ISSN–2230-7346

Journal of Global Trends in Pharmaceutical Sciences

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF TELMISARTAN AND CHLORTHALIDONE IN BULK AND PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC METHOD

S. Ashitha*, M. Ankitha, P.V. Madhavi Latha, A. Ragasudha Sri, P. Uma Devi

Department of Pharmacy, Viswanadha Institute of Pharmaceutical Sciences,

Affiliated to JNTUK, Visakhapatnam - 531173, A.P, INDIA

***Corresponding author:** ashithasundarapu@gmail.com

ARTICLE INFO

Key Words

Telmisartan, Chlorthalidone, RP-HPLC, ICH.

Access this article online Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

A simple, accurate, precise technique was developed for the simultaneous estimation of Telmisartan and Chlorthalidone in Bulk and pharmaceutical dosage form. Chromatogram was run through Phenomenex LunaC18 (150 × 4.6mm, 5µl) column. Mobile phase containing Methanol: water pH3.5 adjusted with ortho phosphoric acid taken in the proportions 80:20%v/v was pumped through column at flow rate of 1ml/min. Temperature was kept ambient. Optimized wavelength selected was 225nm. Retention time of Telmisartan and Chlorthalidone was observed to be 2.9min and 4.6min. %RSD of the Telmisartan and Chlorthalidone were observed to be 0.58 and 0.79 respectively. %Recovery was calculated for Telmisartan at 50%, 100% and 150% were 100.27%, 100.14%, 100.03%respectively and for Chlorthalidone at 50%, 100% and 150% were 101.78%, 100.43% and 100.48% respectively. LOD, LOQ values obtained from regression equation of Telmisartan and were 0.17, 0.19 and 0.48, 1.18 respectively. Regression equation of Telmisartan is y = 11487x -47198, and y = 11237x + 2102 of Chlorthalidone. Retention time were decreased and the run time decreased, so the technique developed was simple conservative that can be embraced in regular quality control test in industries.

INTRODUCTION

Telmisartan and Chlorthalidone is a combination medicine used to treat hyper tension. Telmisartan is an angiotensin ii receptor antagonist (ARB) used in the management of hypertension. Generally, antagonist ii receptors blockers (ARBs) such as telmisartan binds to angiotensin ii (AT 1) receptors with high affinity, causing inhibition of action of angiotensiniion vascular smooth muscle, ultimately leading to reduction in arterial blood pressure. Chlorthalidone is diuretic; it is indicated in the management of hypertension by removing excess water and certain electrolytes from the body. Eventually it also relaxes blood vessels and improves blood flow.[1-2]

MATERIALS AND METHODS

Preparation of diluents: Depending on the nature of solubility of the selected drugs, Acetonitrile and water in the ratio of 80: 20 v/v and pH was adjusted to 3.5 using orthophosphoric acid. The solution was prepared after degassing and filtering the solution using 0.45µm membrane filter.

Stock solution:

Preparation of standard stock solution: The solution was prepared by dissolving 45 mg of accurately weighed Telmisartan and 15mg Chlorthalidone in mobile phase, in two 100.0

ml volumetric flasks separately and sonicate for 20 min.

Preparation of sample stock solution: Twenty tablets were weighed and the average weight of each tablet was calculated, and a quantity of tablet powder equivalent to 45 mg Telmisartan and 15 mg Chlorthalidone were weighed and dissolved in 70 ml mobile phase with the aid of ultra sonication for 20 min. The mixture was diluted to 100 ml with mobile phase to furnish a sample stock solution.

Working solution:

Preparation of working standard solution: From the above stock solution 10 ml from each solution was taken into a 50 ml volumetric flask then madeup the volume with mobile phase and sonicated for 10 min and filtered through 0.45µmmembrane filter.

Preparation of sample working solution: The sample stock solution was filtered through a 0.45 µm nylon syringe filter and 10 ml of the filtrate was diluted into 50 ml volumetric flask to give a sample solution containing 90µg/ml Telmisartan and 30 µg/ml Chlorthalidone.[3 - 5]

RESULTS AND DISCUSSION:

Method validation: Specificity, linearity, range, accuracy, precision, repeatability, intermediate precision, limit of detection, limit of quantification, robustness.[6 – 7]

Specificity: Specificity is the ability to assessing equivocally the analyse in the presence of components which may be expected to be present. Typically these components include impurities, degradants, matrix,etc. Blank solution, standard solution of Telmisartan (90µg/ml) and Chlorthalidone (30 µg/ ml) were injected into the HPLC system. The peak purity data of Telmisartan and Chlorthalidone was compared there should not be any interference at the retention time of the main peak.

Linearity: Linearity for the drugs Telmisartan and Chlorthalidone was determined by preparing the standard solutions at six concentrations levels in six replicates in the range of22.5 – 135 µg/ml for Telmisartan and 7.5 – 45µg/ml for Chlorthalidone from stock solution. The linearity charts of Telmisartan and Chlorthalidone was shown in the figureno.5&6. The correlation coefficient was found to be 0.9954 and 0.999 for both drugs and the method was set to be linear. They were tabulated in table 1.

Accuracy: Accuracy was performed by spiking known amounts of standard solution to sample solution at three different concentrations levels (50%, 100%, 150%) and there by analyzed for overall %RSD should not be more than 2.0.The % recovery was calculated and the results was reported in table no. 2 & 3.

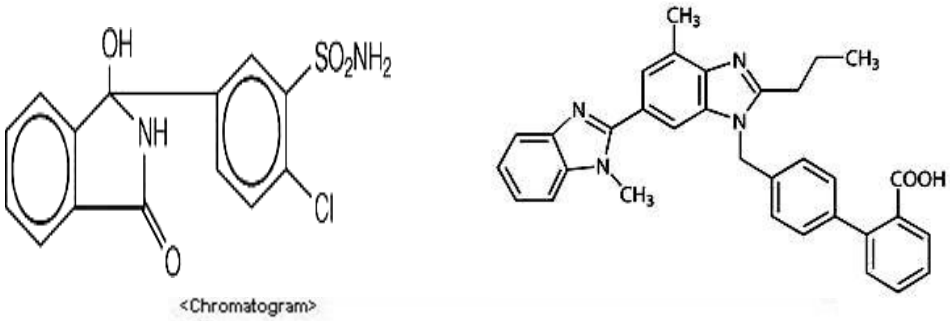
Precision: The precision of the analytical method was studied by injecting six replicates of standard and sample containing 90 µg/ml of Telmisartan and 30 µg/ml of Chlorthalidone were injected into HPLC system. The % RSD was calculated and the results were reported in the table no.4&5.

Limit of Detection (LOD) and Limit of Quantification (LOQ):

The limit of detection (LOD) and limit of quantification (LOQ) were determined by injecting six replicates of mobile phase followed by three concentrations of drug. The limit of detection was defined as the concentration which yields a signal - to – noise ratio 3:1 where as the limit of quantification was calculated to be the lowest concentration that could be measured with signal - to – no iseratio10:1.LOD and LOQ were calculated from slope and standard deviation. The results were tabulated in table no. 6.

Robustness: The smallest deliberate changes in method like flow rate and mobile phase ratio are made but there were no predictable changes in the results and are in the range as per ICH guidelines. Conditions like flow minus (0.8 ml/min), flow plus (1.0 ml/min), mobile phase minus, mobile phase plus, ambient temperature was maintained and sample were injected in duplicate manner. System suitability parameters were not much affected and all the parameters were passed. % RSD was found to be within the limits and Results were tabulated intableno.7 & 8.

Fig-1: structure of Telmisartan and Fig-2: structure of Chlorthalidone



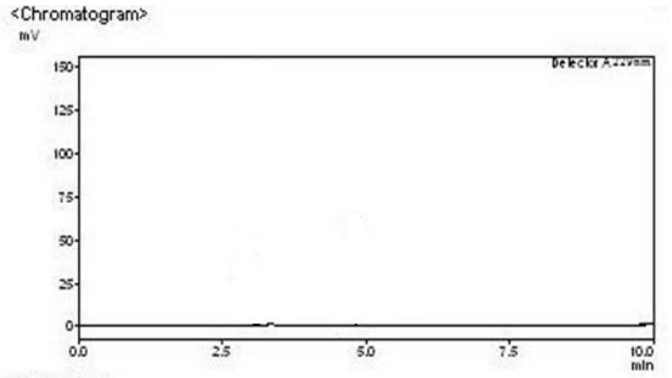


Fig-3: Chromatogram of Blank

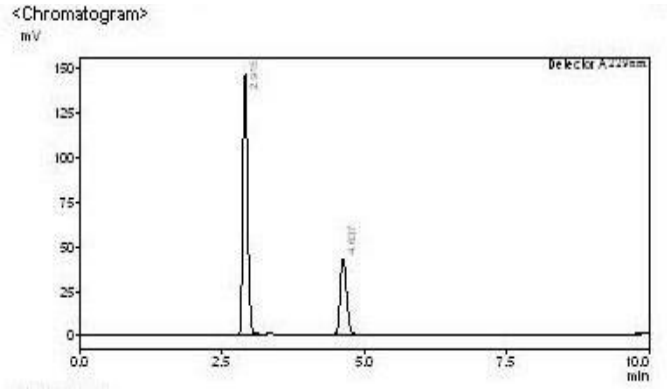


Fig-4: Optimized chromatogram

Table-1: Linearity results of Telmisartan and Chlorthalidon

Telmisartan		Chlorthalidone	
Conc(µg/mL)	Peak area	Conc(µg/ mL)	Peak area
22.5	218093	7.5	85582
45	433120	15	172188
67.5	694264	22.5	255782
90	952350	30	342375
112.5	1244314	37.5	424969
135	1555021	45	503568

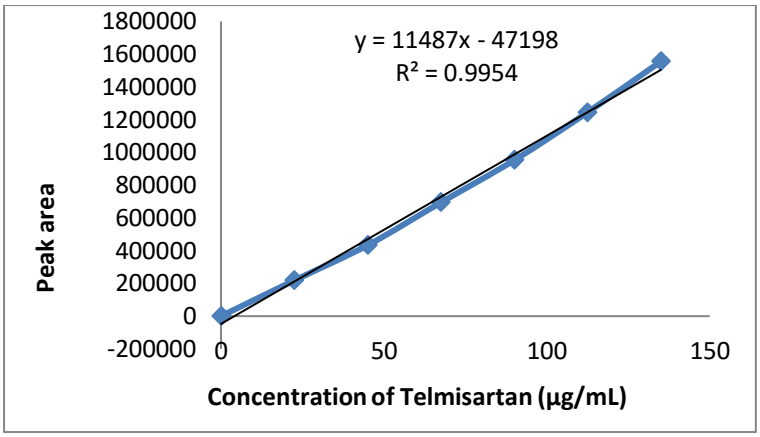


Fig-5: Calibration curve of Telmisartan

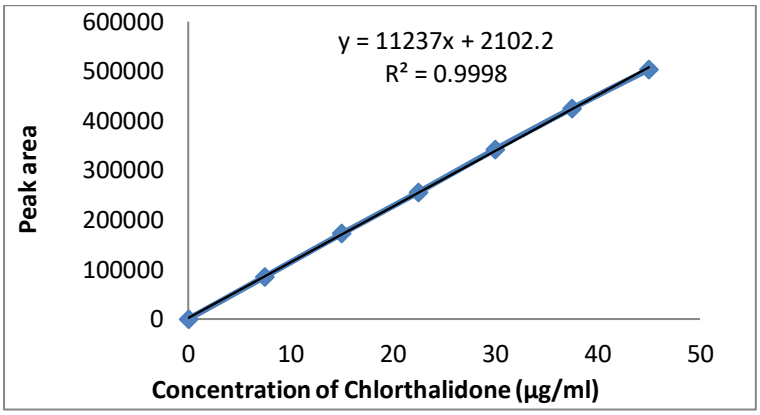


Fig-6: Calibration curve of Chlorthalidone

Table-2: Accuracy data of Telmisartan

%Level	Amountspiked(µg/mL)	Amount recovered(µg/mL)	% Recovery	Mean % Recovery	%RSD
50%	45	45.124	100.28	100.27%	0.12%
	45	45.248	100.55		
	45	45.986	99.97		
100%	90	90.247	100.27	100.14%	0.11%
	90	89.995	99.99		
	90	90.137	100.15		
150%	135	134.896	99.92	100.03%	0.09%
	135	135.086	100.06		
	135	135.138	100.10		

Table-3: Accuracy data of Chlorthalidone

%Level	Amount spiked(µg/mL)	Amount recovered(µg/mL)	% Recovery	Mean% Recovery	%RSD
50%	15	15.267	101.73	101.83	0.35%
	15	15.348	102.32		
	15	15.210	101.40		
100%	30	30.143	100.48	100.43	0.42%
	30	30.257	100.86		
	30	29.986	99.95		
150%	45	45.210	100.47	100.48	0.26%
	45	45.328	100.73		
	45	45.112	100.25		

Table-4: System precision data of Telmisartan and Chlorthalidone

S.NO	Peak Area	
	Telmisartan	Chlorthalidone
1	952468	342375
2	952531	342756
3	952672	342658
4	952289	342325
5	952643	342124
6	952563	342109
Mean	952528	342391
Std dev	138.51	268.31
%RSD	0.58	0.79

Table-5: Method precision data ofTelmisartan and Chlorthalidone

S.NO	Peak Area	
	Telmisartan	Chlorthalidone
1	952348	342258
2	952358	342109
3	952348	342352
4	952548	342428
5	952555	342375
6	952602	342315
Mean	952459.8	342306.2
Std dev	120.35	112.21
%RSD	0.56	0.82

Table-6: LOD and LOQ data of Telmisartan and Chlorthalidone

Drug name	LOD	LOQ
Telmisartan	0.17	0.91
Chlorthalidone	0.48	1.18

Table-7: Robustness data of Telmisartan

S.NO	Condition	%RSD	Tailing factor	Theoretical plates
1	Flow rate(-) 0.8ml/min	0.088	1.168	3942
2	Flow rate(+)1.0ml/min	0.101	1.180	4016
3	Mobile phase(-) 60B:40A	0.126	1.179	3864
4	Mobile phase(+) 50B:50A	0.108	1.158	3998

Table-8: Robustness data of Chlorthalidone

S.NO	Condition	% RSD	Tailing factor	Theoretical plates
1	Flow rate(-)0.8ml/min	0.085	1.126	2220
2	Flow rate(+)1.0ml/min	0.099	1.149	2115
3	Mobile phase(-)60B:40A	0.094	1.138	2093
4	Mobilephase(+) 50B:50A	0.132	1.151	2169

CONCLUSION:

The developed RP-HPLC method was validated as per ICG guidelines. All the system suitability parameters were within the range as stated by ICH guidelines. Interference peaks were not observed in blank, standard and sample chromatogram. Hence simple, precise and accurate, sensitive, specific and robust method was developed and validated. This can be used in quality control department with respect to routine analysis.

Acknowledgement: The author expresses sincere thanks to Pharmazell Vizag private Limited for providing facilities and support to carry out the research work.

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