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UV-Spectrophotometric Determination of Telmisartan and Hydrochlorothiazide in Combined Tablet Dosage Form Using Simultaneous Equation Method

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Abstract

A UV spectrophotometric method was developed for the estimation of Telmisartan & Hydrochlorothiazide in Combined Tablet Dosage Form Using Simultaneous Equation Method. The drug obeyed the Beer's law & shows good correlation near to r^2 = 0.999 for Telmisartan & for Hydrochlorothiazide r^2=0.999.Absorption maxima of Telmisartan 296.8 nm and Hydrochlorothiazide 271.2 nm. Beer's law was obeyed in concentration rang of 5-30 µg/ml for Telmisartan & 2-12 µg/ml for Hydrochlorothiazide. The method has been validated for linearity, accuracy & precision. The recovery was 99.28 % for Telmisartan & 99.26% for Hydrochlorothiazide. The developed method was found to be accurate, simple, precise, economical, and selective for simultaneous estimation of Telmisartan & Hydrochlorothiazide in tablet formulations.

***Keywords*:** Telmisartan, Hydrochlorothiazide, UV-Spectrophotometer simultaneous determination, , development and validation.

1. Introduction

It is antihypertensive drug it selectively blocks AT_1 receptors and prevents stimulation of their receptors by angiotensin it produces vasodilatation and reduces peripheral resistance and blood pressure. Inhibition of central sympathetic tone, Blocks release of adrenaline, Inhibits Na and water retention in kidney and reduces fluid overload and preload. It is mainly used in hypertension. It is used for treating high blood pressure & accumulation of fluid. Works by blocking solute & fluid reabsorption in the kidneys, causing increase urine output. Also used to treat fluid accumulation and swelling (edema) of body caused by heart failure, cirrhosis, chronic kidney failure, corticosteroid medication and nephritic syndrome. TELM is chemically 4'-[(1,4'-Dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-1,1'-biphenyl]-2-carboxylic acid. Hydrochlorothiazide (HCT) is one of the widely used thiazide diuretic which reduces reabsorption of electrolytes from the renal tubules and chemically 6-Chloro-3, 4-dihydro-2H-1, 2, 4-benzothiazidine-7- sulfonamide-1,1-dioxide.

2. Experimental

2.1 Selection of Solvents

On the basis of solubility study methanol was selected as the solvent for dissolving TLM and HCTZ.

2.2 Preparation of Standard Stock Solutions of TLM and HCTZ

A) Telmisartan Standard Stock Solution [T]: An accurately weighed quantity of TLM (25 mg) was taken in 25 mL volumetric flask and dissolved in methanol (20 mL) with the help of ultrasonication for about 10 min. Then the volume was made up to the mark using methanol to get Telmisartan standard stock solution (1 mg / mL).

B) Telmisartan Working Standard Solution [T_1]:

Telmisartan standard stock solution [T] (5 mL) was diluted to 50 mL using 50% v/v methanol to get working standard solution (100 µg / mL)

C) Hydrochlorothiazide Standard Stock Solution [H]:

An accurately weighed quantity of HCTZ (25 mg) was taken in 25 mL volumetric flask and dissolved in methanol (20 mL) with manual shaking. Then the volume was made up to the mark using methanol to get Hydrochlorothiazide standard stock solution (1 mg / mL).

D) Hydrochlorothiazide Working Standard Solution [H_1]:

Hydrochlorothiazide standard stock solution [H] (5 mL) was diluted to 50 mL using 50% v/v methanol to get Hydrochlorothiazide working standard solution of (100 µg / mL)

2.3 Determination of λ Max of Individual Component

An appropriate aliquot portion of TLM (0.5 mL) and HCTZ (0.5 mL) were transferred to two separate 10 mL volumetric flasks, the volume was made up to the mark using 50 %v/v methanol to obtain TLM (5 µg/mL) and HCTZ (5 µg/mL). Drug solutions were scanned separately between 200 nm to 400 nm.

2.4 Determination of Overlay Spectra and Isoabsorptive Point

The overlain spectrum of both drugs was recorded (**Fig. 4)** and two wavelengths 296.8 nm (λ max of TLM) and 271.2 nm (λ max of HCTZ) were selected for further study.

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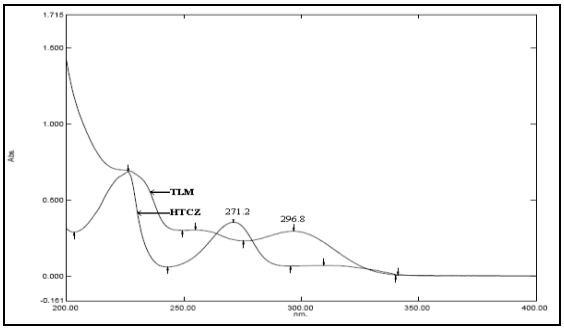
Fig. 1: Overlay Spectra of TLM and HCTZ



2.5 Study of Beer-Lambert's Law [Linearity study]:

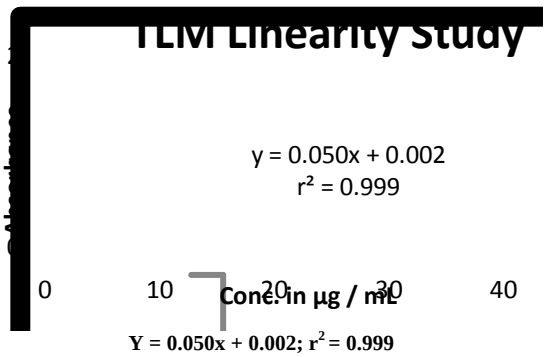
A) Linearity Study for TLM: Accurately measured aliquot portions of working standard solution of TLM [T_1] (0.5 mL to 3 mL) was transferred to seven separate 10 mL volumetric flasks. The volume was made up to the mark using 50% v/v methanol to obtain concentrations (5-30 µg/mL). Absorbance of these solutions was measured at 296.8 nm, **(Table2)** Calibration curve was plotted, absorbance Vs concentration as shown in **(Fig. 5)**.

B) Linearity Study for HCTZ: Accurately measured aliquot portions of working standard solution of HCTZ [H_1] (0.2 mL to 1.2 mL) were transferred to seven separate 10 mL volumetric flasks. The volume was made up to the mark using 50% v/v methanol to obtain concentrations (2 – 12 µg/mL). Absorbance of these solutions was measured at 271.2 nm, (**Table 3)**. Calibration curve was plotted, absorbance Vs concentration as shown in (**Fig. 6).**

Table 2: Linearity Study of TLM at 296.8 nm

Sr. No.	Concentration of TLM in [µg/mL]	Absorbance Mean ± S.D. [n = 5]	% R.S.D.
1	0	0	0
2	5	0.252±0.0016	0.63
3	10	0.497±0.0048	0.96
4	15	0.748± 0.0060	0.80
5	20	1.137±0.0047	0.41
6	25	1.258±0.0094	0.74
7	30	1.488±0.0034	0.22

Fig. 2: Calibration Curve of Telmisartan at 296.8 nm Wavelength



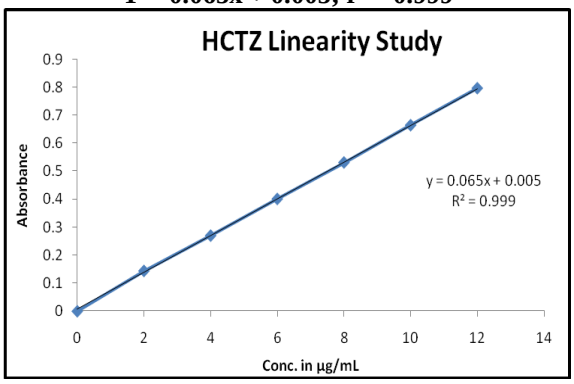
Y = 0.050x + 0.002; r^2 = 0.999

Table3: Linearity Study of HCTZ at 271.2 nm

Sr. No.	Concentration of HCTZ [µg/mL]	Absorbance Mean ± S.D. [n = 5]	% R.S.D.
1	0	0	0
2	2	0.144 ± 0.0025	1.736
3	4	0.270 ± 0.0021	0.77
4	6	0.401 ± 0.0017	0.42
5	8	0.531 ± 0.0044	0.82
6	10	0.664 ± 0.0024	0.36
7	12	0.796 ± 0.0079	0.99

Fig. 6: Calibration Curve of HCTZ at 271.2 nm Wavelength

Y = 0.065x + 0.005; r^2 = 0.999



2.6 Determination of E (1%, 1cm) at Selected Wavelengths: Aliquot portion of TLM working standard solution [T_1] (3.2 mL) was transferred to five different 10 mL volumetric flaks and volume was made up to the mark to obtain the concentration (32 □ g / mL). Similarly, aliquot portion of HCTZ from working standard solution [H_1] (1 mL) was transferred to five different 10mL volumetric flask and volume was made up to the mark to obtain concentration (10 □ g / mL). The absorbance of each solution was measured at 296.8 nm and 271.2 nm.

E (1%, 1cm) values of drugs were calculated using following formula;

$$E\ (1\%, 1cm) = \frac{\text{Absorbance}}{\text{Cocentration (g/100mL)}}$$

Results of E (1%, 1cm) are shown in **(Table 4)**

Table4: E (1%, 1cm) Values of TLM and HCTZ at 296.8 nm and 271.2 nm

Sr. No.	at 296.8 nm		at 271.2 nm	
	TLM	HCTZ	TLM	HCTZ
1	497.8	79	356.5	664
2	498.7	79	356.8	664
3	498.1	78	356.8	663
4	498.75	79	357.1	665
5	499.3	78	355.9	663
6	498.75	80	355.9	666
Mean	**ax_1 = 498.51**	**ay_1= 78.8**	**ax_2 = 356.5**	**Ay_2= 664.1**
S.D	0.52	**0.752**	0.501	1.169
% RSD	0.1043	0.9543	0.140	0.176

2.7 Estimation of Laboratory Mixture by Proposed Method

In order to see the feasibility of proposed method for simultaneous estimation of TLM and HCTZ in marketed pharmaceutical formulations, the method was first tried for estimation of drugs in standard laboratory mixture. Accurately weighed TLM (40 mg) and HCTZ (12.5 mg) were taken in 100 mL volumetric flask, dissolved in methanol (60 mL) with the help of ultrasonication for about 10 min and the volume was made up to mark using the same. Appropriate aliquot portion (1 mL) was transferred to 10 mL volumetric flask and further diluted using 50% v/v methanol to get TLM (40 µg/ mL) and HCTZ (12.5 µg/ mL). The absorbance was recorded at 296.8 nm and 271.2 nm against solvent as blank.

Amount of each drug was estimated using following equations,

$$C_x = \frac{A_2 \times ay_1 - A_1 \times ay_2}{ax_2\, ay_1 - ax_1\, ay_2}$$

$$C_y = \frac{A_1 \times ax_2 - A2 \times ax_1}{ax_2\, ay_1 - ax_1\, ay_2}$$

Where;

A1 and A2 are the absorbance of diluted mixture at λ_1 and λ_2

Cx and Cy are the concentration of X and Y respectively

ax1 and ax2 are absorptivities of X at λ_1 and λ_2 respectively

ay1 and ay2 are absorptivities of Y at λ_1 and λ_2 respectively

The results are reported in (**Table 5).**

Table5: Results of Estimation of Telmisartan and Hydrochlorothiazide Standard Laboratory Mixture

Sr. No.	Absorbance of Mixture at 296.8nm	Absorbance of Mixture at 271.2 nm	Amount of TLM Taken (mg)	Amount of TLM Estimated (mg)	% TLM Estimated	Amount of HCTZ Taken (mg)	Amount of HCTZ Estimated (mg)	% HCTZ Estimated
1.	2.078	2.215	40.05	39.81	99.41	12.58	12.58	100.05
2.	2.077	2.215	40.10	39.86	99.42	12.51	12.51	100.06
3.	2.076	2.213	39.95	39.69	99.37	12.55	12.53	99.87
4.	2.078	2.216	40.13	39.89	99.41	12.55	12.61	100.5
5.	2.079	2.214	40.15	39.96	99.53	12.57	12.52	99.62
				Mean	99.42			100.02
				SD	0.0601			0.3222
				% RSD	0.0604			0.3222

2.8 Application of the Proposed Method for Estimation of Drugs in Tablets: Twenty '**Telista-H'** Tablets containing TLM (40 mg) and HCTZ (12.5 mg) were weighed and ground to fine powder. A quantity of sample equivalent to TLM (40 mg) and HCTZ (12.5 mg) was transferred into 100 mL volumetric flask containing methanol (60 mL), sonicated for 15 min and the volume was made up to the mark and filtered through Whatman filter paper (No. 45). This solution was (1 mL) transferred to 10 mL volumetric flaks, dissolved and volume was adjusted to the mark. The absorbance of the solutions were measured at 296.8 nm and 271.2 nm against blank. The concentrations of two drugs in sample were determined by using simultaneous equations**.**

The results are reported in the (**Table 6).**

Table6: Results of Estimation of Telmisartan and Hydrochlorothiazide in Tablets.

Tablet- Telista-H						**Average Weight of Tablet- 348.85 mg.**	
Sr. No.	**Quantity Tablet Powder Taken (mg)**	**Absorbance of Mixture at 296.8nm**	**Absorbance of Mixture at 271.2 nm**	**Amount of Drug Estimated (mg)**		**% of Drug Estimated.**	
				TLM	**HCTZ**	**TLM**	**HCTZ**
1.	348.90	2.081	2.212	39.86	12.40	99.65	99.25
2.	348.82	2.08	2.214	39.83	12.45	99.58	99.62
3.	348.88	2.078	2.213	39.79	12.46	99.48	99.68
4.	348.91	2.085	2.211	39.95	12.34	99.88	98.72
5.	348.87	2.087	2.207	40.02	12.21	100.07	97.72
					Mean	99.73	98.99
					SD	0.2395	0.8102
					% RSD	0.2401	0.8184

2.9 Validation of Proposed Method:

The Proposed method was validated as per the ICH guidelines.

1] Accuracy [Recovery Study]:

Accuracy of proposed method was ascertained on the basis of recovery study performed by standard addition method. A known amount of standard drug solutions were added to the tablet powder to make final concentrations in the range of 80%, 100% and 120% and re-analyzed it by the proposed method. The absorbance were recorded and the % recoveries were calculated using formula.

% Recovery = [A - B/ C] X 100

Where,

A = Total amount of drug estimated

B = Amount of drug found on preanalysed basis

C = Amount of Pure drug added

The results are reported in (Table 7).

Table 7: Recovery Study

Tablet- Telista-H							Average Weight of Tablet = 348.85 mg.	
Sr. No.	Quantity Tablet Powder Taken (mg)	Percentage %	Amount of Pure Drug Added (mg)		Total Amount of Drug Recovered (mg) ± S.D. (n = 3)		% of Drug Recovered (n = 3)	
			TLM	HCTZ	TLM	HCTZ	TLM	HCTZ
1.	348.80	80	24.03	7.54	63.22 ±0.017	19.92 ±0.043	98.97	99.11
2.	348.86	100	40.08	12.52	79.68 ±0.069	24.93 ±0.033	99.62	99.78
3.	348.82	120	55.85	17.55	95.24 ±0.025	29.62 ±0.056	99.25	98.93
						Mean	99.28	99.26
						SD	0.326	0.447
						% RSD	0.328	0.451

2] Precision:
Precision was determined as intra-day and inter-day variations. Intra-day precision was determined by analyzing TLM (19.2, 25.6, and 32 µg/mL) and HCTZ (6, 8, and 10 µg/mL) for three times on the same day. Inter-day precision was determined by analyzing the same concentration of solutions for three different days over a period of week. The results are reported in (Table 8).

Table 8: Precision Study

Drug	Conc. [µg/mL]	Intra-day Amount Found		Inter-day Amount Found	
		Mean [N=3]	% R.S.D.	Mean ± [S.D. [*n* = 3]	% R.S.D.
TLM	19.2	19.3 ± 0.01527	0.0791	19.26 ± 0.0230	0.1198
	25.6	25.7 ± 0.01520	0.0591	25.71 ± 0.0231	0.0898
	32	32.18 ± 0.08082	0.2511	32.16 ± 0.0577	0.1795
HCTZ	6	5.91 ± 0.02	0.0849	5.89 ± 0.02	0.3395
	8	7.69 ± 0.02516	0.3271	7.88 ± 0.0264	0.3356
	10	9.97 ± 0.04725	0.04739	9.97 ± 0.0707	0.7091

3] Ruggedness: Ruggedness of the proposed method was determined by analysis of aliquots from homogenous slot by two different analyst using same operational and environmental conditions. The results are reported in **(Table 9).**

Table 9: Ruggedness Study

	TLM 40 µg/mL		HCTZ 12.5 µg/mL	
	Amount Found in µg/mL Mean ± S.D. (n = 3)	% RSD	Amount Found in µg/mL Mean ± S.D (n = 3)	% RSD
Analyst I	40.17 ± 0.075498	0.1879	12.41 ± 0.02645	0.2104
Analyst II	39.98 ± 0.1892	0.4732	12.57 ± 0.06658	0.5296
Day-I	39.91 ± 0.03294	0.0824	12.52 ± 0.1953	1.559
Day-II	39.96 ± 0.09470	0.2369	12.48 ± 0.08911	0.7140

4] LOD: Limit of detection of Telmisartan and Hydrochlorothiazide were found to be **0.123** µg and **0.208** µg respectively.

5] LOQ: Limit of Quantitation of Telmisartan and Hydrochlorothiazide were found to be **0.375** µg and **0.632** µg respectively.

3. Result and Discussion

The values of standard deviation are satisfactorily low and recovery was close to 100% (99.28 %) for Telmisartan and **(**99.26%) for Hydrochlorothiazide indicating reproducibility and accuracy of this method. Recovery studies were satisfactory which shows that there is no interference of excipients.

3.1 Method Validation

Linearity- Linearity of Telmisartan and Hydrochlorothiazide was observed in the range of 5-30 µg/ml and 2-12µg/ml at all wavelengths 296.8 nm and 271.2 nm for one method. The calibration curve yielded coefficient of correlation (r) near to 0.9999.

Assay results- A tablet dosage form of Telmisartan and Hydrochlorothiazide was analyzed by Simultaneous equation, the percentage in dosage form were determined and presented, 99.73 %& 98.99 %.Assay results obtained are within limit.

Accuracy and precision –The low values of % RSD interval indicate that method is precise. % recovery by using simultaneous equation method was found to be within limit indicate the non interference from the formulation excipients and confirm the accuracy and precision of the method.

4. Conclusion

All above results indicate that, the Simultaneous equation method employed here are very simple, accurate, economical, and rapid for routine analyses of drug, Telmisartan and Hydrochlorothiazide. The recovery was 99.28 % and 99.26% for simultaneous equation method, which is close to 100% indicating reproducibility & accuracy of method.

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