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Research Article

Simultaneous Estimation of Telmisartan and Indapamide in Tablet Dosage Form by RP-HPLC Method and its Method Validation

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ABSTRACT

A new simple, accurate, rapid and precise isocratic RP-HPLC was developed and validated for the determination of Telmisartan and Indapamide in Pharmaceutical tablet dosage form. The Method employs Shimadzu LC system on Symmetry C8 (4.6 x 150mm, 3.5µm, Make: X Terra) and flow rate of 1ml/min with a load of 20µl. Potassium Dihydrogen Orthophosphate buffer and Acetonitrile was used as mobile phase in the composition of 43:57 v/v. The Detection was carried out at 254 nm. Linearity ranges for Telmisartan and Indapamide were 200-600µg/ml and 9-22.5µg/ml respectively for HPLC. Retention Time of Telmisartan and Indapamide were found to be 2.2 & 5.8 min respectively. Percent Recovery study values of Telmisartan and Indapamide were found 100.56 % and 99.4 % respectively. This newly developed method was successfully utilized for the Quantitative estimation of Telmisartan and Indapamide in tablet dosage form. This method was validated for, linearity, precision, Accuracy, System suitability Robustness, Ruggedness as per ICH guidelines.

Keywords: Telmisartan and Indapamide, RP-HPLC, validation.

1. INTRODUCTION

Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. Generally, angiotensin II receptor blockers (ARBs) such as Telmisartan bind to the angiotensin II type 1 (AT1) receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, ultimately leading to a reduction in arterial blood pressure. Recent studies suggest that Telmisartan may also have PPAR-gamma agonistic properties that could potentially confer beneficial metabolic effects. Chemically described as 2-(4-{[4-methyl-6-(1-methyl-1H-1, 3-benzodiazol-2- yl)-2-propyl-1H-1, 3-benzodiazol-1-yl] methyl} phenyl)benzoic acid. In the present study the authors report a rapid, sensitive, accurate and precise HPLC method for the estimation of Telmisartan in bulk samples and in tablet dosage forms.

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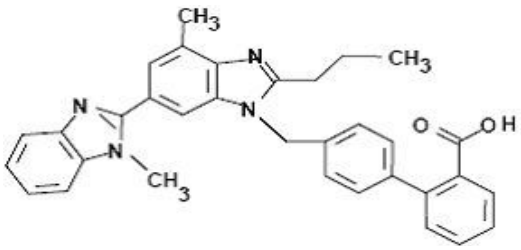

Fig.1: Chemical structure of Telmisartan

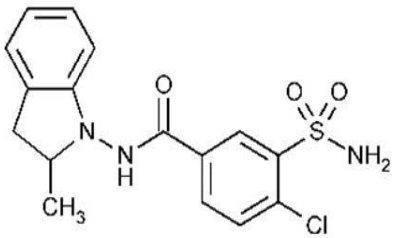

Fig.2: Chemical structure of Indapamide

Indapamide is chemically 4 – chloro –N - (2 – methyl - 2,3-dihydroindol –1 – yl) - 3- sulfamoyl - benzamide (Fig-2). Indapamide is a thiazide diuretic generally used in the treatment of hypertension. It enhances sodium chloride and

water by interfering with the transport of sodium ions across the renal tubular epithelium. Indapamide blocks the slow component of delayed rectifier potassium current without altering the rapid component or the inward rectifier current. Indapamide is also thought to stimulate the synthesis of vasodilatory hypotensive prostaglandin. Simultaneous estimation of Indapamide and Telmisartan was not official in any pharmacopoeia. The method was validated according to ICH guidelines. The Linearity, Accuracy, Precision, Intermediate precision, Robustness parameters were validated

2. MATERIALS AND METHODS

2.1 Materials

Analytically pure samples of Telmisartan and Indapamide were obtained as a gift sample from Dr. Mliton laboratories pvt.ltd, Pondicherry, respectively, Marketed formulation sample inditel-d telmisartan40mg and Indapamide 1.5mg claim Cadila Healthcare limited. Chemicals used for this experiments were, Methanol (HPLC grade), Ortho phosphoric acid (AR grade) was purchased from Merck Specialized Pvt Ltd, Mumbai, Acetonitrile (HPLC grade), anhydrous Potassium Dihydrogen Phosphate (AR grade) is from Merck Pvt. Ltd.

2.2 Instrument

.The development and validation of the assay was performed on a HPLCShimadzu LC 2010 ,Isocratic pump, equipped with an auto injectorPAD detector, LC 2010 CHT, UV-Visible spectrophotometer SHIMADZU UV-Probe 2.33

2.3 Chromatographic conditions

Chromatographic conditions were obtained using a stainlesssteel column (Symmetry C8 (4.6 x 150mm, 3.5µm, Make: XTerra), which was maintained at Ambient temperature. The analytical wavelength was set at 254 nm and samples of 20µl were injected to HPLC system. The mobile phase was Phosphate Buffer pH adjusted to 4.5 with orthophosphoric acid): acetonitrile in ratio of 43:57 at a flow rate of 1.0ml/min

2.4 Preparation of mobile phase

Mobile phase was prepared by Potassium Dihydrogen Orthophosphate buffer and acetonitrile in ratio of 43:57 v/v respectively. Buffer solution was prepared by dissolving 7.0 gm of potassium dihydrogen orthophosphate to 1000ml of HPLC grade water and pH is adjusted to 4.5 with orthophosphoric acid. The content of mobile phase and buffer solution were filtered before use through 0.45µm filter and degassed for 10min by sonication.

2.5 Diluent Preparation: Mobile phase was used as a Diluent.

2.6 Preparation of standard drug solution

The standard stock solution was prepared by dissolving 40mg of Telmisartan and 1.5mg of Indapamide in 10ml of mobile phase (stock solution). Then take1ml of solution from stock solution and dilute upto 10ml with mobile phase to get working concentration of Telmisartan(400µg/ml) and Indapamide (15µg/ml).

2.7 Preparation of sample solution

Weigh and crush tablets in to a clean and dry mortar pestle to get the average weight. The sample of the powdered tablets claimed to contain 40mg of Telmisartan and 1.5mg of Indapamide of active ingredient was taken in a 10ml volumetric flask diluted up to mark with mobile phase and sonicated for 20min(stock solution). Take 1ml of solution from stock solution and dilute up to 10ml with mobile phase to get working concentration of Telmisartan and Indapamide .The solution was then filtered through0.45µm membrane filter.

2.8 Method Validation

2.8.1 Linearity

Solutions were prepared containing200µg/ml, 300µg/ml, 400µg/ml,500µg/ml & 600µg/ml concentrations of Telmisartan and 9µg/ml, 12µg/ml, 15µg/ml, 18.75µg/ml, 22.5µg/ml concentrations of Indapamide which corresponding to ,50, 75,100,125 and 150% respectively of the test solution concentration. Each solution was injected, linearity was evaluated by linear- regression analysis.

2.8.2 Accuracy

Accuracy was determined by the recovery studies at three different concentrations (corresponding to 50, 100 and 150% of the test solution concentration) by addition of known amounts of standard to pre-analysed sample preparation. For each concentration, three sets were prepared and injected.

2.8.3 Precision

Intraday and Rggedness variations were determined by using Three replicate injections of standard concentration and

analyzed on the same day and different days. Precision of an analytical method is usually expressed as the standard deviation or relative standard deviation (coefficient of variation) of a series of measurements.

2.8.4 Robustness

The robustness was evaluated by assaying test solutions after slight but deliberate changes in the analytical conditions. The factors chosen for this study were the flow rate (±0.2ml/min), Hence it indicates that the method is not robust even by change in the Mobile phase ±10.

2.8.5 Ruggedness

Ruggedness test was determined between two different analysts, instruments and Columns. The value of percentage RSD was below 2.0%, showed ruggedness of developed analytical method.

3. RESULTS AND DISCUSSION

RP-HPLC method has been developed for the simultaneous estimation of Telmisartan and Indapamide in bulk and pharmaceutical dosage form. Chromatographic separation was performed on a stainless steel column (Symmetry C8 (4.6 x 150mm, 3.5µm, Make: X Terra), which was maintained at Ambient temperature using mobile phase consisting phosphate buffer: acetonitrile (43:57) at pH 4.5 at a flow rate of 1ml/min. Detection was carried out at 254nm. Telmisartan and Indapamide obeyed linearity in concentration range of 200-600µg/ml and 9-22.5µg/ml respectively. The percentage recovery studies of Telmisartan and Indapamide were found 100.56 %, 99.4 % respectively. The method was validated and found to be simple, accurate, sensitive and precise.

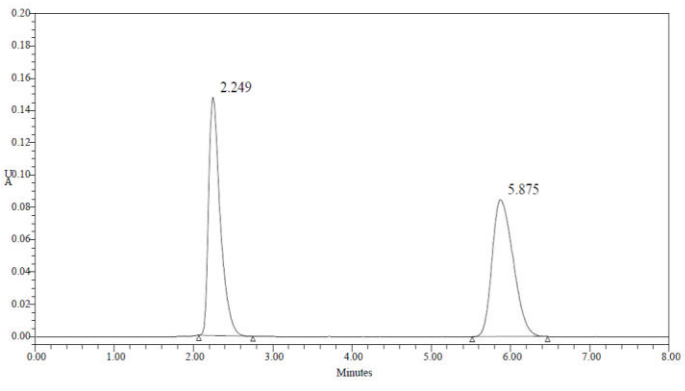

Fig. 3: Chromatogram of Telmisartan (40µg/ml) and Indapamide (1.5µg/ml) standard

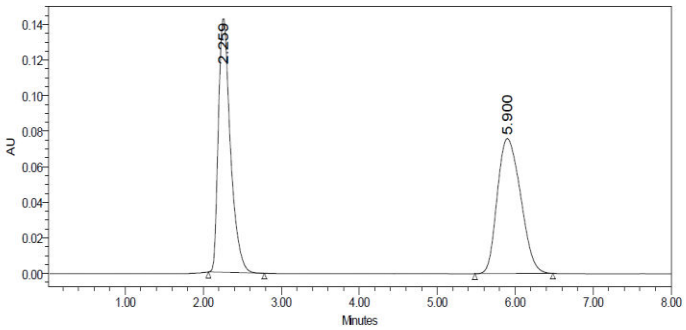

Fig.4: Chromatogram for Sample

Table 1: Analysis data of tablet formulation

S. No	Tablet	Lable Claim	%Assay	Relative standard deviation
1.	Telmisartan	40mg	100.56	0.14
2.	Indapamide	1.5mg	99.4	1.76

Table 2: Result of Linearity

S. No	Telmisartan		Indapamide	
	Conc. (µg/ml)	Peak area	Conc. (µg/ml)	Peak area
1	200	3843675	9	298791
2	300	5786567	12	357431
3	400	7526542	15	383408
4	500	9354556	18.75	439576
5	600	11086576	22.5	494721

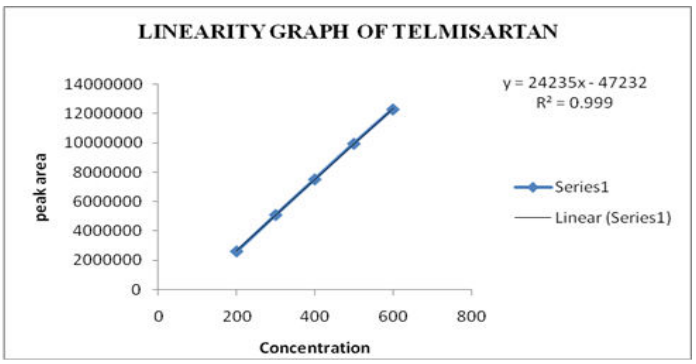

Fig. 5: Calibration curve for Telmisartan

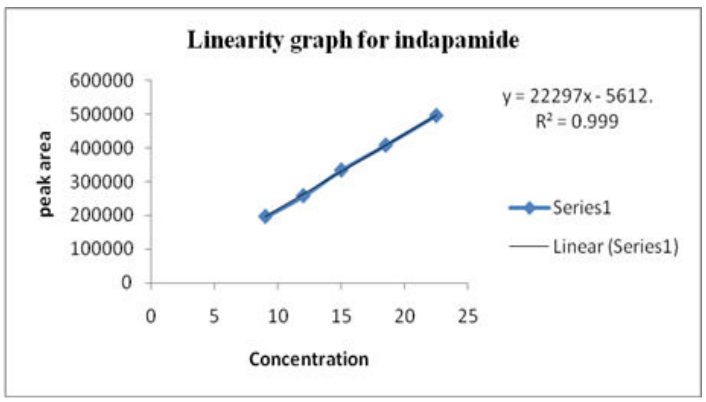

Fig.6: Calibration curve for Indapamide

Table 4: System suitability studies

Parameters	Telmisartan	Indapamide	Acceptance criteria
Theoretical plates	4103.7	3683.4	More than 2000
USP Tailing factor	0.7	0.9	Less than 2
Retention time(min)	2.249	5.875	More than 2

Table 5: Recovery studies for Telmisartan and Indapamide

Drug	%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
TEL	50%	3864243	20.0	20.07	101.4%	100.56%
	100%	7567396	40.0	39.98	99.8%	
	150%	1219728	60.0	60.08	100.5%	
IND	50%	198196	0.75	0.79	98.6%	99.4%
	100%	382695	1.5	1.52	99.6%	
	150%	565792	2.25	2.23	100.%	

Table 6: Results of Precision

Telmisartan	Injection number	Retention time of Telmisartan	Retention time of Indapamide	Area of Telmisartan	Area of Indapamide
1	Injection-1	2.259	6.374	7549491	379612
2	Injection-2	2.259	6.374	7530248	374521
3	Injection-3	2.259	6.374	7530713	366564
4	Injection-4	2.259	6.374	7530578	373452
5	Injection-5	2.259	6.374	7548473	365423
6	Injection-6	2.259	6.374	7545445	375643
	AVG			7539158	372535
	%RSD			0.12	1.46

Table 7: Results of Telmisartan Robustness study

Proposed variations		USP Plate Count	USP Tailing
Variation in mobile phase composition	10% less	3963.1	0.9
	Actual	4103.7	0.7
	10% more	3768.8	1.1
Variation in flow rate	0.8ml/min	3519.4	1.0
	1ml/min	3903.7	0.7
	1.2ml/min	3474.4	1.1

Table 8: Results of Indapamide Robustness study

Proposed variations		USP Plate Count	USP Tailing
Variation in mobile phase composition	10% less	3396.9	1.1
	Actual	3683.4	0.9
	10% more	3518.9	1.0
Variation in flow rate	0.8ml/min	3228.3	1.3
	1ml/min	3475.4	0.9
	1.2ml/min	3142.7	1.1

Table 9: Ruggedness of Telmisartan and Indapamide

Number of injections	Retention time of Telmisartan	Retention time of Indapamide	Area of Telmisartan	Area of Indapamide
Injection-1	2.293	5.951	7576857	390948
Injection-2	2.291	5.955	7571778	393690
Injection-3	2.290	5.944	7570279	395386
AVG			7572971	393341
STD			3447.5	2239.4
% Relative Standard deviation			0.04	0.56

4. CONCLUSION

A simple, accurate, fast and precise reverse phase high pressure liquid chromatographic method has been developed for the quantification simultaneous determination in bulk and Pharmaceutical dosage form. The developed method is suitable for routine quality control Analysis work.

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