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Analytical method development and validation for the simultaneous estimation of telmisartan and hydrochlorothiazide by RP-HPLC

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ABSTRACT

The present research work deals with the development, optimization and validation of RP-HPLC method for the simultaneous estimation of Telmisartan and Hydrochlorothiazide in combined dosage form. Market is folded with combination of drugs in various dosage forms. The multi-component formulations have gained a lot of importance now days due to greater patient acceptability, increased potency, multiple action, fewer side effects and quicker reliefs. For simultaneous estimation of drugs present in multi-component dosage form, High Pressure Liquid Chromatography (HPLC) is considered to be most suitable since it is extremely precise, accurate, sensitive, linear and rapid. So the objective of the present work is to develop HPLC method for simultaneous estimation of drugs in combined dosage form for which no better analytical method has been previously reported. The Method employs Waters HPLC system on XTerra, Symmetry C18 (4.6 x 150mm, 5µm) Column. The flow rate was 1.0ml/min and the detection was carried out at 274 nm. Selected mobile phase was a combination of Methanol: Buffer (Potassium dihydrogen phosphate) in the ratio of 70:30 and PH 2.5 (adjusted with Orthophosphoric acid).The Retention times of Hydrochlorothiazide and Telmisartan were found to be 1.723 and 3.769 minutes respectively. Linearity ranges for Hydrochlorothiazide and Telmisartan were 6.25 - 31.25ppm and 20-100ppm respectively. The correlation co-efficient of Telmisartan and Hydrochlorothiazide was found to be 0.999. Percent recovery was found to be within the range of 98.0 % to 102.0%.Theproposed method was found to be precise, selective, rapid and economical. It can be successfully utilized for the simultaneous determination of Telmisartan and Hydrochlorothiazide in pharmaceutical dosage form.

Keywords: Telmisartan, Hydrochlorothiazide, precision, accuracy, linearity, HPLC

INTRODUCTION

Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. It is Insoluble in H_2O and in pH range of 3 to 9, sparingly soluble in alcohol, strong acid (except HCl) and soluble in strong base. Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I. Hence, it antagonizes the effect of angiotensin II (vasoconstriction and aldosterone secretion) by blocking the angiotensin II (AT_1 receptor) in vascular smooth muscle and the adrenal gland, producing decreased blood pressure.[1-5]

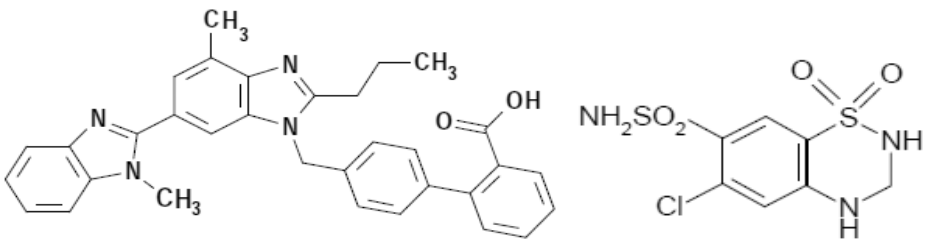

Fig 1: Structure of Telmisartan and Hydrochlorothiazide

Hydrochlorothiazide, a 'water pill,' is used to treat high blood pressure and fluid retention caused by various conditions, including heart disease. It causes the kidneys to get rid of unneeded water and salt from the body into the urine. Slightly soluble in water, and freely soluble in sodium hydroxide solution. Hydrochlorothiazide, abbreviated HCTZ, HCT, or HZT, is a first-line diuretic drug of the thiazide class that acts on the kidney tubule to decrease reabsorption of sodium. So, more sodium and water is sent into the urine. This reduces the volume of the blood, decreasing blood return to the heart and thus cardiac output and lowers the blood pressure. Used to treat High blood pressure, heart attacks, Diabetes Insipidus, act as a diuretic, reduces extra fluid in the body (edema), reduces the symptoms like shortness of breath, swelling in ankles and joints.[6-9]

The tablets are available in combination containing either telmisartan 40 mg and hydrochlorothiazide 12.5 mg, or telmisartan 80 mg and hydrochlorothiazide 12.5 mg or 25 mg. A patient whose blood pressure is not adequately controlled with telmisartan monotherapy may be switched to combination tablets, telmisartan 40mg/hydrochlorothiazide 12.5 mg.[10-12]

MATERIALS AND METHOD

Telmisartan and Hydrochlorothiazide gift samples obtained from pharma industry were used for the study. All the solvents and reagents used were of HPLC grade.

Equipment

Alliance Waters HPLC with Autosampler with Empower 2.0 Software, dual λ UV detector was provided. The chromatographic analysis was performed using Symmetry C18 (4.6 x 150mm, 5µm, Make: XTerra) as a stationary phase.

Chromatographic Conditions

Mobile phase was pumped at a flow rate of 1 mL/min using a binary mixture of Methanol and Phosphate buffer (70:30v/v) in isocratic mode. The injection volume of 20 µL was given and the detection wavelength for Telmisartan and Hydrochlorothiazide was set at 274 nm and the separation was achieved at room temperature.

Preparation of standard solutions

Accurately weigh and transfer 6.25 mg of Hydrochlorothiazide and 20mg of Telmisartan working standard into a 10mL clean dry volumetric flask add about 7ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 0.3ml of Hydrochlorothiazide and Telmisartanthe above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent.

Preparation of sample solution

Accurately weigh and transfer to 133 mg of Hydrochlorothiazide and Telmisartan Tablet Powder into a 100ml clean dry volumetric flask add about 70ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution). Further pipette 1.5ml of Hydrochlorothiazide and Telmisartan of the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluents.

RESULTS AND DISCUSSION

Optimized chromatographic conditions

Equipment	: High performance liquid chromatography equipped with Auto Sampler and DAD or UV detector
Column	: Symmetry C18 (4.6 x 150mm, 5µm, Make: XTerra) or equivalent
Mobile phase	: Methanol and Phosphate buffer (70:30)
Flow rate	: 1.0 mL per min
Wavelength	: 274 nm
Injection volume	: 20 µl
Column oven	: Ambient
Run time	: 7 min

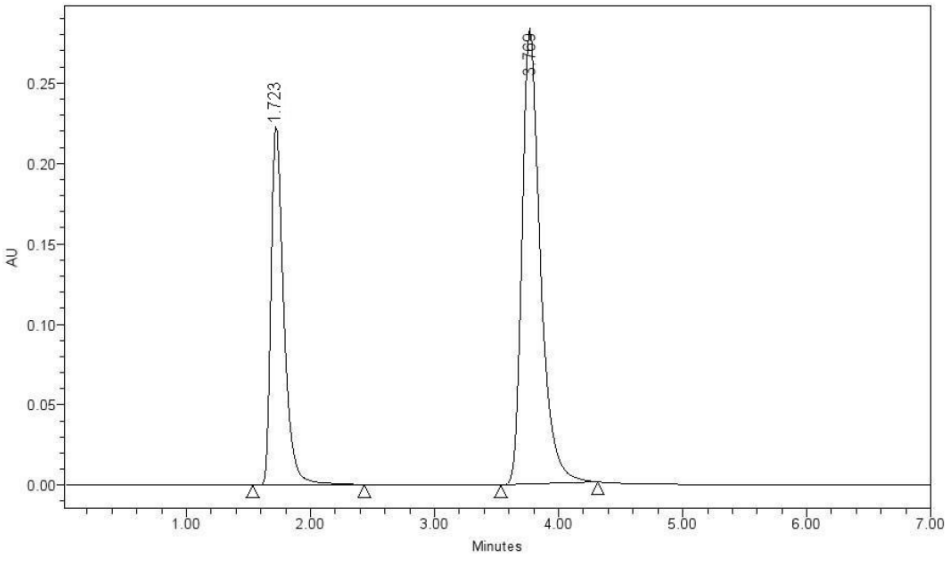

Fig 2: Typical Chromatogram of Telmisartan and Hydrochlorothiazide

Assay

Table 1: Assay Results

	Name	RT	Area	USP Plate Count	USP Tailing
1	Hydrochlorothiazide	1.725	1626625	2404	1.4
2	Hydrochlorothiazide	1.725	1625152	2409	1.4
3	Hydrochlorothiazide	1.725	1608660	2421	1.4
Mean			1622215	2411.3	1.4
Std.Dev			2237.3		
%RSD			**0.14**		

Table 2: Assay Results

	Name	RT	Area	USP Plate Count	USP Tailing	USP Resolution
1	Telmisartan	3.759	2907257	3295	1.4	8.83
2	Telmisartan	3.759	2938398	3302	1.39	8.83
3	Telmisartan	3.759	2960622	3347	1.4	8.89
Mean			2967626	3314.6	1.4	
Std.Dev			7306.1			
%RSD			**0.25**			

Validation of the HPLC Method: The proposed method was validated as per ICH guidelines[12].

Linearity and range

Linearity of detector response of assay method was found by injecting standard solutions with concentration ranging from 50 % to 150 % of the test concentration Peak area is measured and each level injected into the chromatographic system and the. A graph plotted of peak area versus concentration the correlation coefficient calculated.

Table 3: Linearity of Hydrochlorothiazide

S.NO	LINEARITY LEVEL	CONCENTRATION	AREA
1	I	6.25ppm	950530
2	II	12.5ppm	1251176
3	III	18.75ppm	1648170
4	IV	25.0ppm	1965704
5	V	31.25ppm	2316007
Correlation Coefficient			0.999

Table 4: Linearity of Telmisartan

S.NO	LINEARITY LEVEL	CONCENTRATION	AREA
1	I	20ppm	1613754
2	II	40ppm	2357123
3	III	60ppm	3066687
4	IV	80ppm	3792417
5	V	100ppm	4419759
Correlation Coefficient			0.999

Accuracy

The % Recovery results indicate that the test method has an acceptable level of accuracy for the assay of hydrochlorothiazide and telmisartan in the range of 50% to 150%.

Table 5: Recovery results for hydrochlorothiazide

%Concentration (at specification level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	1179422	3.10	3.12	100.8%	
100%	2358274	6.25	6.25	100.0%	100.8%
150%	3603242	9.40	9.55	101.6%	

Table 6: Recovery results for Telmisartan

%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	2185178	10.0	9.92	99.9%	
100%	4402202	20.0	19.9	99.9%	100.3%
150%	6732427	30.0	30.5	101.9%	

Precision

Sample preparations of Telmisartan and Hydrochlorothiazide were prepared as per the method and injected into the column. And the relative standard deviation of assay results was calculated. The results were shown in Table 7, 8.

Table 7: Results for Method precision of Hydrochlorothiazide

INJECTION	AREA
Injection-1	1612121
Injection-2	1613799
Injection-3	1612432
Injection-4	1607736
Injection-5	1614913
AVERAGE	1612200
STD.DEVIATION	2734.0
%RSD	0.17

Table 8: Results for Method precision of Telmisartan

INJECTION	AREA
Injection-1	2949740
Injection-2	2929827
Injection-3	2941727
Injection-4	2927105
Injection-5	2941828
AVERAGE	2938046
STD.DEVIATION	9378.9
%RSD	0.32

Intermediate Precision/Ruggedness

Precision was performed by different analysts by using different columns of same dimensions and method evaluated. The area was measured in HPLC for the five times injected standard solution. The results were shown in Table 9.

Table 9: Results for Ruggedness

Hydrochlorothiazide	AREA	Telmisartan	AREA
Injection-1	1610414	Injection-1	2945785
Injection-2	1609420	Injection-2	2936585
Injection-3	1618938	Injection-3	2951312
Injection-4	1616343	Injection-4	2955626
Injection-5	1609045	Injection-5	2950608
AVERAGE	1612832	**AVERAGE**	2947983
STD.DEVIATION	4512.3	**STD.DEVIATION**	7265.4
%RSD	0.28	**%RSD**	0.25

Robustness

Chromatographic conditions variation

The prepared solution is injected at different variable conditions like Temperature and wavelength as per test method. System suitability parameters were compared with that of method precision. The results were shown in Table 10

Table 10: Result of Robustness study

S.NO	ROBUSTNESS PARAMETER FLOW RATE(ml/min)	USP RESOLUTION
1.	ACTUAL FLOW (1 ml/min)	8.83

2.	LESS FLOW (0.9 ml/min)	8.9
3.	MORE FLOW (1.1 ml/min)	8.6
S.NO	**ROBUSTNESS PARAMETER**	**USP RESOLUTION**
	ORGANIC COMPOSITION IN MOBILE PHASE	
1.	ACTUAL ORGANIC	8.83
2.	LESS ORGANIC	12.4
3.	MORE ORGANIC	6

CONCLUSION

From the above it can be concluded that all validation parameters such as precision, accuracy, linearity and Ruggedness met the predetermined acceptance criteria as mentioned in ICH guidelines. The developed RP-HPLC method is simple, rapid, accurate, and precise and can be applied for routine analysis of Telmisartan and Hydrochlorothiazide in bulk and its dosage forms

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