ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Spectrophotometric Methods for Simultaneous Determination of Telmisartan and Hydrochlorothiazide in Tablet Dosage Form

K Ilango[1*] and Shiji Kumar PS[2]

[1*]Department of Pharmaceutical Chemistry, S.R.M. College of Pharmacy, S.R.M. University, Kattankulathur – 603 203, Kancheepuram (Dt), Tamil Nadu, India.
[2]Research scholar, Karpagam University, Coimbatore (Dt), Tamil Nadu – 641021, India.

ABSTRACT

The study aims to develop simple, sensitive, rapid, accurate and precise spectrophotometric methods for simultaneous determination of telmisartan (TELM) and hydrochlorothiazide (HTZ) in tablet dosage forms. Method I was based on derivative spectrophotometry and absorbance were measured at 270 and 296nm being the zero crossing points for telmisartan and hydrochlorothiazide respectively. Method II involves determination using multicomponent mode method; the sampling wavelengths selected were 296 and 270nm. Method III was based on dual wavelength analysis, in which two wavelengths were selected (253, 284 nm and 245, 296nm) at which the absorbance of the other component were the same. Both telmisartan and hydrochlorothiazide obey Beer's law in the concentration range employed for the methods. The developed methods were successfully applied to analysis of telmisartan and hydrochlorothiazide in laboratory prepared mixtures and tablets with good recoveries and their validation was carried out following International Conference on Harmonization (ICH) guidelines. The utility of the developed methods has been demonstrated by analysis of commercially available tablet dosage form.

Keywords: Derivative spectrophotometry, Multicomponent analysis, two wavelength method, Telmisartan, Hydrochlorothiazide, Validation.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Telmisartan (Fig. 1a) 4'-[(1, 4'- Dimethyl-2'-propyl-[2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1, 1'-biphenyl]-2-carboxylic acid, is a non-peptide angiotensin-II receptor antagonist. It inhibits angiotensin-II AT_1 receptor subtype selectively and insurmountably without affecting other systems involved in cardiovascular regulation. Hydrochlorothiazide (Fig.1b) 6-Chloro-3, 4-dihydro-2H-1, 2, 4-benzothiazidin-7-sulfonamide-1,1-dioxide, is a thiazide type diuretic which reduces reabsorption of electrolytes from the renal tubules. TELM and HTZ are available in combined tablet dosage form for the management of hypertension.

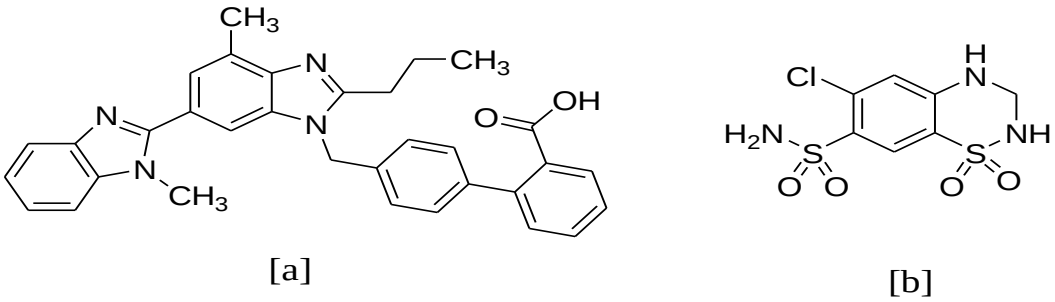

Fig.1 Chemical structure of (a) Telmisartan (b) Hydrochlorothiazide

The literature survey revealed that TELM is not yet official in any pharmacopoeia. Several analytical methods have been reported for the determination of TELM in biological fluids, and formulation includes HPLC, HPTLC, electrophoretic and fluorimetric methods [1-5]. Few analytical methods were reported for determination of TELM and HTZ in combination which includes HPLC, TLC-densitometric and spectrophotometric methods [6, 7] and few methods for the determination of HTZ in combination with other drugs [8-12]. To the best of author's knowledge, no previous article concerning simultaneous spectrophotometric determination of TELM and HTZ by above three methods was published. Therefore the aim of the present work was to develop and validate three different UV spectrophotometric techniques for simultaneous determination of TELM and HTZ in tablets without previous separation.

MATERIALS AND METHODS

Chemicals and Reagents

Pharmaceutical grade TELM and HTZ were supplied by M/S. A to z Laboratories, Chennai, India. Telma-H tablets, labeled to contain 40 mg TELM and 12.5 mg HTZ per tablet were manufactured and supplied by M/S. Glenmark Pharmaceuticals Ltd, Nasik, India. Spectroscopy grade methanol was used throughout study.

Equipment

A double beam UV-visible spectrophotometer (Shimadzu, Japan) model UV-170 with quartz cell 1 cm path length, connected to HP computer version 2.21 was used. Shimadzu balance (AUW-120D) was used for all weighing.

ISSN: 0975-8585

Standard stock solution

Standard stock solution (1.0 mg/mL) each of TELM and HTZ was separately prepared by dissolving in methanol. These stock solutions were further diluted to get working standard stock solutions each 100 µg/mL.

Sample preparation

Twenty tablet were accurately weighed and tablet powder equivalent to 100 mg TELM and HTZ was transferred into 100 mL volumetric flask, 50 mL methanol was added, dissolved and completed to 100 mL with same solvent. The resulting solution is filtered through Whatmann filter paper, discarding first few millilitres. From the above solution suitable aliquots were completed to volume with methanol to get a concentration in the ratio of 3.2:1 taking into consideration its amount present in combined tablet formulation.

Method I: First order derivative spectroscopy

The first derivative (D^1) overlain spectra of each pure drug was found to show zero crossing point and assisted in their simultaneous estimation. The first derivative wavelength considered for TELM was 270 nm and 296 nm for HTZ. Calibration curves were constructed with six different concentrations in the range between 4-24µg/mL and 2-12µg/mL for TELM and HTZ respectively (Fig. 2). Each concentration was analysed thrice. The sample solution of final concentration 20µg/mL of TELM and 6.25µg/mL of HTZ was measured at 270 and 296nm. The procedure was repeated five times and concentration of TELM and HTZ was calculated from calibration graph.

Method II: Multicomponent mode method

Five mixed standard solutions of each containing TELM and HTZ in the concentration ratio of 6.4:2, 9.6:3, 12.8:4, 16:5 and 19.2:6 as in commercial tablets was prepared in methanol. All the mixed standard solutions were scanned over the range of 200 – 400 nm in the multicomponent mode (Fig. 3). The overlain spectrum obtained was employed to determine the concentration of drugs in sample solutions with reference to mixture standards (Fig. 4).

Method III: Dual wavelength method

TELM was determined by plotting the difference in absorbance at 253 and 284nm (difference is zero for HTZ) against its corresponding concentration. Similarly, for determination of HTZ, the difference in absorbance at 245 and 296nm (difference is zero for TELM) was plotted against corresponding concentration. The concentrations of two drugs were calculated from the corresponding regression equation.

ISSN: 0975-8585

RESULTS AND DISCUSSION

The aim of this work is to establish and validate simple, sensitive and accurate spectrophotometric method according to ICH guidelines with satisfactory precision and accuracy [13].

Linearity and sensitivity

The linearity of methods was evaluated thrice by analysing six concentrations of each drug. The linearity was best fitted by the equation y = mx + c. Table 1 reveals correlation coefficients, standard deviation of slope (s_b) and intercept (S_a). The sensitivity determined by detection and quantification limit, were calculated based on standard deviation of response and slope.

Accuracy

The validity and reliability of proposed methods were assessed by recovery studies by standard addition method. The value for %RSD found to be < 1.0 for all the methods, which indicate excellent recoveries as revealed in Table 2.

Precision

Precision was ascertained by triplicate estimation of standard drugs on same day (intraday) and on three consecutive days (inter day). The %RSD reveals good precision (Table 3).

Assay of tablet formulation

The assay results of tablets (labeled to contain TELM 40mg and HTZ 12.5mg) for three methods were reported in Table 4. The standard deviation of five replicate analyses for all three methods was found to be < 1. The assay values indicate that interference of the excipients matrix is insignificant for the estimation of TELM and HTZ by proposed methods.

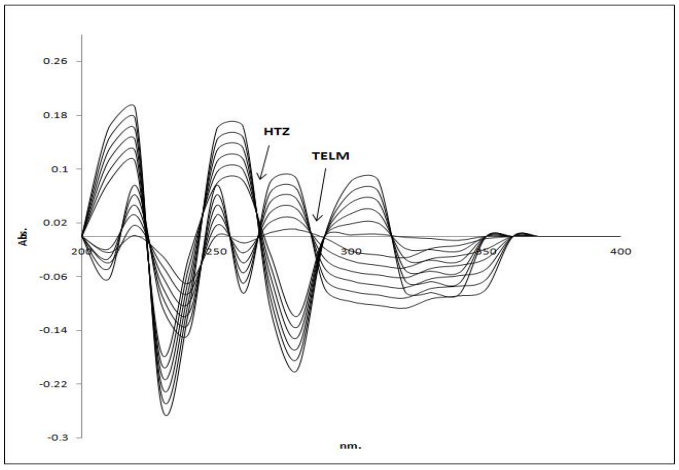

Fig. 2: First order derivative spectra of TELM and HTZ for different linear concentrations

ISSN: 0975-8585

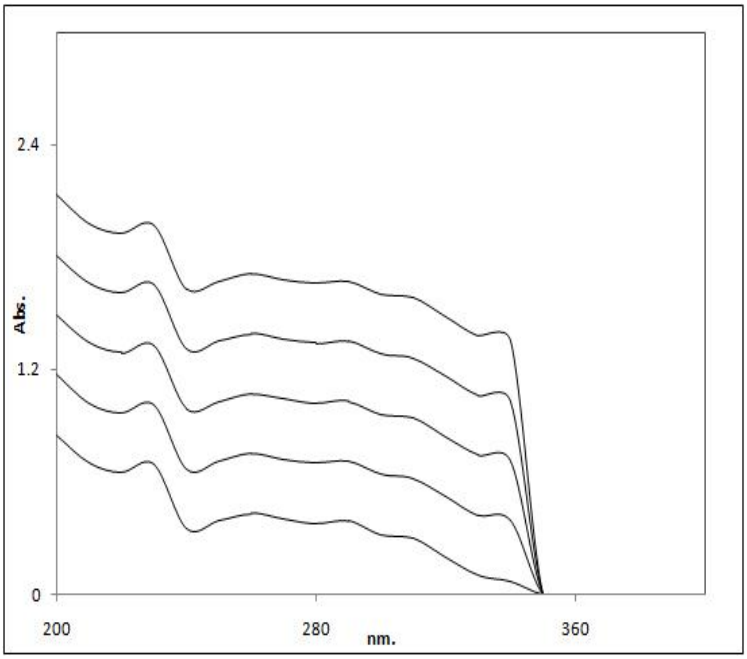

Fig. 3: Overlain spectra of binary mixtures of TELM and HTZ in multicomponent mode

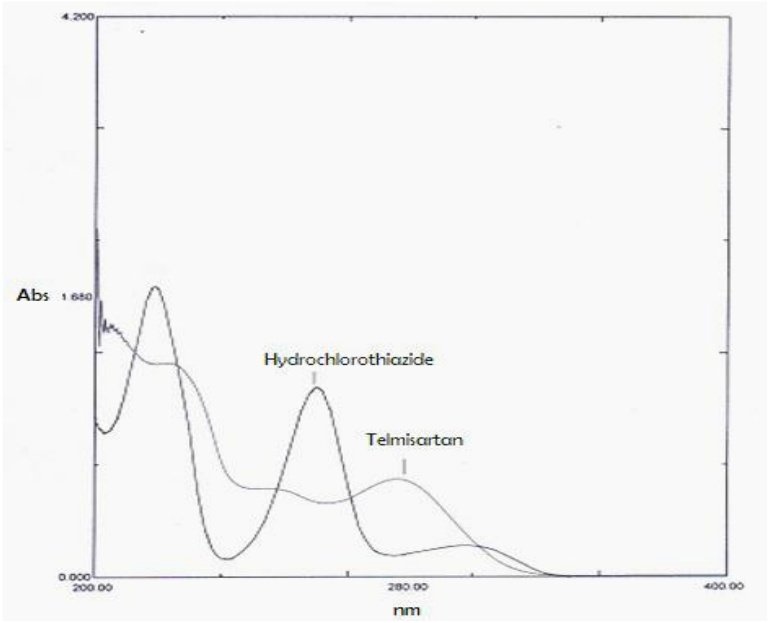

Fig. 4: Overlain spectra of TELM and HTZ

ISSN: 0975-8585

Table 1: Optical characteristics obtained for TELM and HTZ by first derivative, multicomponent mode and dual wavelength method

Parameters	First derivative (D^1)		Multicomponent mode		Dual wavelength	
	TELM	HTZ	TELM	HTZ	TELM	HTZ
Range of linearity (µg/mL)	4 – 24	2 – 12	4 – 24	2 – 12	5 – 30	3 – 15
S_a	0.00053	0.00012	0.00032	0.00015	0.00023	0.00054
S_b	0.0004	0.00070	0.00041	0.00033	0.00057	0.0051
Correlation coefficient (r^2)	0.9991	0.9989	0.9998	0.9994	0.9995	0.9997
LOD (µg/mL)	0.63	0.29	0.50	0.25	0.54	0.29
LOQ (µg/mL)	2.38	1.08	2.12	1.01	1.23	1.11
Regression coefficient (r)	0.997	0.996	0.999	0.998	0.987	0.999

LOD = 3.3×SD/slope, LOQ = 10×SD/slope, S_a = Standard deviation of intercept of regression line, S_b = Standard deviation of slope of regression line

Table 2: Results of recovery study

Drug	Amount taken (µg/mL)	Amount added (µg/mL)	Amount recovered ± SD* (µg/mL)	% RSD	Amount recovered ± SD* (µg/mL)	% RSD	Amount recovered ± SD* (µg/mL)	% RSD
			Method I		Method II		Method III	
TELM	16	5	20.34 ± 0.017	0.084	21.21 ± 0.086	0.405	20.97 ± 0.130	0.620
		10	26.46 ± 0.029	0.110	25.09 ± 0.054	0.215	26.93 ± 0.097	0.360
		15	30.93 ±0.048	0.155	31.08 ± 0.091	0.293	30.92 ± 0.083	0.268
HTZ	5	2	07.04 ± 0.003	0.043	06.98 ± 0.020	0.287	06.46 ± 0.043	0.666
		4	09.03 ± 0.007	0.078	09.43 ± 0.009	0.095	09.86 ± 0.010	0.101
		6	11.21 ± 0.040	0.357	11.15 ± 0.060	0.538	11.93 ± 0.080	0.671

Method I: First order derivative, Method II: Multicomponent mode, Method III: Dual wavelength method
*Mean of three determinations

ISSN: 0975-8585

Table 3: Results of intraday and inter day precision

Method	Precision	Amount taken (µg/mL)		% Mean*		% RSD	
		TELM	HTZ	TELM	HTZ	TELM	HTZ
I	Intraday	10	4	98.71	99.56	0.063	0.115
	Inter day	10	4	101.52	98.31	0.860	0.644
II	Intraday	10	4	100.76	100.72	1.12	1.32
	Inter day	10	4	102.16	101.12	0.570	0.240
III	Intraday	10	4	99.53	100.86	0.232	0.080
	Inter day	10	4	100.72	99.54	1.06	0.812

Method I: First order derivative, Method II: Multicomponent mode, Method III: Dual wavelength method
*Mean of three determinations

Table 4: Results of tablet analysis

Parameters	Method I		Method II		Method III	
	TELM	HTZ	TELM	HTZ	TELM	HTZ
Label claim (mg per tablet)	40	12.5	40	12.5	40	12.5
Drug content % ± SD*	101.73 ± 0.13	99.54 ± 0.79	100.86 ± 0.32	98.43 ± 0.52	101.21 ± 0.86	98.72 ± 0.46
% RSD	0.13	0.79	0.32	0.53	0.85	0.47

Method I: First order derivative, Method II: Multicomponent mode, Method III: Dual wavelength method
*Mean of five determinations

CONCLUSION

The developed spectrophotometric methods found to be suitable for determination of TELM and HTZ in bulk and tablet dosage form without any interference from excipients. Statistical analysis proves that the method is repeatable and selective for the analysis of both drugs. Its advantages are simple, economic, sensitive, accurate and precise. The method has lower LOD and LOQ values and high recovery.

REFERENCES

[1] Palled MS, Rajesh PMN, Chatter M, Bhat AR. Ind J Pharm Sci 2005; 108-110.
[2] Nageswara rao R, Sen S, Nagaraju P, Sumanth Reddy V, Radha Krishnamurthy P, Uday Bhaskar S. Asian J Chem 2006; 18(2): 775-782.
[3] Yihua Li Bing Guo-Ping, Yang Da-Wei Xiao, Wang Xuefeng. Chi J Clin Pharm 2006; 15(4): 200-203.
[4] Christel Hempen, Liane Glasle-Schwarz, Ulrich Kunz, Uwe Karst. Analy Chimi Acta 2006; 560: 35-40.
[5] Christel Hempen, Liane Glasle-Schwarz, Ulrich Kunz, Uwe Karst. Analy Chemi Acta 2006; 560: 41-49.
[6] Lories I, Bebawy, Samah S, Abbas, Laila A Fattah, Heba H.Refaat. J Pharm Biomed Anal 2003; 31(2): 329-339.
[7] Shah N, Suhagia B, Shah R and Shah C. IPC 57th Scientific Abstracts 2005; G-5.
[8] Hillaert S and Van den Bossche W. J Pharm Biomed Analy 2005; 39(3): 523-529.
[9] Suhagia BN, Shah RR, Patel DM. Ind J Pharm Sci 2005; 67(1): 37-42.

ISSN: 0975-8585

[10] Baing MM, Vaidya VV, Singh G, Mhaske H, Dhotre O. Ind Drug 2006; 43(4): 333-337.
[11] Sahu R and Vandana PB. Ind Drug 2006; 43(3): 226-230.
[12] Shailesh A Shah, Ishwarsinh S Rathod, Bhanubhai N Suhagia, Shrinivas S, Savale Jignesh, Patel B. J AOAC Inter 2001; 84(6): 1715-1723.
[13] ICH Topic Q2 (R1) November 2005, Validation of analytical procedures methodology and CPMP/ICH/281/95, 1995.