INTERNATIONAL JOURNAL OF RESEARCH CULTURE SOCIETY ISSN: 2456-6683 Volume - 4, Issue - 4, Apr – 2020
Monthly, Peer-Reviewed, Refereed, Indexed Journal Scientific Journal Impact Factor: 5.245
Received on : 04/04/2020 Accepted on : 17/04/2020 Publication Date: 30/04/2020

Validation and analysis of Telmisartan drug Pharmaceutical dosage forms by RP-HPLC method

[1]Jagadeesh Kumar Ega, [2]Sateesh Kuna, [3]Kumara Swamy Jella, [4]Kavitha Siddoju
[1, 4] Department of Chemistry, Chaitanya Deemed to be University, Hanamkonda, Warangal Urban, Telagana State-506001
[2] Vignan's Institute of Management and Technology for Women, Ghatkesar, Medchal-Malkajgiri, Telangana State-501301
[3] R.D Women's P.G. College, Hanamkonda, Telangana State-506009

Abstract: *Telmisartan drug acts as angiotensin II receptor antagonist as a vasoconstrictor. Here within discuss the suitable RP-HPLC method for the analysis of Telmisartan in formulations, attempts were made to develop simple, precise and accurate analytical method for estimation of Telmisartan and extend it for their determination in formulation. A rapid and precise Reverse Phase High Performance Liquid Chromatographic method has been developed for the validated of Telmisartan, in its pure form as well as in tablet dosage form. Chromatography was carried out on a Hypersil C18 (4.6×150mm, 5µ) column using a mixture of Methanol and water (15:85 v/v) as the mobile phase at a flow rate of 1.0ml/min, the detection was carried out at 284nm. The retention time of the Telmisartan was 3.515 ±0.02min. The method produce linear responses in the concentration range of 25-125µg/ml of Telmisartan. The method precision for the determination of assay was below 2.0%RSD. The method is useful in the quality control of bulk and pharmaceutical formulations.*

Key Words: *Telmisartan, RP-HPLC, validation.*

1. INTRPODUCTION:

Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT1-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland[1-2]. 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. Chromatography is a method in which the components of a mixture are separated on an adsorbent column in a flowing system [3-4]. High Performance Liquid Chromatography [5] is now one of the most powerful tools in analytical chemistry. It has the ability to separate, identify, and quantitative the compounds that are present in any sample that can be dissolved in a liquid [6]. The validated of drug as per ICH guidelines and specificity, linearity & range, accuracy, precision and robustness was performed. HPLC can be applied to just about any sample, such as pharmaceuticals, food, cosmetics, environmental matrices, forensic samples, and industrial chemicals. Reversed phase HPLC consists of a non-polar stationary phase and an aqueous, moderately polar mobile phase. RPC operates on the principle of hydrophobic interactions [6-7], which result from repulsive forces between a polar eluent, the relatively non-polar analyte, and the non-polar stationary phase. The binding of the analyte to the stationary phase is proportional to the contact surface area around the non-polar segment of the analyte molecule upon association with the ligand in the aqueous eluent. Drug interactions are may enhance the hypotensive effect of Angiotensin II Receptor Blockers, enhance the nephrotoxic effect of Angiotensin II Receptor Blockers.

2.MATERIALS AND METHODS:

The utility of the developed method to determine the content of drug in commercial formulation was also demonstrated. Validation of the method was done in accordance with USP and ICH guideline for the assay of active ingredient. The method was validated for parameters like system suitability, linearity, precision, accuracy, specificity, ruggedness and robustness, limit of detection and limit of quantification. This method provides means to quantify the component. This method was suitable for the analysis of Pharmaceutical dosage forms [8-12].The analytical method was developed by studying different parameters. All maximum absorbance was found to be at 284nm and the peak purity was excellent. Injection volume was selected to be 10µl which gave a good peak area. The column used for study was Hypersil C18 (4.6 x 150mm, 5m) because it was giving good peak. 40 ° C temperatures was found to be suitable for the nature of drug solution. The flow rate was fixed at 1.0ml/min because of good peak area and satisfactory retention time. Mobile phase is Methanol: water was fixed due to good symmetrical peak. So this mobile phase was used for the proposed study. Methanol: water was selected because of maximum extraction sonication time was fixed to be 10min at which all the drug particles were completely soluble and showed good recovery. Run time was selected to be 6min because analyze gave peak around 3.5 and also to reduce the total run time.

The percent recovery was found to be 98.0-102 was linear and precise over the same range. Both system and method precision was found to be accurate and well within range. The analytical method was found linearity over the

range of 25-125µg/ml of the target concentration. The analytical passed both robustness and ruggedness tests. On both cases, relative standard deviation was well satisfactory.

Table-1: List of Instruments and Apparatus:

S.No	Instruments And Glassware's	Model
1	HPLC	WATERS Alliance 2695 separation module, software: Empower 2, 996 PDA detector.
2	pH meter	Lab India
3	Weighing machine	Sartorius
4	Volumetric flasks	Borosil
5	Pipettes and Burettes	Borosil
6	Beakers	Borosil
7	Digital ultra sonicator	Labman

Table-2: List of used Chemicals:

S.No	Chemicals	Brand names
1	Telmisartan	Sura labs
2	Water and Methanol for HPLC	LICHROSOLV (MERCK)
3	Acetonitrile for HPLC	Merck

Table-3: Optimized Chromatographic conditions

Instrument used	:	Waters HPLC with auto sampler and PDA detector 996 model.
Temperature	:	40ºC
Column	:	Hypersil C18 (4.6 x 150mm, 5µm)
Mobile phase	:	Methanol: Water (15:85 v/v)
Flow rate	:	1ml/min
Wavelength	:	284nm
Injection volume	:	10µl
Run time	:	6minutes

VALIDATION

Preparation of mobile phase:

Accurately measured 150 ml (15%) of HPLC Methanol and 850 ml of HPLC Water (85%) were mixed and degassed in a digital ultrasonicater for 10 minutes and then filtered through 0.45 µ filter under vacuum filtration.

Diluent Preparation: The Mobile phase was used as the diluent. Five level of preparation of Telmisartan displayed as 25µg/ml, 50µg/ml, 75µg/ml, 100µg/ml and 125µg/ml**.(Tables 1-3)**

3. RESULTS AND DISCUSSION:

Shown in **Table-4 t0 15 and Fig: 1-30**

Table-4: Results of system suitability for Telmisartan

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Telmisartan	3.513	2947505	275462	7462	1.1
2	Telmisartan	3.516	2958475	275361	7462	1.1
3	Telmisartan	3.515	2965847	275144	6472	1.1

4	Telmisartan	3.517	2952642	275837	7183	1.1
5	Telmisartan	3.512	2951645	275948	7428	1.1
Mean			2955223			
Std. Dev.			7114.704			
% RSD			0.24075			

Table-5: Peak results for assay standard:

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Telmisartan	3.518	2967593	275837	1.1	6583
2	Telmisartan	3.517	2967399	275922	1.1	5938
3	Telmisartan	3.515	2960183	271844	1.1	5883

Table-6: Peak results for Assay sample:

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Telmisartan	3.511	2983744	275833	1.1	7584
2	Telmisartan	3.511	2958374	275984	1.1	6294
3	Telmisartan	3.514	2957262	275481	1.1	8194

Table-7: Chromatographic data for Linear study:

Concentration Level (%)	Concentration µg/ml	Average Peak Area
33	25	1083048
66	50	1973321
100	75	2955166
133	100	4063921
166	125	5006038

Table-8: Results of repeatability for Telmisartan

S. No	Peak name	Retention time	Area(µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Telmisartan	3.528	2958333	275983	7583	1.1
2	Telmisartan	3.516	2951049	275911	7593	1.1
3	Telmisartan	3.514	2959294	275955	8674	1.1
4	Telmisartan	3.519	2953391	275921	7958	1.1
5	Telmisartan	3.512	2950744	275221	9745	1.1
Mean			2954562			
Std.dev			4028.083			
%RSD			0.136334			

Table-9: Results of Intermediate precision Day 1 for Telmisartan

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate count	USP Tailing
1	Telmisartan	3.517	2957344	275838	7194	1.1
2	Telmisartan	3.514	2951847	275629	8573	1.1
3	Telmisartan	3.517	2950834	276931	7655	1.1
4	Telmisartan	3.517	2957155	275623	7944	1.1
5	Telmisartan	3.512	2950185	275184	7562	1.1
6	Telmisartan	3.518	2951750	275193	7585	1.1
Mean			2953186			
Std. Dev.			3207.331			
% RDS RSD			0.108606			

Table-10: Results of Intermediate precision Day 2 for Telmisartan

S.No	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate count	USP Tailing
1	Telmisartan	3.513	2951848	275929	7937	1.1
2	Telmisartan	3.511	2958275	275222	7284	1.1
3	Telmisartan	3.516	2950185	275857	7684	1.1
4	Telmisartan	3.518	2957462	275163	7917	1.1
5	Telmisartan	3.511	2957541	275164	7585	1.1
6	Telmisartan	3.519	2951164	275154	7192	1.1
Mean			2954413			
Std. Dev.			3715.025			
% RSD			0.125745			

Table-11: Results of Accuracy for concentration-50%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Telmisartan	3.519	1493763	275837	1.1	6453
2	Telmisartan	3.520	1493923	275819	1.1	7584
3	Telmisartan	3.519	1492575	275083	1.1	6785

Table-12: Results of Accuracy for concentration-100%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Telmisartan	3.516	2983722	275829	1.1	7483
2	Telmisartan	3.518	2984722	275143	1.1	6935
3	Telmisartan	3.519	2967382	275063	1.1	6285

Table-13: Results of Accuracy for concentration-150%

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Telmisartan	3.517	4462011	275622	1.1	7483
2	Telmisartan	3.519	4469483	275922	1.1	7265
3	Telmisartan	3.520	4489583	276331	1.1	7194

Table-14: The accuracy results for Telmisartan

%Concentration (at specification Level)	Area	Amount Added (ppm)	Amount Found (ppm)	% Recovery	Mean Recovery
50%	1483420	37.5	36.96	98.5%	98.8%
100%	2978609	75	74.1	98.8%	
150%	4473692	112.5	111.56	99.1%	

Table-15: Results for Robustness

Parameter used for sample analysis	Peak Area	Retention Time	Theoretical plates	Tailing factor
Actual Flow rate of 1.0 mL/min	2955764	3.513	7483	1.1
Less Flow rate of 0.9 mL/min	2958393	3.897	6028	1.1
More Flow rate of 1.1 mL/min	2956411	3.218	6928	1.2
Less organic phase	2950683	3.707	6733	1.2
More organic phase	2957265	3.350	6285	1.1

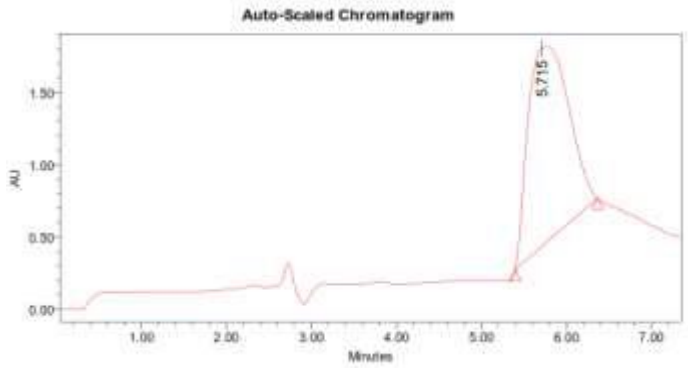

Figure 1: chromatogram for trail 1

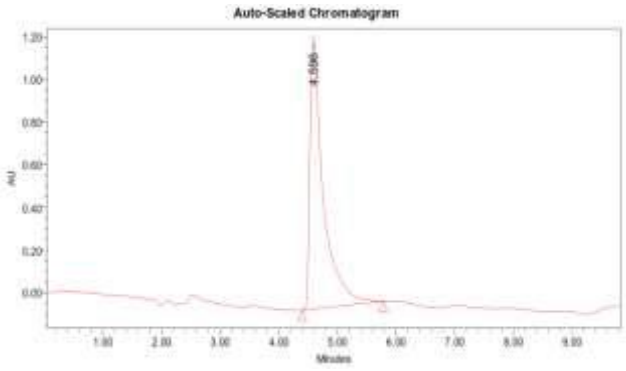

Figure 2: chromatogram for trail 2

INTERNATIONAL JOURNAL OF RESEARCH CULTURE SOCIETY ISSN: 2456-6683 Volume - 4, Issue - 4, Apr – 2020
Monthly, Peer-Reviewed, Refereed, Indexed Journal Scientific Journal Impact Factor: 5.245
Received on : 04/04/2020 Accepted on : 17/04/2020 Publication Date: 30/04/2020

Figure 3: chromatogram for trail 3

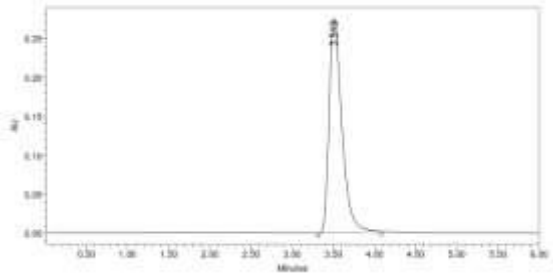

Figure 4: Optimized Chromatogram (Standard)

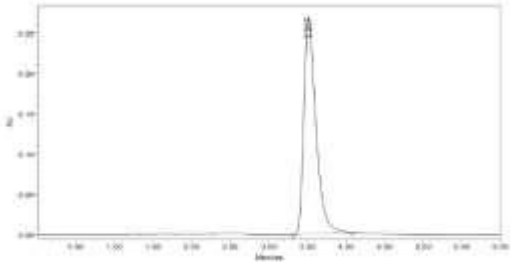

Figure 5: Optimized Chromatogram (Sample**)**

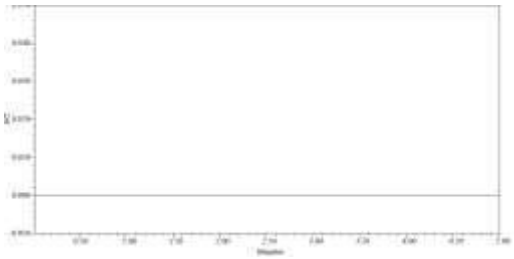

Figure 6: Chromatogram showing blank (mobile phase preparation)

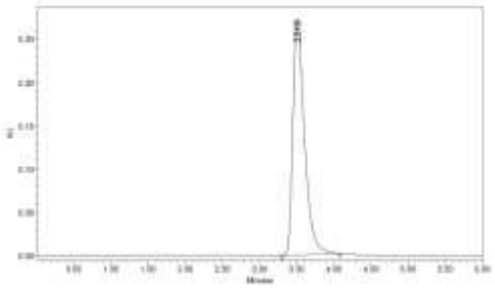

Figure 7: Chromatogram showing injection -1

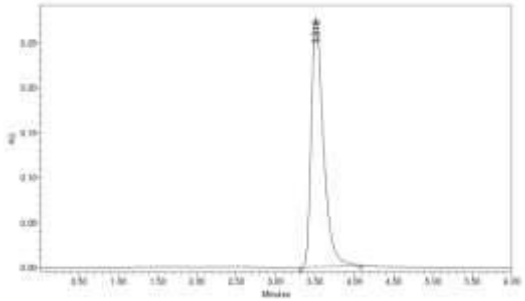

Figure 8: Chromatogram showing injection -2

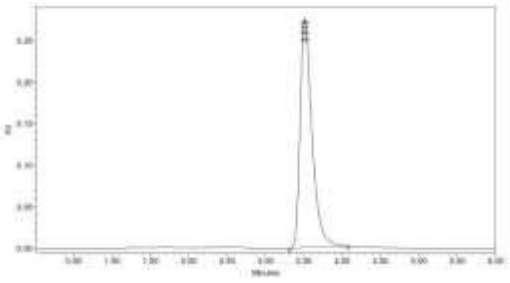

Figure 9: Chromatogram showing injection -3

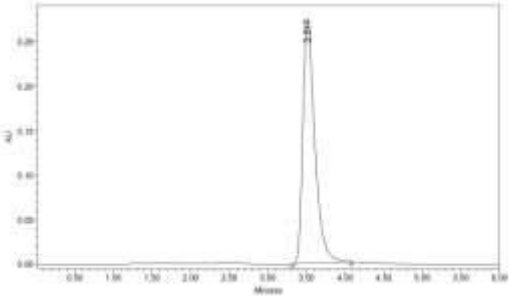

Figure 10: Chromatogram showing injection -4

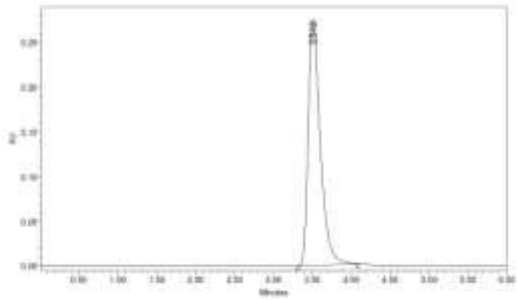

Figure 11: Chromatogram showing injection -5

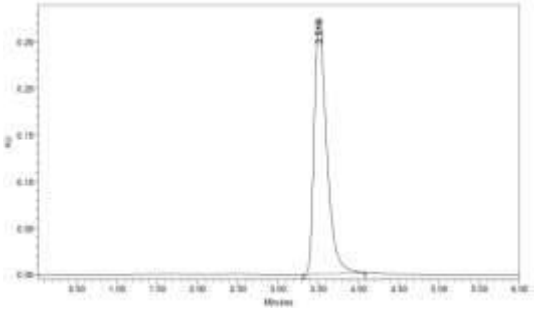

Figure 12: Chromatogram showing assay of standard injection -1

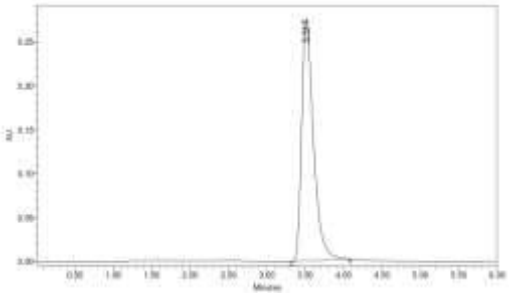

Figure 13: Chromatogram showing assay of standard injection-2

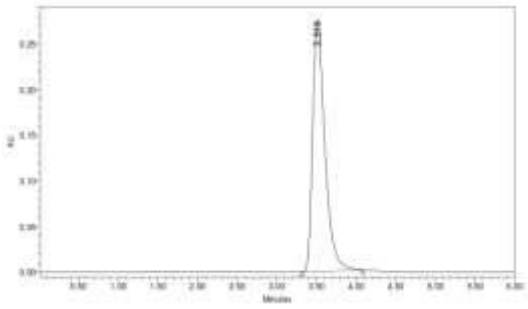

Figure 14: Chromatogram showing assay of standard injection-5

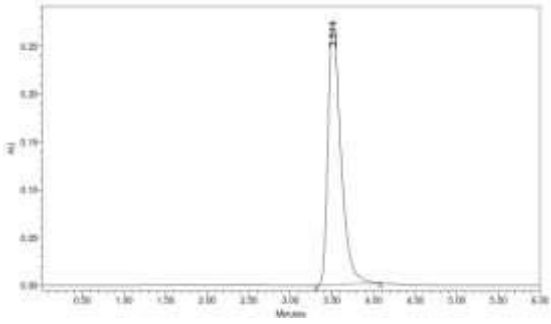

Figure 15: Chromatogram showing assay of sample injection-1

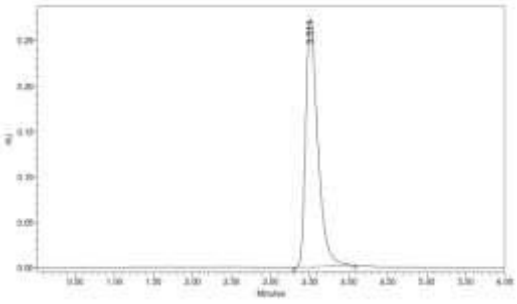

Figure 16: Chromatogram showing assay of sample injection-2

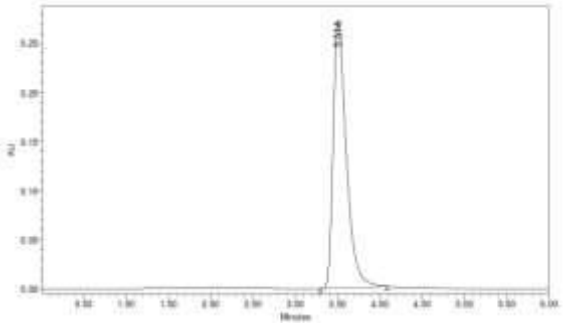

Figure 17: Chromatogram showing assay of sample injection-3

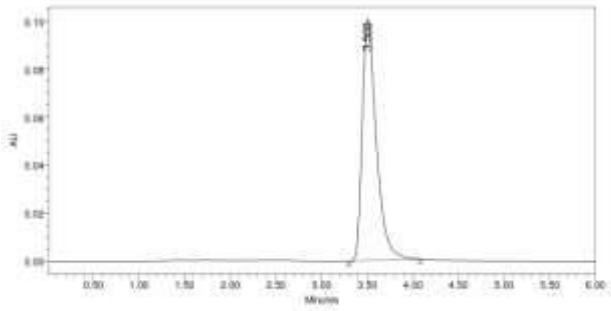

Figure 18: Chromatogram showing linearity level-1

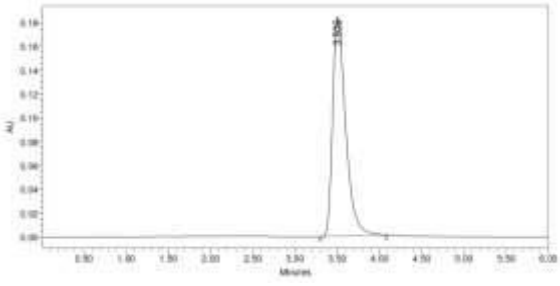

Figure 19: Chromatogram showing linearity level-2

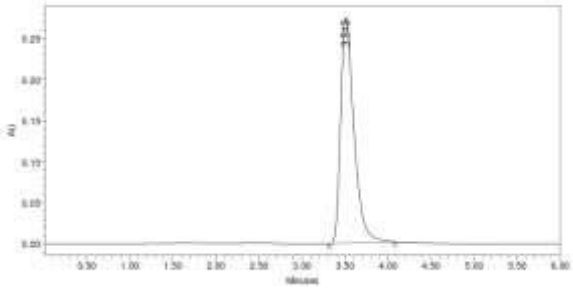

Figure 20: Chromatogram showing linearity level-3

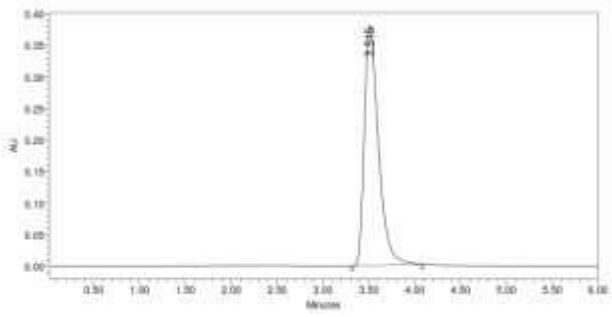

Figure 21: Chromatogram showing linearity level-4

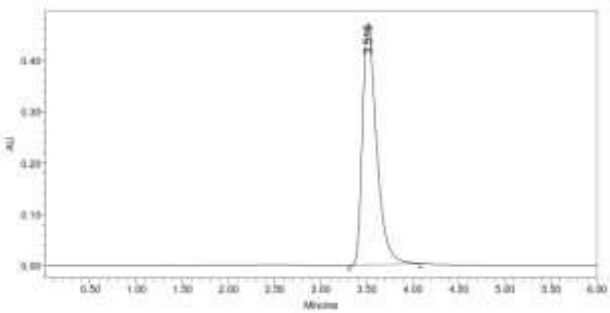

Figure 22: Chromatogram showing linearity level-5

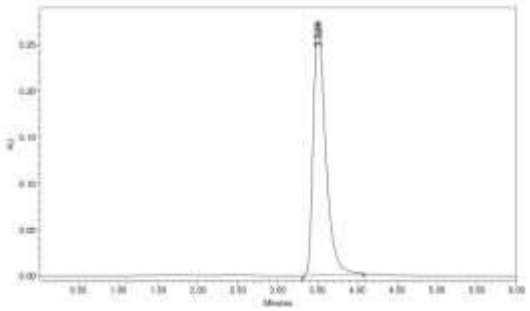

Figure 23: Chromatogram showing precision injection -1

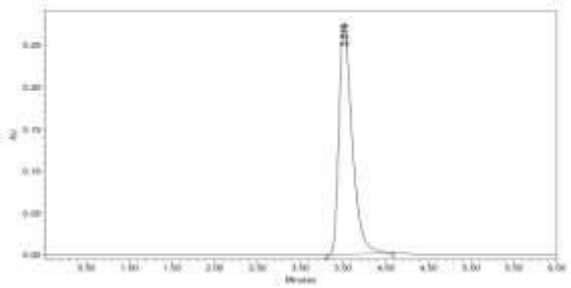

Figure 24: Chromatogram showing precision injection-2

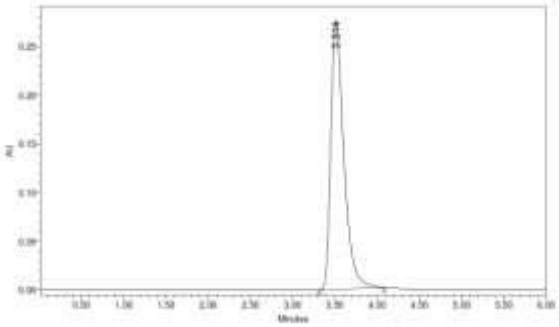

Figure 25: Chromatogram showing precision injection -3

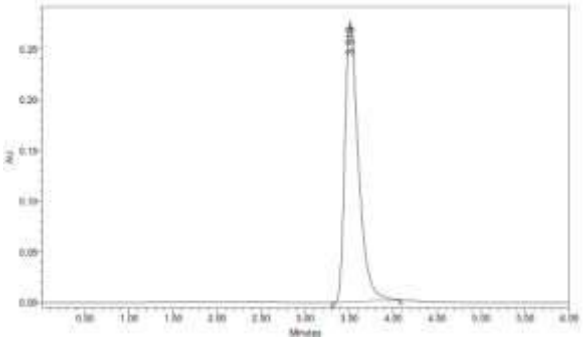

Figure 26: Chromatogram showing precision injection -4

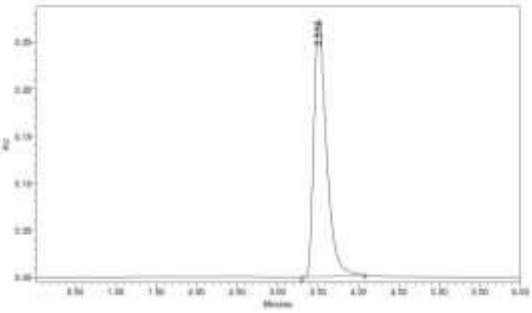

Figure 27: Chromatogram showing precision injection -5

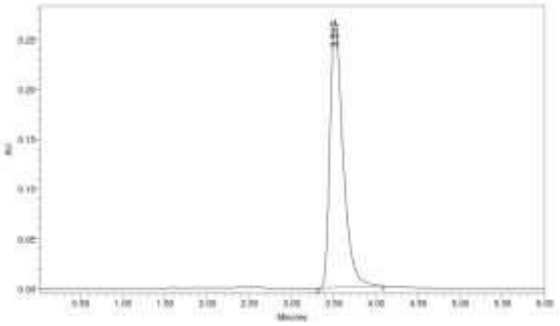

Figure 28: Chromatogram showing Day1 injection -1

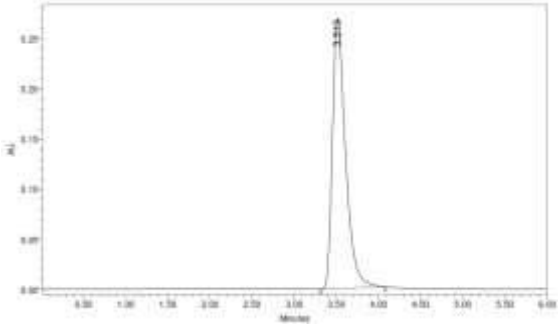

Figure 29: Chromatogram showing Day2 injection -1

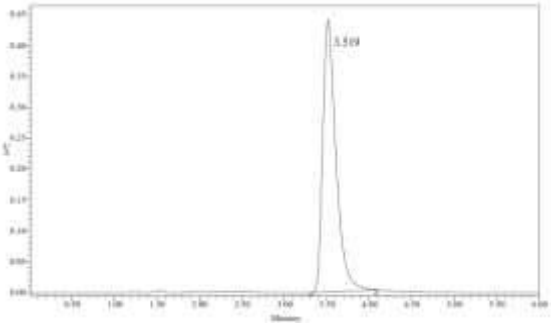

Figure 30: Chromatogram showing accuracy-50% injection-1

4. CONCLUSION:

The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods.We have investigated, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Telmisartan in bulk drug and pharmaceutical dosage forms. This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps. Telmisartan was freely soluble in ethanol, methanol and sparingly soluble in water. Methanol: water was chosen as the mobile phase. The solvent system used in this method was economical. The %RSD values were within 2 and the method was found to be precise. This method can be used for the routine determination of Telmisartan in bulk drug and in Pharmaceutical dosage forms. Accuracy, precision, standard deviation, linearity and assay are displayed .

REFERENCES:

1. Dr. Kealey and P.J Haines, Analytical Chemistry, 1st edition, Bios Publisher, **2002,**PP 1-7.
2. A.BraithWait and F.J.Smith, Chromatographic Methods, 5th edition, Academic Publisher, **1996,**PP 1-2.
3. Andrea Weston and Phyllisr. Brown, HPLC Principle and Practice, 1st edition, Academic press, **1997**, PP 24-37.
4. Yuri Kazakevich and Rosario Lobrutto, HPLC for Pharmaceutical Scientists, 1st edition,Wiley Interscience, A John Wiley & Sons, Inc., Publication, **2007**, PP15-23.
5. Chromatography, (online). URL:http://en.wikipedia.org/wiki/Chromatography.
6. Meyer V.R. Practical High-Performance Liquid Chromatography, 4th Ed. England, John Wiley & Sons Ltd, **2004**, PP 7-8.
7. Sahajwalla CG a new drug development, vol 141, Marcel Dekker Inc., New York, **2004**, PP 421–426.
8. Introduction to Column. (Online),URL:http://amitpatel745.topcities.com/index_files/study/column care.pdf
9. Detectors used in HPLC (online)URL:http://wiki.answers.com/
10. Detectors (online) ,URL:http://hplc.chem.shu.edu/NEW/HPLC_Book/Detectors/det_uvda.html
11. Detectors (online) ,URL:http://www.dionex.com/enus/webdocs/64842-31644-02_PDA-100.pdf
12. Detectors (online),URL:http://www.ncbi.nlm.nih.gov/pubmed/8867705