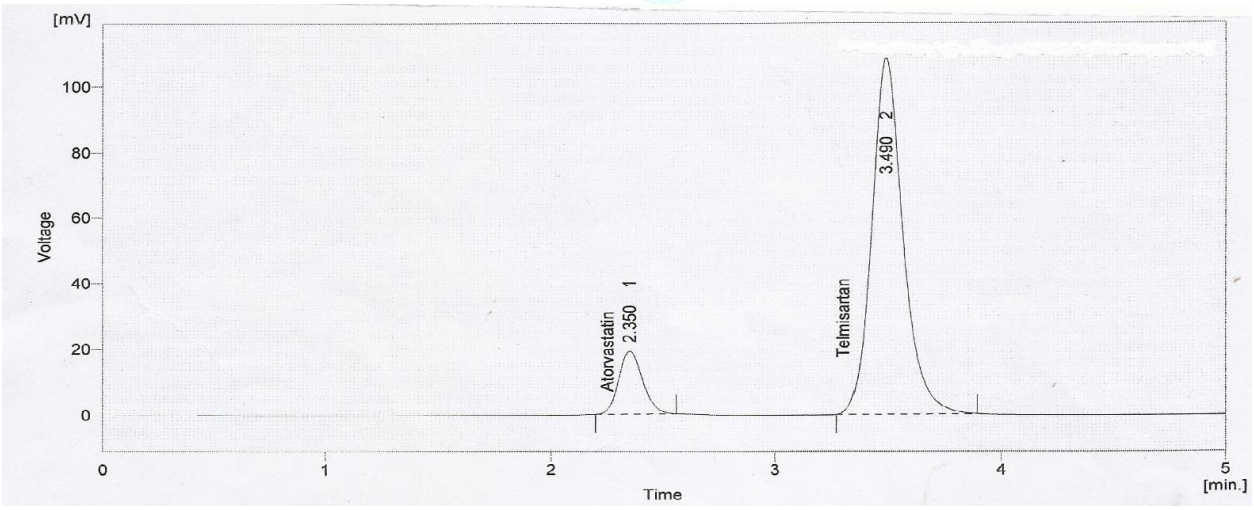
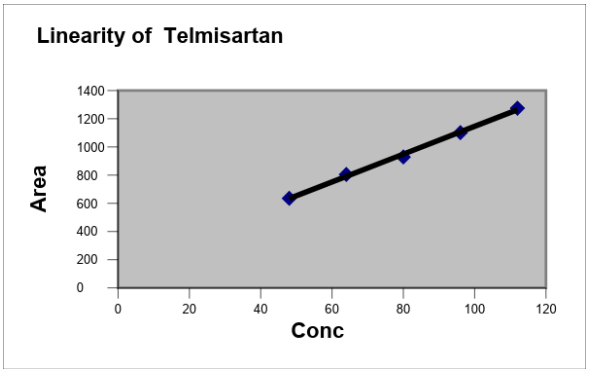


Figure 3: chromatogram

S.NO	Name	RT(min)	Asymmetry	Theoritical plates	Area	Resolution
1	AC	2.350	1.370	2382	136.161	--
2	TM	3.490	1.316	3284	1035.333	5.227

Linearity:

The linearity study was performed for the concentration of 60ppm to 140ppm level. Each level was injected into chromatographic system the area of each level was used for calculation of correlation coefficient. The linearity study was performed and the correlation coefficient of Telmisartan and Atorvastatin calcium was found to be 0.999 and 0.997 respectively (NMT 0.999).



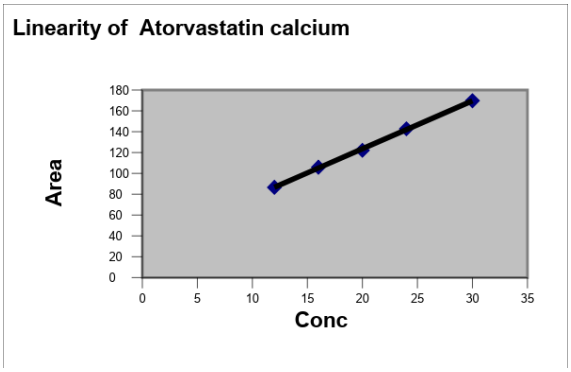


Figure 4: Calibration curve of Telmisartan

Figure 5: Calibration curve of Atorvastatin calcium

Table 1: Results of linearity study

S.No	Linearity Level	Concentration	Area of Telmisartan	Area of Atorvastatin calcium
1	I	60ppm	635.316	86.613
2	II	80ppm	804.182	105.914
3	III	100ppm	928.411	122.129
4	IV	120ppm	1101.576	142.812
5	V	140ppm	1274.763	169.731
Correlation coefficient			**0.999**	**0.997**

Accuracy

Accuracy of the method was determined by Recovery studies. To the formulation (pre analysed sample), the reference standards of the drugs were added at the level of 80%, 100%, 120%. The recovery studies were carried out three times and the percentage recovery and percentage mean recovery were calculated for drug.

Table 2: Results for accuracy of Telmisartan

Recovery level	Accuracy of telmisartan					Average % Recovery
	Amount taken (mcg/ml)	Area	Average area	Amount recovered (mcg/ml)	%Recovery	
80%	64	1035.01	1032.530	81.16	101.45	100.943 %
	64	1026.185				
	64	1036.395				
100%	80	1101.576	1104.674	95.19	99.15	
	80	1102.274				
	80	1110.173				
120%	96	1328.71	1313.850	114.50	102.23	
	96	1322.727				
	96	1290.113				

Table 3: Results for accuracy of Atorvastatin calcium

Recovery level	Accuracy of Atorvastatin calcium					Average % Recovery
	Amount taken (mcg/ml)	Area	Average area	Amount recovered (mcg/ml)	%Recovery	
80%	16	130.148	133.703	20.20	100.99	100.576 %
	16	135.519				
	16	135.443				
100%	20	142.812	144.957	23.74	98.91	
	20	143.275				
	20	148.784				
120%	24	172.511	169.660	28.51	101.83	
	24	167.307				
	24	169.163				

Precision:

The precision study was performed for six injections of Telmisartan and Atorvastatin calcium. Each standard was injected into chromatographic system. The area of each standard injection was used for calculation of %RSD.

Table 4: Method precision results for Telmisartan and Atorvastatin calcium

S.NO.	Telmisartan		Atorvastatin calcium	
	Retention Time	Area	Retention Time	Area
1	3.510	1015.834	2.363	126.473
2	3.500	1026.375	2.35	135.444
3	3.510	1023.904	2.36	133.190
4	3.513	1023.366	2.363	133.075
5	3.470	1041.225	2.32	135.357
6	3.503	1021.136	2.357	133.526
Average	3.501	1025.307	2.3522	132.844
SD	0.016	8.572	0.0165	3.296
%RSD	0.46	0.84	0.70	2.48

Robustness:

Chromatographic conditions variation:

To demonstrate the robustness of the method, prepared solution as per test method are injected at different variable conditions like using different conditions like flow rate and wavelength. System suitability parameters were compared with that of method precision.

Table 5: Robustness results for Telmisartan and Atorvastatin calcium

Parameter	Telmisartan		Atorvastatin calcium	
	Retention time(min)	Asymmetry	Retention time(min)	Asymmetry
Flow Rate				
0.8 ml/min	4.450	1.319	2.987	1.294
1.2 ml/min	2.830	1.273	1.900	1.292
Wavelength				
233nm	3.490	1.316	2.347	1.286
237nm	3.500	1.324	2.350	1.333

Ruggedness:

Ruggedness of the method was studied by determining the analyst to analyst variation by performing the Assay by two different analysts

Table 6: Ruggedness results for Telmisartan and Atorvastatin calcium

Parameter	Telmisartan		Atorvastatin calcium	
	Retention time(min)	Asymmetry	Retention time(min)	Asymmetry
Analyst 1				
Standard	3.510	1.324	2.363	1.259
sample	3.500	1.277	2.350	1.346
Analyst 2				
Standard	3.510	1.263	2.360	1.296
sample	3.500	1.297	2.350	1.333

Table 7: Results for system suitability of Telmisartan and Atorvastatin calcium

Injection	Telmisartan				Atorvastatin calcium			
	RT	Peak area	Theoretical plates	Asymmetry	RT	Peak area	Theoretical plates	Asymmetry
1	3.510	1015.834	3482	1.324	2.363	126.473	2557	1.259
2	3.500	1026.375	3463	1.297	2.350	135.444	2382	1.333
3	3.510	1023.904	3482	1.263	2.360	133.190	2550	1.297
4	3.513	1023.366	3329	1.289	2.363	133.075	2409	1.250
5	3.470	1041.225	3403	1.324	2.320	135.357	2621	1.280
6	3.503	1021.136	3310	1.263	2.357	133.526	2395	1.259
Mean	3.501	1025.307			2.3522	132.844		
SD	0.016	8.572			0.016	3.296		
%RSD	0.70	2.48			0.70	2.48		

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