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Research Article

A Validated RP-HPLC Method for Tablets Containing Amlodipine Besylate and Telmisartan HCl as Active Pharmaceutical Ingredient

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ABSTRACT

The LC method for the determination of test procedures of Assay for Amlodipine Besylate and Telmisartan HCl in bulk drug, and tablets were simple, reliable, sensitive and less time consuming. The positivity of the present working procedures was a simple isocratic method. The present method can be used for rapid and precise quantification of Amlodipine Besylate and Telmisartan HCl. The present work showing a validation with highly sensitive and selective method for the estimation of Amlodipine Besylate and Telmisartan HCl in pharmaceutical dosage forms.

Keywords: HPLC; Amlodipine Besylate; Telmisartan HCl; Chromatogram; Validation

INTRODUCTION

Importance of Chromatography

The importance of Chromatography is increasing rapidly in pharmaceutical analysis. The precise differentiation, selective identification and quantitative determination of structurally closely related compounds [1,2].

High performance Liquid Chromatography (HPLC)

The cutting edge kind of chromatography has been called superior, high, high goal and fast fluid chromatography.

Guideline of division in HPLC

The standard of partition in typical stage HPLC is adsorption. At the point when blends of segments are acquainted in with a HPLC section, they travel predictable with their relative affinities towards the fixed stage. (Figure 1). The segment which has greater partiality towards the adsorbent ventures more slowly [3].

Solvent reservoir

The dissolvable or portable stage store has a few attributes. The arrangement of repository should render it latent to an assortment of watery and non-fluid is to be pressurized; glass is to be kept away from.

Pumps

HPLC is every now and again conveyed as elite fluid chromatography; the siphon must be equipped for creating weights of up to 3 ml/min for diagnostic arrangements. The dissolvable stream from the siphon ought to be beat less or ought to be hosed so as to expel beats, since the weight of heartbeats in the stream may cause deceptive outcomes with certain indicators.

Injection device

The infusion of the example on to the segment presents some one of a kind issues in light of the high-pressure associated with HPLC. While septum injectors can be utilized in HPLC, the circle injectors find greatest use in HPLC. Initially, the example ought to infuse in tight fitting [4]. Column, Detector, and Recorder are according to the experimentally needed.

MATERIALS AND METHODS

Instrument used: Younglin HPLC - ACME-9000

Detector: UV/Visible detector

Integration: done by using AutoChro-3000 software package

Solvents used: HPLC Grade (Merck)

Reagents and Chemicals

Water (purified using Millipore Milli Q system), Methanol, Acetonitrile, Amlodipine Besylate and Telmisartan Hcl, Preparation of 0.02 M Ammonium acetate buffer,Buffer was prepared by dissolving 2.72 g of Potassium dihydrogenorthophosphate (KH_2PO_4) in 1L of water and followed by the degassing of the solution (Figure 2).

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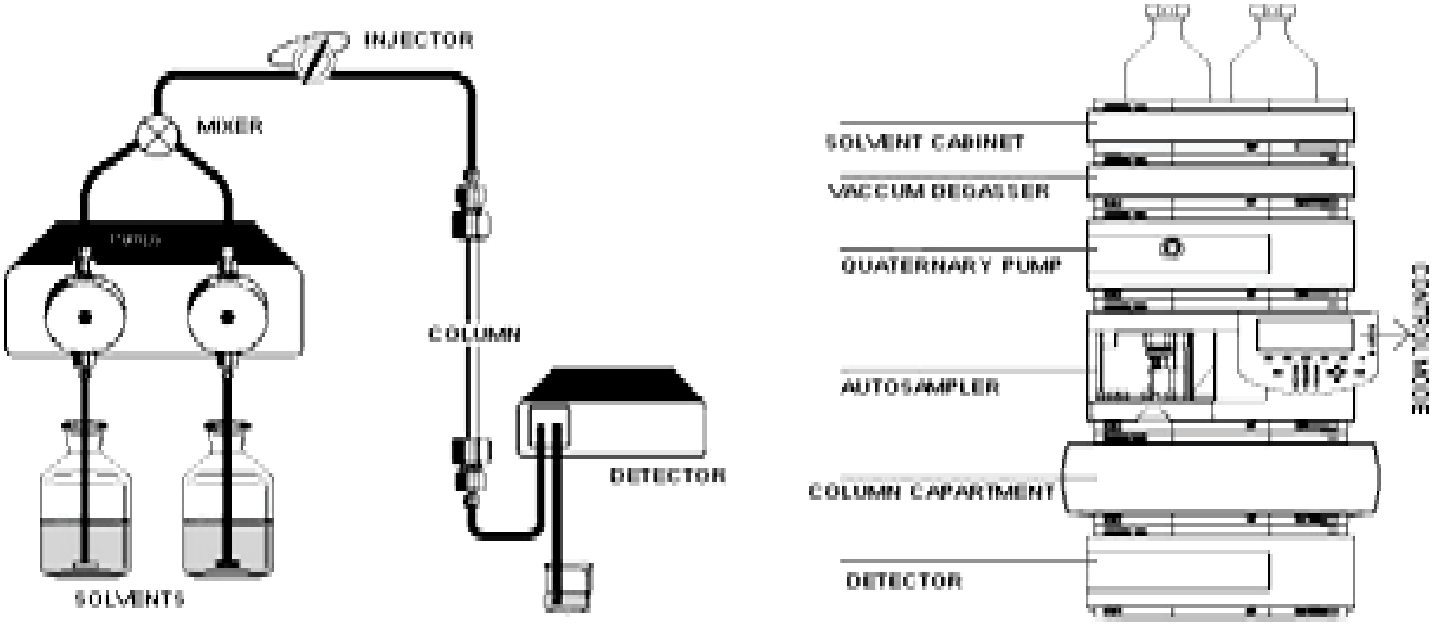

Figure 1: The essential parts of high performance liquid chromatography are: Solvent Reservoir, Pumps, Injection Device, Column, Detector, and Recorder.

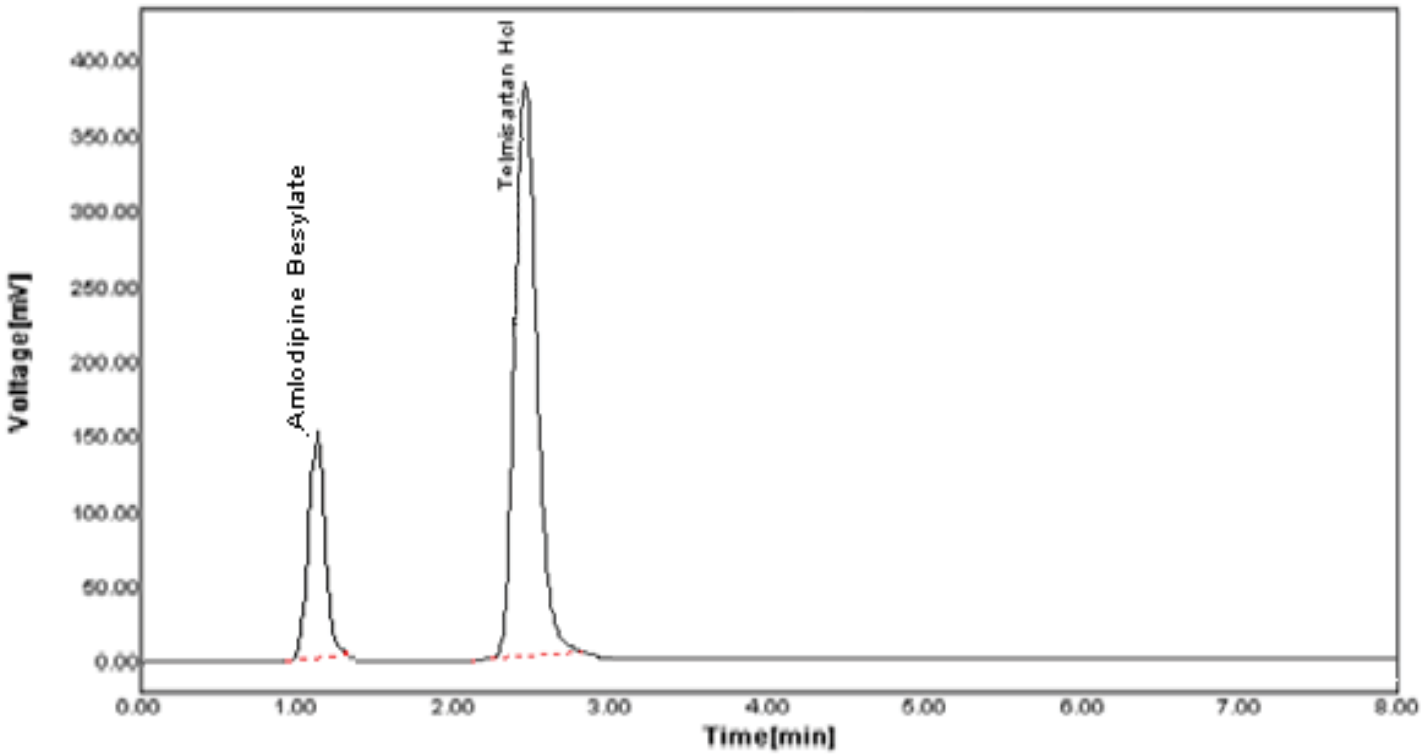

Figure 2: Mobile phase-100% Methanol. Faster elution of the analyst.

Diluent preparation

1L of diluent was prepared by mixing 450 ml of 0.02 M Phosphate Buffer, 300 ml of Acetonitrile and 250 ml of Methanol.

Preparation of stock solution

Accurately weighed 10 mg of the both Amlodipine Besylate and Telmisartan HCl was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the Methanol and mixed well. This yielded a stock solution with concentration 1000 ppm of Amlodipine Besylate and Telmisartan HCl mixture (Figure 3).

Preparation of standard solution

Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well. (Figure 4). This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively [5].

Standard solution were prepared as per the test method and injected six times to test the performance of the chromatographic instrument.

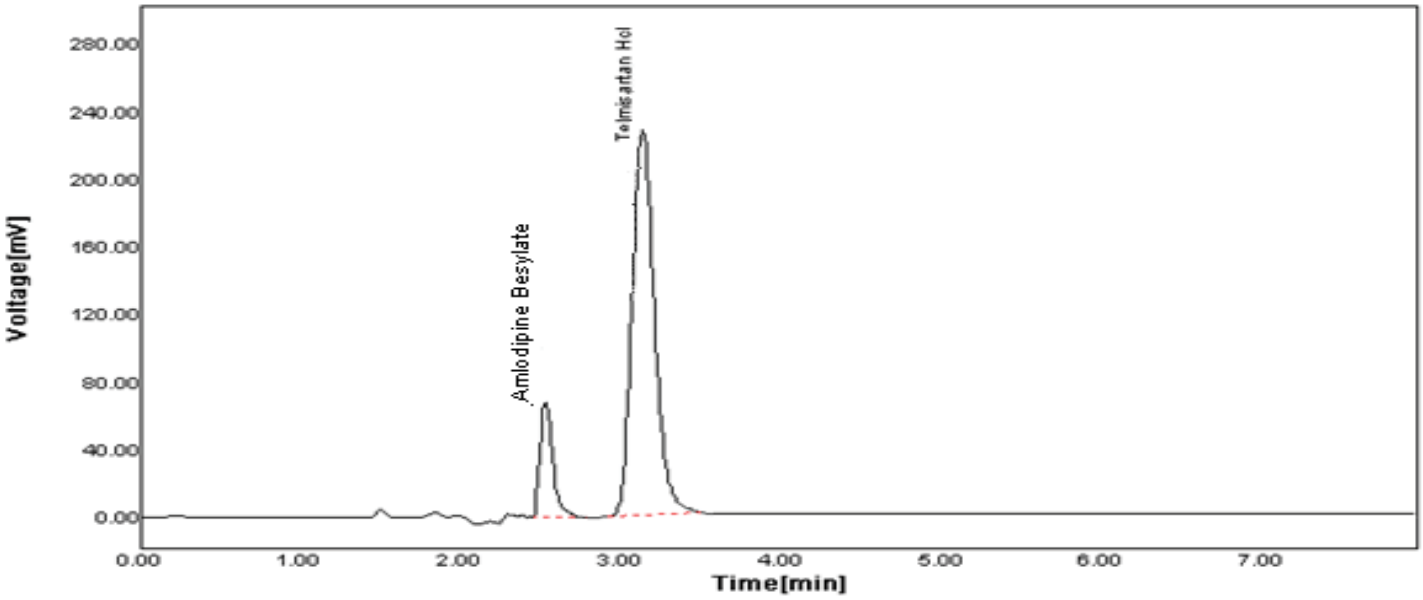

Figure 3: 0.025M Ammonium acetate: Methanol (82:18). Couldn't get consistent retention time.

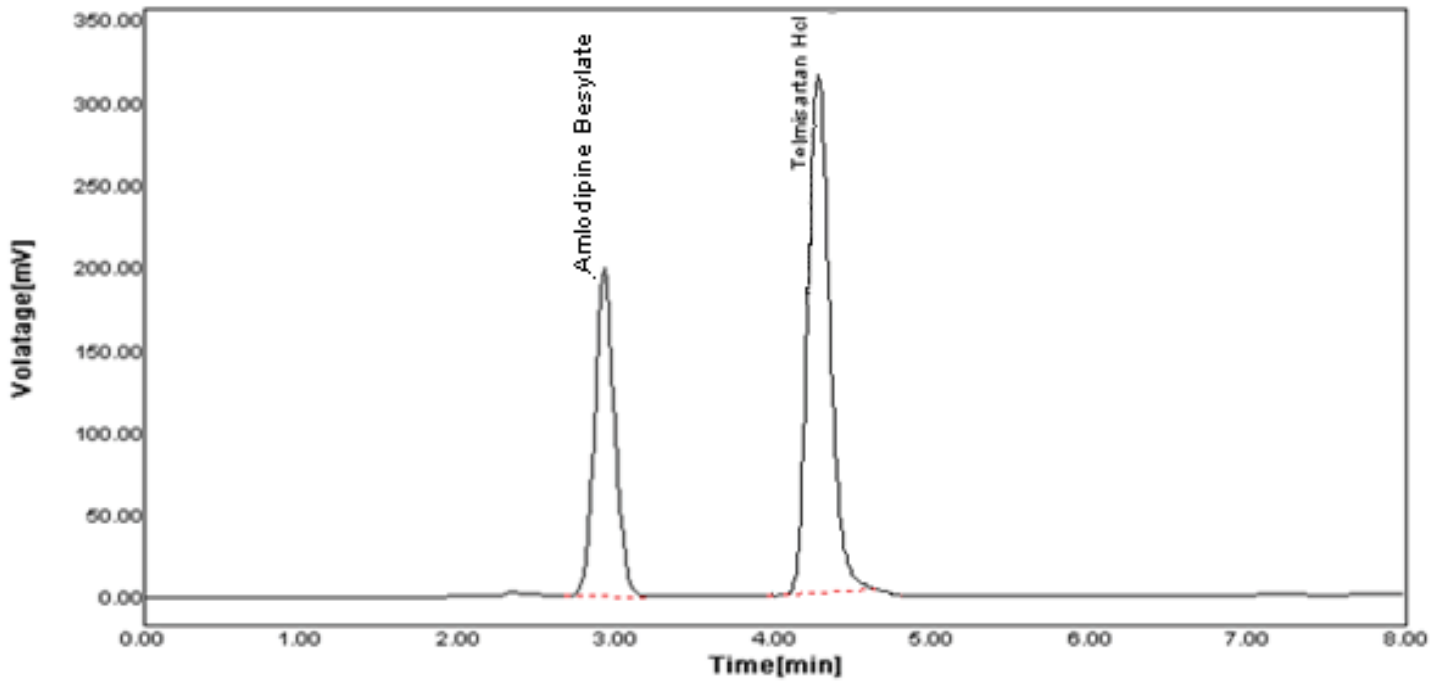

Figure 4: 0.025M Phosphate Buffer: Methanol (75:15). Couldn't get consistent retention time.

Method precision

Six preparations were prepared individually using single batch of Amlodipine Besylate and Telmisartan HCl working standard as per test method and injected each solutions in duplicate [6].

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

Procedures

RSD criteria: Series of working standard solutions of different concentrations below two specification level were prepared (generally about 10%, 20%, 30%, 40% and 50% of the specification concentration) and injected six replicate injections into HPLC. The solution was prepared at predicted concentration (for LOQ/LOD) and injected six replicates as per methodology.

Acceptance criteria for LOD and LOQ

RSD criteria: Concentration at which RSD< 33.0% (LOD); Concentration at which RSD<10.0 (LOQ)

Linearity

Procedure: Prepared a series of standard solutions not less than five in the specified concentration range and analyze them as per method.

Acceptance criteria: The correlation coefficient should be not less than 0.9990.

Accuracy

Accuracy normally refers to the difference between the mean of the set of results and the true or correct value for the quantity measured.

According to IUPAC accuracy relates to the difference between results (or mean) and the true value. For analytical methods, there are two possible ways of determining the accuracy, absolute method and comparative method [7]. Accuracy is best reported as percentage bias, which is calculated from the expression.

Since for real samples the true value is not known, an approximation is obtained based on spiking drug-free matrix to a nominal concentration. The accuracy of analytical method is then determined at each concentration by assessing the agreement between the measured and nominal concentrations of the analytes in the spiked drug–free matrix sampler. Acceptance criteria: Assay recovery should be between 98% to 102%.

Specificity

Procedure: Acid hydrolysis: Sample was treated with 5 ml of acid (1N Hcl) and kept for 1 hr. After 1 hr the solution was neutralized with 1N NaOH and analyzed using HPLC.

Oxidation: Amlodipine Besylate and Telmisartan HCl solution 100 ppm was mixed with 5 mL of 30% aqueous hydrogen peroxide solution.

Alkali hydrolysis: Sample was treated with 5 ml of alkali (1N NaOH) and kept for 1 hr. After 1 hr the solution was neutralized with 1 N HCl and analyzed using HPLC.

Photolysis: Samples were kept under UV light for different time intervals (15-60 mins) and observed by HPLC. [8].

Heat: Samples were heated at 90°C for 1-2 hrs and analyzed.

Range

The range of an analytical procedure is the interval between the upper and lower concentrations (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.

Acceptance criteria

Linearity, precision and recovery should be shown. The logic behind this parameter was–typical concentration range was essential between which the actual concentration should fall when performing real sample analysis.

Robustness

Measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides indication of its reliability during its normal usage.

Procedure: Samples were analyzed under the following conditions.

Ruggedness

Method/Procedure: Samples were prepared as per the test method the test method and injected in duplicate using different system, analyst on different day.

Calculated mean area, SD, % RSD.

Stability studies

In the rational design and evaluation of dosage forms for the drugs, the stability of the activity components must be a major criterion in determining their stability. The medicine has to reach the patient in an active and acceptable form maintaining the criteria for acceptable equality.

RESULTS AND DISCUSSION

Method validation: System suitability.

Acceptance criteria:

1. RSD should not be more than 2.0% for five replicate injections of standard.
2. USP Tailing for Amlodipine Besylate and Telmisartan HCl peak in not more than 2.0.
3. The column efficiency as determined for Amlodipine Besylate and Telmisartan Hcl, USP Plate Count should not be more than 2000.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well. This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 1).

HPLC method development

The above trials indicating that RT for the drug was not constant and elution time was faster which not prefered for the analysis. The above trials indicating that RT for the drug was not constant and elution time was faster which not preferred for the analysis (Table 2).

Remaining experiments were done with above method and the results are satisfactory (Table 3).

System suitability for Amlodipine Besylate and Telmisartan HCl

Precision

Acceptance criteria: RSD should not be more than 2.0% for five replicate injections of standard.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl (Figure 5) stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well (Table 4). This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 5).

Method precision: Six individual preparations were prepared using single batch of Amlodipine Besylate and Telmisartan HCl working standard as per test method and injected each solutions.

Summary of results of method precision parameter for Amlodipine Besylate and Telmisartan Hcl

Injection precision: Standard solution were prepared as per test method and injected six times.

Table 1: Optimized chromatographic conditions.

Parameters	Method
Stationary phase (column)	Phenomenix C18 (250 × 4.6 mm, 5 µm)
Mobile Phase	40:35:25 v/v/v, (0.02 M Ammo. Phosphate buffer: Acetonitrile: methanol)
pH	7.2 ± 0.02
Flow rate (ml/min)	1
Run time (minutes)	8
Column temperature (°C)	Ambient
Volume of injection loop (ml)	20
Detection wavelength (nm)	254
Drugs RT (min)	2.65 & 4.966

Table 2: Developed Chromatogram.

No.	Name	RT [min]	Area [mV × s]	TP	TF	Resolution
1	Amlodipine Besylate	2.65	820575	4401.9	1.3125	0
2	Telmisartan Hcl	4.9667	11774356	7419.7	0.9986	7.4555
Sum		-	12594931	-	-	-

Table 3: The %RSD, PC and TF results were found to be satisfactory.

Conc. of Amlo. & Gliclˆ	Injection	Area of Amlo.	RT	Area of Telmi. Hcl	RT
10 & 80ppm	Inj-1	825624	2.65	11777624	4.969
	Inj-2	823624	2.62	11774518	4.972
	Inj-3	824680	2.64	11775810	4.964
	Inj-4	823728	2.67	11783917	4.97
	Inj-5	824936	2.66	11774356	4.969
	Inj-6	822937	2.64	11770629	4.966
	Mean	824254.8	2.646667	11776142	4.968333
Statistical Analysis	SD	993.1325	0.017512	4449.214	0.002875
	% RSD	0.120489	0.661659	0.037782	0.05787
	Tailing Factor	1.31	-	0.99	-
	Plate Count	4401.9	-	7419.7	-

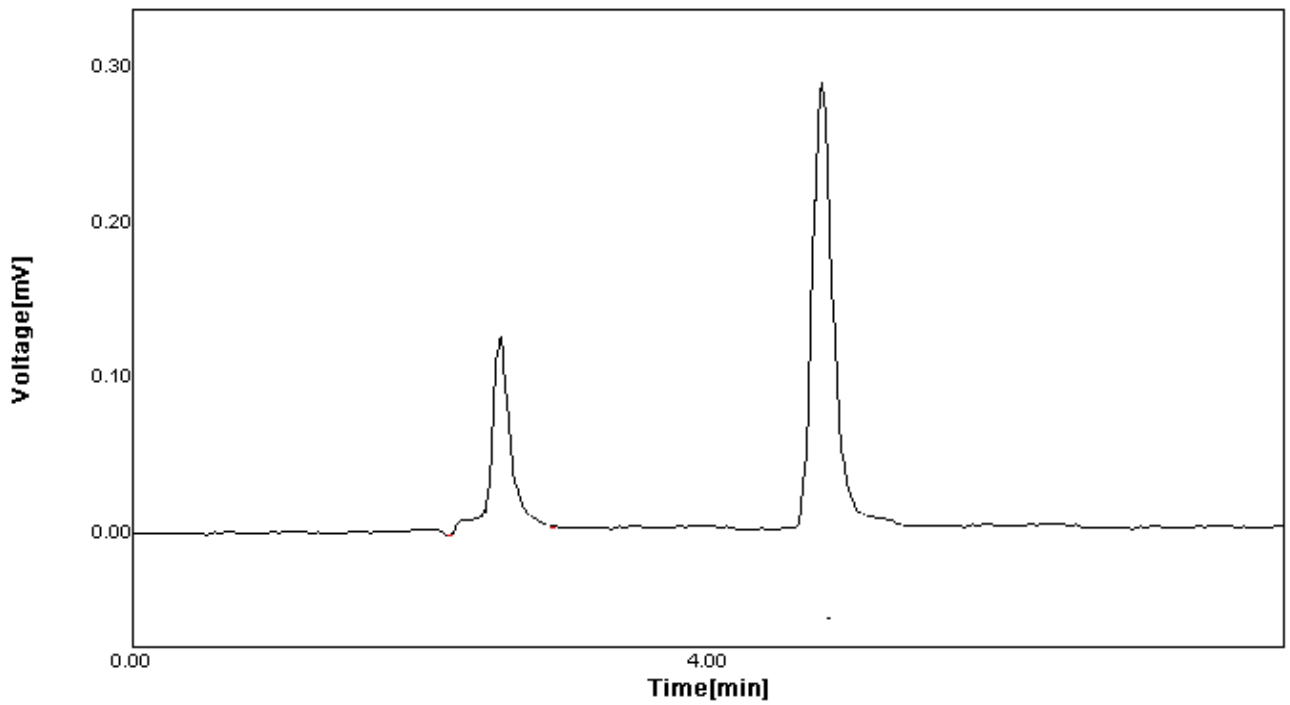

Figure 5: The LOD results were found to be satisfactory.

Table 4: The % RSD value from six preparations observed to be less than 2 and hence the result found to be satisfactory.

Variables	Inj-1	Inj-2	Avg	Mean	SD	% RSD
			Amlodipine Besylate			
MP-1	820575	820876	820725.5	823077.6	1795.99	0.2182
MP-2	822816	823925	823370.5			
MP-3	821274	824680	822977			
MP-4	820914	823817	822365.5			
MP-5	822924	824680	823802			
MP-6	824624	825826	825225			
			Telmisartan Hcl			
MP-1	11775382	11779725	11777554	11777845	4374.288	0.03714
MP-2	11777918	11774517	11776218			
MP-3	11783917	11775810	11779864			
MP-4	11784612	11774356	11779484			

Table 5: Parameter for Amlodipine Besylate and Telmisartan Hcl.

No. I.P	Amlodipine Besylate	Telmisartan Hcl
I.P-1	821429	11777624
I.P-2	822267	11774518
I.P-3	820072	11775810
I.P-4	821279	11783917
I.P-5	820785	11774356
I.P-6	822547	11770629
Mean	821396.5	11776142
SD	919.1861	4449.214
% RSD	0.111905	0.037782

Summary of results of Injection Precision parameter for Amlodipine Besylate and Telmisartan HCl

Limit of Detection

LOD: Lowest amount of analyte in a sample that can be detected but not necessarily quanities, under the stated experimental conditions.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well. This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 6).

Method procedure: The mobile phase was allowed to run equilibrate with stationary phase upto good baseline was obtained. The different concentration ranging from 0.001 to 0.1 ppm of Amlodipine Besylate and 0.008 to 0.8 ppm Telmisartan HCl was injected and peaks were recorded. 0.003 and 0.024 ppm for Amlodipine Besylate and Telmisartan HCl concentrations were detected respectively.

Chromatogram obtained for Chromatogram of Amlodipine Besylate and Telmisartan HCl showing LOD

Limit of Quantification

LOQ: Lowest amount of analyte in a sample, which can be quantitatively, determined with suitable precision and accuracy.

Table 6: Signal-to- Noise Ratio for LOD.

Approach	LOD
Visual Inspection	Minimum level detectable
Signal-to- Noise Ratio	3:1
SD of response (σ) & slope (S)	(3.3×σ)/s

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well (Figure 6). This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 7).

Method procedure: The mobile phase was allowed to run equilibrate with stationary phase upto good baseline was obtained. The different concentration ranging from 0.001 ppm to 0.1 ppm of Amlodipine Besylate and 0.008 to 0.8 ppm of Telmisartan HCl was injected and peaks were recorded. 0.01 ppm and 0.08 ppm for Amlodipine Besylate and Telmisartan HCl concentrations were detected respectively (Table 8).

Summary of results of LOQ for Amlodipine Besylate and Telmisartan HCl

Linearity & range

Acceptance Criteria: R2 value should be not more than 1.

Preparation of standard stock solution:

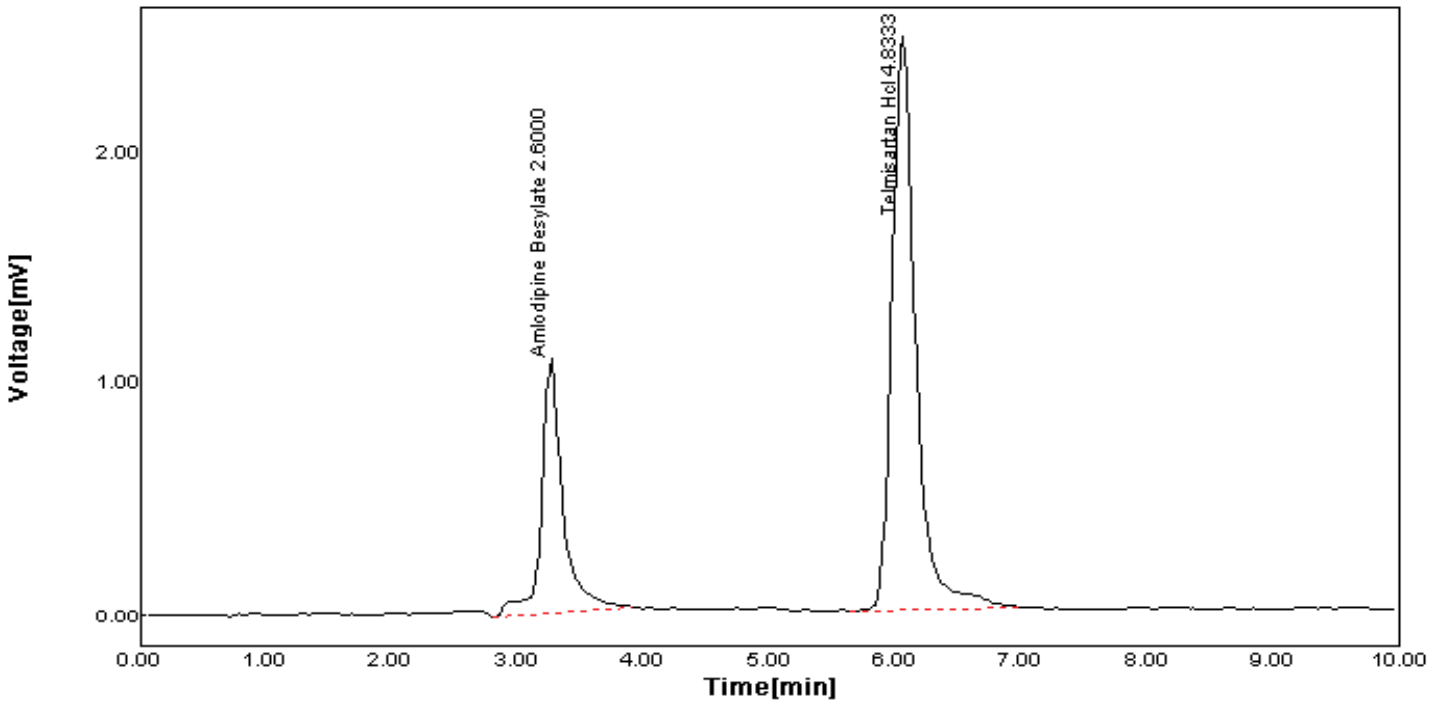

Figure 6: Chromatogram obtained for Chromatogram of Amlodipine Besylate and Telmisartan Hcl showing LOQ.

Table 7: Signal-to- Noise Ratio for LOQ.

Approach	LOQ
Visual Inspection	Minimum level quantifiable
Signal-to- Noise Ratio	10:1
SD of response (σ) & slope (S)	{10.0×σ}/s

Table 8: The % RSD value for LOQ was found to be less than 2 and hence the result found to be satisfactory.

Injection	Area of Amlo. (0.01ppm)	Area of Telmi. Hcl (0.08ppm)
Inj-1	70916	185238
Inj-2	71926	184826
Inj-3	72068	185193
Inj-4	71672	184927
Inj-5	72143	185017
Inj-6	71783	185516
Mean	71751.33	185119.5
SD	444.8072	249.1431
% RSD	0.619929	0.134585

Accurately weighed 10 mg of the both Amlodipine Besylate and Telmisartan HCl was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the Methanol and mixed well (Table 9). This yielded a stock solution with concentration 1000 ppm of Amlodipine Besylate and Telmisartan HCl mixture.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask.

Summary of results of Linearity parameter for Amlodipine Besylate and Telmisartan HCl

Then the volume was made up to the mark with the diluent and mixed well. This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively.

Table 9: Parameter for Amlodipine Besylate and Telmisartan Hcl.

Amlodipine Besylate Conc. (ppm)	Average	Telmisartan Hcl Conc. (ppm) 1ppm	Average
0.1	72068	0.8	180283
1	169058	8	1508607
8	684555	64	9240280
10	820575	80	11774356
12	973654	96	14519419
20	1602430	160	23629730

Method procedure: The mobile phase was allowed to run equilibrate with stationary phase upto good baseline was obtained (Figure 7). The various concentrations ranging from 0.1 ppm to 20 ppm for Amlodipine Besylate and 0.8 ppm to 160 ppm for Telmisartan HCl was injected then peaks were detected (Figure 8). The linearity graph was plotted as concentration *vs.* peak area is depicted (Figure 9).

Accuracy

Acceptance criteria: Recovery should be in between 95% to 105%.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well. This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 10).

Method precision: Prepared solutions in triplicate at levels 80%, 100% and 120% of test concentrations using for Amlodipine Besylate and Telmisartan HCl working Standards as per the test method and injected each solution in triplicate (Figure 10).

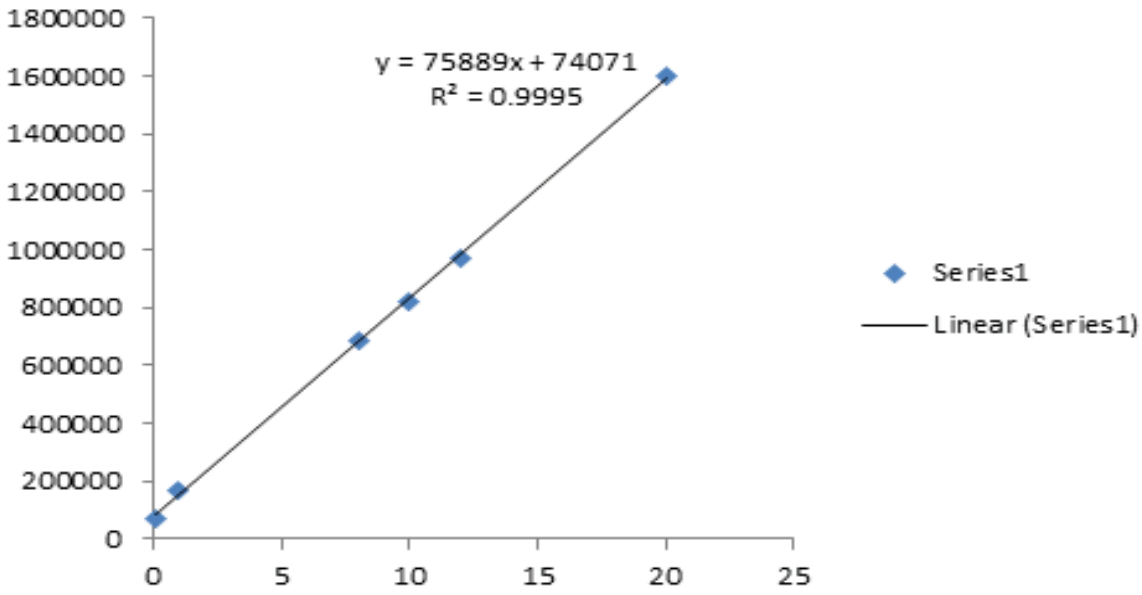

Figure 7: Linearity Curve of Amlodipine Besylate.

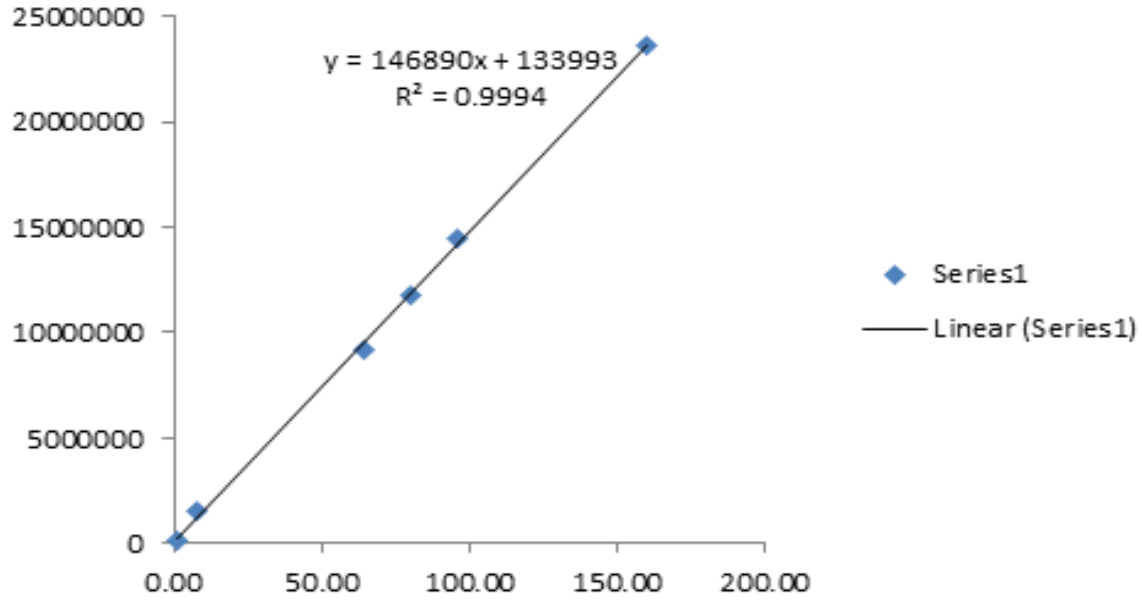

Figure 8: Linearity Curve of Telmisartan Hcl.

Summary of results of Accuracy parameter for Amlodipine Besylate and Telmisartan HCl

Robustness

Acceptance criteria: Overall RSD should not be more than 2.0%.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well. This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively.

Method procedure

1. Flow: The standard solution was prepared and injected for the two times with (+1) flow rate.
2. Mobile phase: The standard solution was prepared and injected for the two times with (+5) Mobile Phase composition

Ruggedness

Acceptance criteria: Overall RSD should not be more than 2.0%.

Preparation of standard solution: Accurately amount of 0.1 ml and 0.8 ml of the Amlodipine Besylate and Telmisartan HCl stock was transferred to 10 ml clean and dry volumetric flask. Then the volume was made up to the mark with the diluent and mixed well (Table 11). This yielded a standard stock solution with concentrations of 10 ppm and 80 ppm of Amlodipine Besylate and Telmisartan HCl respectively (Table 12).

Method procedure: The standard solution was individually prepared as per the test method and injected each solution in six times using different system, analyst and date.

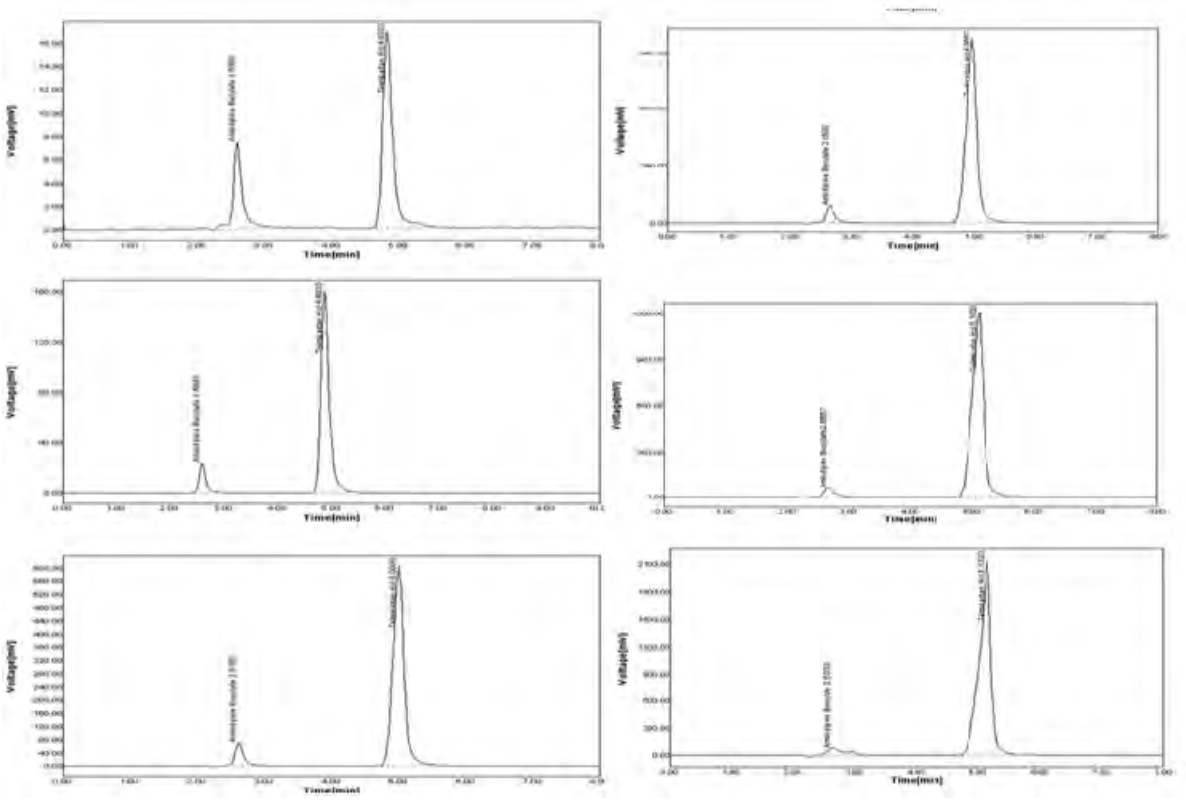

Figure 9: Linearity Chromatograms for Amlodipine Besylate (0.1-20 ppm) and Telmisartan Hcl (0.8-160 ppm).

Table 10: The recovery results showing that the test method was acceptable level of accuracy for the assay of Amlodipine Besylate and Telmisartan Hcl was from 80% to 120% of test concentration.

Amlodipine Besylate								
Conc.		Inj-1	Inj-2	Inj-3	Mean	% Recovery	STD	% RSD
8 pm	1	402682	404572	403782	403679	98.389	949.23	0.23514
10 ppm	1	820365	820472	820575	820471	99.987	105.01	0.0128
12 pm	1	1.00E+06	1.00E+06	1231075	1.00E+06	100.02	270.58	0.02198
Telmisartan Hcl								
64 ppm	1	9.00E+06	9.00E+06	9289274	9.00E+06	98.408	18744	0.20221
80 ppm	1	1.00E+07	1.00E+07	1.20E+07	1.00E+07	99.993	672.83	0.00572
96 ppm	1	1.00E+07	1.00E+07	1.40E+07	1.00E+07	100.32	110196	0.77747

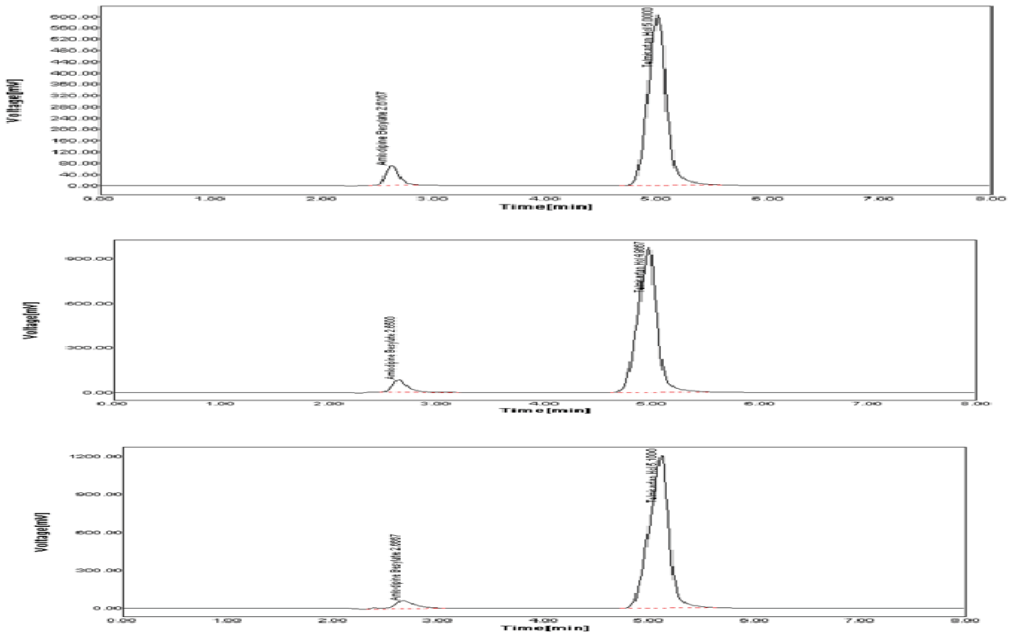

Figure 10: Accuracy Chromatograms for Amlodipine Besylate and Telmisartan Hcl (80%, 100% and 120%).

Table 11: aAvg. Area = Six Repeatable injections.

Parameters	Adjusted TO	Avg. Area	RT	SD	% RSD
Amlodipine Besylate					
Flow Rate As per method 1.2 ml/min	1	947592	3.31	1357.18	0.33
	As it is	820575	2.65	1032.11	0.31
	1	787279	2.03	2675.91	1.09
Mobilephasecompn (40:35:25 v/v, (Buffer: Acetonitrile: Methanol)	35:37.5:27.5	851939	2.27	3784.67	0.98
	As it is	820575	2.65	1032.11	0.31
	45:33.5:22.5	792894	2.94	3097.23	1.04
Telmisartan Hcl					
Flow Rate As per method 1.2 ml/min	1	2.00E+07	5.72	12826.9	0.82
	As it is	1.00E+07	4.96	1301.76	0.12
	1	8.00E+06	4.13	7390.12	0.83
Mobilephasecompn (40:35:25 v/v, (Buffer: Acetonitrile: Methanol)	35:37.5:27.5	1.00E+07	4.39	15528.6	0.74
	As it is	1.00E+07	4.96	1301.76	0.12
	45:33.5:22.5	9.00E+06	5.48	8126.6	0.83

Table 12: The %RSD value found to be less than 2 and hence the result found to be satisfactory.

Inj. No.	Amlodipine Besylate	Telmisartan Hcl
I.P-1	817397	11751826
I.P-2	818035	11716829
I.P-3	805762	11728925
I.P-4	814628	11710276
I.P-5	808935	11742516
I.P-6	811926	11720629
Mean	812780.5	11728500
SD	4839.6794	15943.71
% RSD	0.5954473	0.13594

CONCLUSION

The present method can be used for rapid and precise quantification of Amlodipine Besylate and Telmisartan HCl. The present work showing a validation with highly sensitive and selective method for the estimation of Amlodipine Besylate and Telmisartan HCl in pharmaceutical dosage forms.

DISCLOSURE

There is no conflict of interests.

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