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Validated simultaneous spectrophotometric estimation of telmisartan, hydrochlorthiazide and amlodipine besylate in combined tablet dosage form

Manish A. Raskar*[1], Ganesh R. Godge[2], Ashok B. Chitale and Pritam D. Giri

[1]*Department of Pharmaceutical Chemistry, Padmashree Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, MS, India*
[2]*Department of Pharmaceutics, Padmashree Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, MS, India*

ABSTRACT

Two simple, accurate, precise, economical and reproducible UV spectrophotometric methods have been developed for simultaneous estimation of Telmisartan (TEL), Hydrochlorthiazide (HTZ) and Amlodipine besylate (AML) in pure bulk drug and tablet dosage form. The stock solutions were prepared in methanol followed by further required dilutions with distilled water. Method I is based on first order derivative spectrophotometry and absorbances were measured at 252 nm, 271 nm and 239 nm, being the zero-crossing points for telmisartan, hydrochlorthiazide and amlodipine respectively. Method II is based on the muticomponent analysis. The absorbance maxima of telmisartan, hydrochlorthiazide and amlodipine was found to be at 296 nm, 272nm and 238nm respectively. All the three drugs obey Beer's law in the concentration range of 5-30µg/ml. The results of analysis for both methods were tested and validated for various parameters according to ICH guidelines. The utility of the developed methods has been demonstrated by analysis of commercially available dosage form.

Keywords: Derivative spectrophotometry, muticomponent analysis, Telmisartan, Hydrochlorthiazide, Amlodipine besylate

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INTRODUCTION

Telmisartan (TEL), is an angiotensin receptor blocker, chemically it is 4'-[(1,4'- dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol] - 1'-yl) methyl] [1,1'-biphenyl] - 2- carboxylic acid[1]. Hydrochlorthiazide (HTZ) is chemically 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulphonamide-1,1-dioxide. It is a thiazide diuretic & used as an antihypertensive agent which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium and chloride ions and consequently of water. Hydrochlorthiazide is official in IP [2] and USP [3] which describe liquid chromatography method for its estimation. Amlodipine besylate (AML), is a **c**alcium channel blocker, chemically it is [3-ethyl-5-methyl (4RS)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-methyl-1-dihydropyridine-3,5-dicarboxylate benzenesulfonate [4]. It is used in the treatment of hypertension and angina. Literature survey reveals that several analytical methods were reported for the determination of telmisartan alone or in combination with other drugs in pharmaceutical preparations and biological fluids, viz. spectrophotometry [5,6], HPLC [7,8] and HPTLC [9,10]. Also several methods like spectroscopic [11-13] and chromatographic [14-16] methods were reported for individual estimation of amlodipine besylate and hydrochlorothiazide or combination with other drugs. However, there is no evidence in literature for simultaneous determination of telmisartan, hydrochlorothiazide and amlodipine besylate using first order derivative and multicomponent UV

spectrophotometric methods. Hence present work describes two simple, sensitive, accurate and economical spectrophometric methods for simultaneous estimation of telmisartan, hydrochlorothiazide and amlodipine besylate in bulk and tablet dosage form. The developed methods were validated and found to be accurate, precise and reproducible.

MATERIALS AND METHODS

Apparatus

A double beam UV/Visible spectrophotometer (Jasco, model V-630) was employed with a pair of 1 cm quartz cells for all analytical work.

Reagents and chemicals

Telmisartan, Hydrochlorothiazide and Amlodipine besylate were obtained as a gift sample and were used as working standards. A commercial pharmaceutical preparation, Telma AMH-40, Glenmark Pharmaceutical Ltd, India (Label claim: 40mg TEL, 12.5 mg HTZ and 5 mg AML) was procured from the local market. Methanol and distilled water were used throughout the analysis.

Preparation of standard stock solution

Standard stock solutions (100 µg/ml) of AML, TEL & HTZ were prepared by dissolving separately 10 mg of each drug in 100 ml methanol. From this stock solution, working standard solutions were prepared by appropriate dilution with distilled water. Working standard solutions of each drug were scanned in UV range 200-400 nm. The spectral data was processed to obtain first order derivative spectrum of each drug.

Method I: Derivative spectrophotometry

The first derivative (D1) overlain spectra of each pure drug was found to show zero crossing point (ZCP) and assisted in their simultaneous estimation as shown in **Fig.1**. The first derivative wavelength considered for TEL was 252nm at which HTZ and AML show zero absorbance. Similarly the estimation of HTZ and AML was carried out at 271 nm and 239 nm at which other two shows zero absorbance. Calibration curves were plotted between absorbance observed at D1, for three drugs at all the three wavelengths against the concentrations, in the range of 5-30µg/ml for TEL, HTZ and AML respectively.

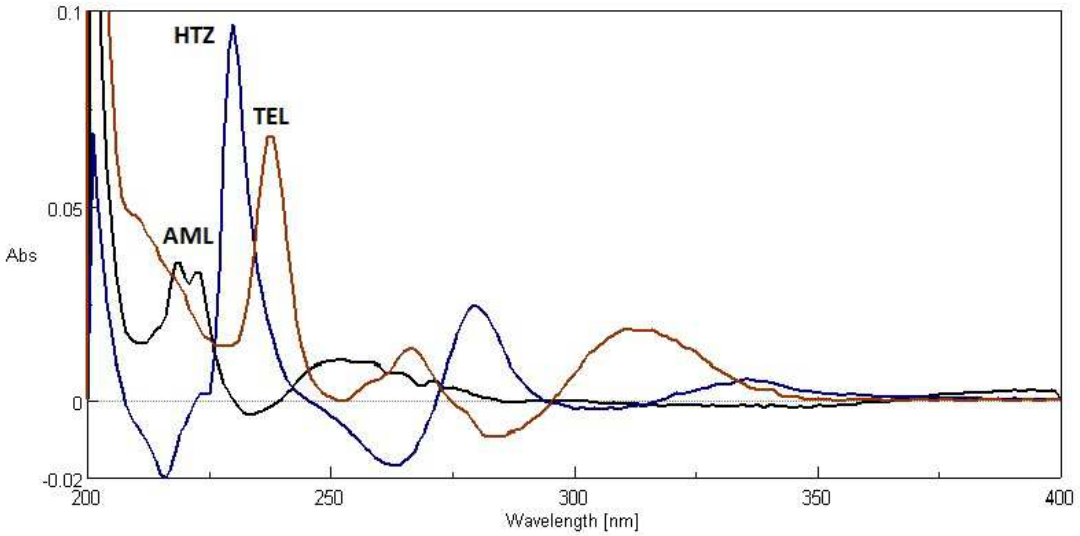

Fig. 1. First order derivative overlain spectra of AML, TEL & HTZ

Method II: Multi-component analysis

The use of five mixed standards and three sampling wavelengths like 296, 272 & 238 nm were found to serve the purpose of this experiment. Five mixed standard solutions of each containing TEL, HTZ and AML in the concentration ratio of 8:2.5:1, 16:5:2, 24:7.5:3, 32:10:4 and 40:12.5:5 as in Telma AMH-40 were prepared in distilled water. All the mixed standard solutions were scanned over the range of 200 -400 nm in the multi-component mode using the previously mentioned three sampling wavelengths. The overlain spectra of the five

mixed standards were then employed to determine the concentration of the drugs in sample solutions by analysis of the spectral data of sample solution with reference to that of mixed standards. The overlain spectra of mixed standards of TEL, HTZ and AML are shown in **Fig. 2**.

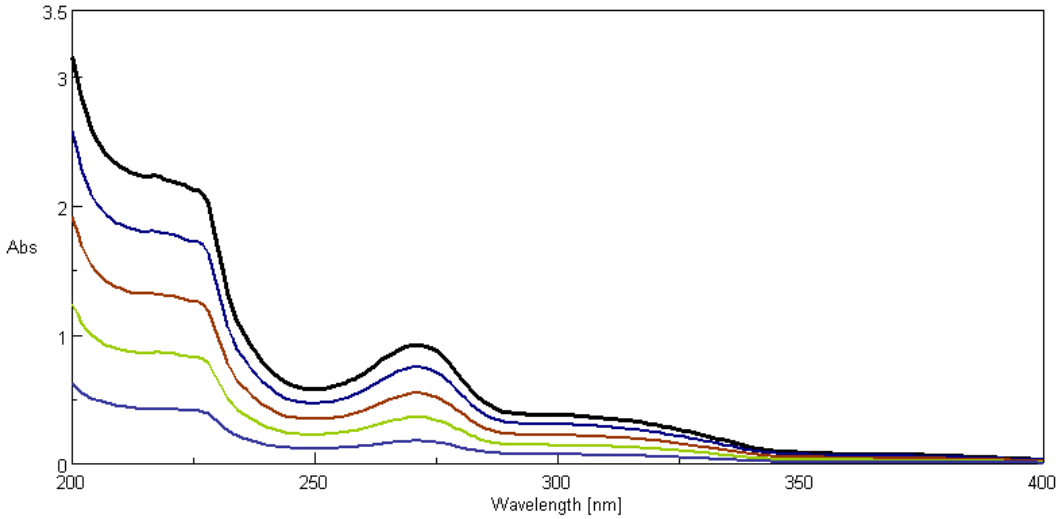

Fig. 2. Overlain spectra of mixed standards of AML, TEL and HTZ for Multicomponent analysis

Analysis of Tablet formulation

Twenty tablets (Telma AMH-40) were weighed and powdered. An accurately weighed powder equivalent to 10 mg of TEL was dissolved in methanol, sonicated for 10 min. and diluted to 100 ml with methanol. Then it is filtered through Whatman filter paper (No. 41). After appropriate dilutions, absorbance of sample solutions were measured at corresponding wavelengths and the results were recorded as shown in **Table 1**.

Table 1. Result of Tablet Analysis

Parameters	Method I			Method II		
	TEL	HTZ	AML	TEL	HTZ	AML
% Drug content	99.40	99.52	99.48	99.74	99.43	99.70
S.D.*	0.01291	0.03162	0.02863	0.01923	0.02966	0.03605
% R.S.D.*	0.01292	0.03163	0.02863	0.01925	0.02966	0.03605

**Mean of six determinations, Where method I is Derivative spectrophotometry and method II is Multicomponent analysis*

Validation of developed methods

The proposed methods were validated according to International Conference on Harmonization (ICH) Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for each analyte [17]. Both precision and accuracy were determined with standard samples prepared in triplicates at different concentration levels covering the entire linearity range.

RESULTS AND DISCUSSION

Linearity

The linearity was determined ranging from 5-30 µg/ml for TEL, HTZ, and AML respectively for both methods.

Precision

Precision was determined by studying the repeatability and intermediate precision. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. Repeatability result indicates the precision under the same operating conditions over a short interval time and inter-assay precision. The results are presented in **Table 2**. The intermediate precision study is expressed within the laboratory variation on different days. The % COV in intra and inter-day precision studies for both the methods was not more than 1.0%, which indicates excellent repeatability and intermediate precision.

Table 2. Optical characteristics and validation Parameters

Parameters	TEL		HTZ		AML	
	I	II	I	II	I	II
Working wavelength (nm)	252	296	271	272	239	238
Beer- Lambert's Law range (µg/ml)	5-30	5-30	5-30	5-30	5-30	5-30
Precision*:						
Interday Precision	0.14	0.16	0.21	0.20	0.26	0.14
Intraday Precision	0.125	0.165	0.156	0.165	0.195	0.169
LOD (µg/ml)*	0.12	0.16	0.13	0.15	0.18	0.19
LOQ(µg/ml)*	0.30	0.35	1.20	0.97	0.69	0.45
Regression values:						
Slope*	0.0329	0.0349	0.0057	0.0027	0.0039	0.0328
Intercept*	0.0002	0.0125	0.0007	0.0001	0.0004	0.0025
Regression coefficient(r^2)	0.9992	0.9998	0.9992	0.9993	0.9996	0.9990

**Average of six estimations*

Accuracy

The validity and reliability of proposed methods were assessed by recovery studies by standard addition method. The results of recovery studies are shown in **Table 3**.

Table 3. Result of Recovery Studies

Drug	Recovery level	% Recovery ± R.S.D.#	
		Method I	Method II
TEL	80%	99.04±0.63	100.56±0.87
AML		99.30±0.91	99.90±0.23
HTZ		99.39±0.67	99.63±0.45
TEL	100%	99.67±0.80	99.87±0.86
AML		99.56±0.43	99.65±0.46
HTZ		99.78±0.56	99.49±0.84
TEL	120%	99.89±0.37	99.91±0.53
AML		99.70±0.48	99.54±0.76
HTZ		99.85±0.57	99.43±0.65

#Average of three estimations at each level of recovery, R.S.D: Relative Standard deviation

CONCLUSION

The proposed UV spectrophotometric methods for simultaneous estimation of telmisartan, hydrochlorthiazide and amlodipine besylate were found to be accurate, precise, economical and easy to perform. The developed methods were validated as per ICH guidelines in terms of accuracy, precision and linearity. Hence the proposed methods can be routinely used for estimation of telmisartan, hydrochlorthiazide and amlodipine besylate in pure and combined tablet dosage form in quality control laboratories.

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