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Validated Simultaneous Derivative Spectrophotometric Estimation of Telmisartan, Hydrochlorthiazide and Amlodipine Besylate in Combination Tablet Dosage Form

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ABSTRACT

A simple, accurate, precise, economical and reproducible UV spectrophotometric method has 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. This method is based on second order derivative spectrophotometry and absorbances were measured at 222 nm, 234 nm and 227 nm being the zero-crossing points for telmisartan, hydrochlorthiazide and amlodipine respectively. All the three drugs obey Beer's law in the concentration range of 5-30 µg/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.

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1. 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 calcium 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 second order derivative UV spectrophotometric method. Hence present work describes a simple, sensitive, accurate and economical spectrophotometric method for simultaneous estimation of telmisartan, hydrochlorothiazide and amlodipine besylate in bulk and tablet dosage form. The developed method was validated and found to be accurate, precise and reproducible.

2. MATERIALS AND METHODS

Experimental

2.1. Instrumentation:

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

2.2. Chemicals and Reagents:

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: 40 mg TEL, 12.5 mg HTZ and 5 mg AML) was procured from the local market. Methanol and distilled water were used throughout the analysis.

2.3. 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 second order derivative spectrum of each drug.

2.4. Derivative spectrophotometry method

The second derivative (D2) overlain spectra of each pure drug was found to show zero crossing point (ZCP) and assisted in their simultaneous estimation as shown in Figure 1.

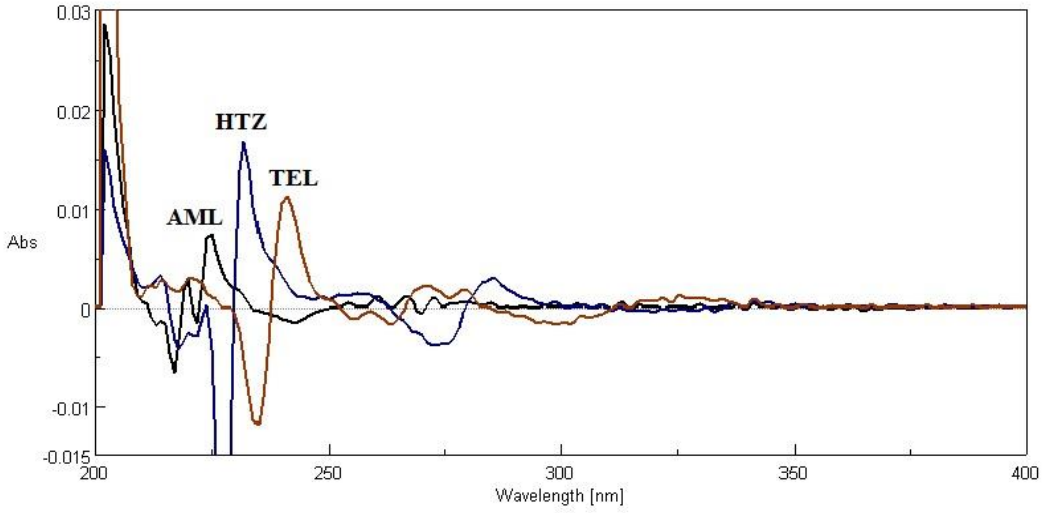

Figure 1: Second order derivative overlain spectra of AML, TEL & HTZ

The second derivative wavelength considered for TEL was 222 nm at which HTZ and AML show zero absorbance. Similarly the estimation of HTZ and AML was carried out at 234 nm and 227 nm at which other two shows zero absorbance. Calibration curves were plotted between absorbances observed at D2, for three drugs at all the three wavelengths against the concentrations, in the range of 5-30 µg/ml for TEL, HTZ and AML respectively. An overlain spectra of mixed standards of AML, TEL and HTZ is shown in Figure 2.

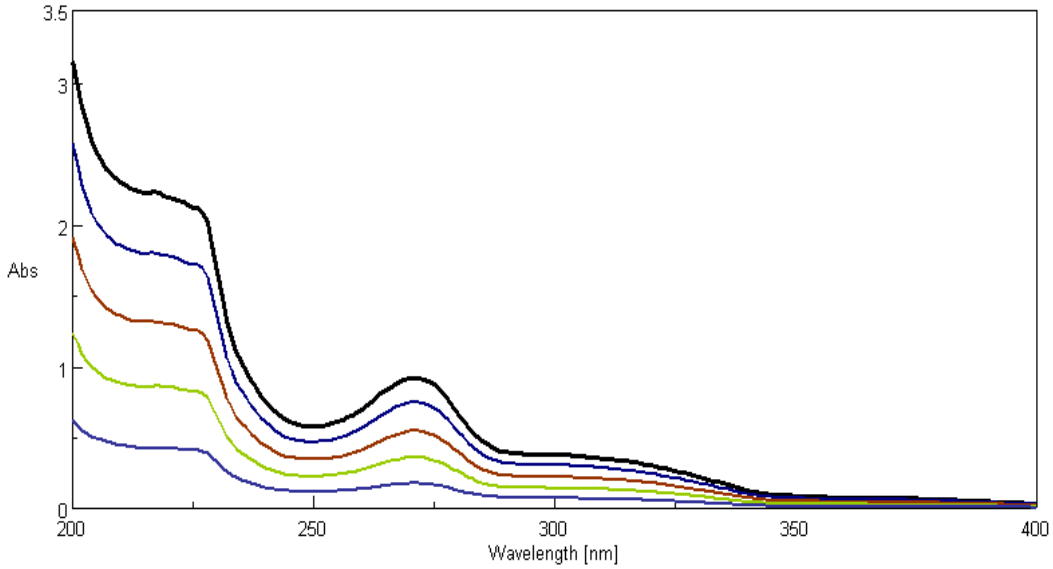

Figure 2: Overlain spectra of mixed standards of AML, TEL and HTZ

2.5. 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, absorbances of sample solutions were recorded at corresponding wavelengths and the results were recorded as shown in Table 1.

Table 1: Result of Tablet Analysis

Parameters	**TEL**	**HTZ**	**AML**
% Drug content	99.47	98.52	99.72
S.D.*	0.01131	0.03351	0.03625
% R.S.D.*	0.01142	0.03952	0.04523

*Mean of six determinations

3. RESULTS AND DISCUSSION

3.1. Method Validation

The proposed method was 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.

3.1.1. Linearity

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

3.1.2. 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.

Table 2: Optical characteristics and validation Parameters

Parameters	**TEL**	**HTZ**	**AML**
Wavelength (nm)	222	234	227
Beer's Law range (µg/ml)	5-30	5-30	5-30
Precision*:			
Interday Precision	0.15	0.17	0.24
Intraday Precision	0.135	0.154	0.188
LOD* (µg/ml)	0.13	0.14	0.18
LOQ*(µg/ml)	0.36	1.26	0.77
Regression values:			
Slope*	0.0324	0.0056	0.0038
Intercept*	0.0005	0.0006	0.0003
Regression coefficient (r^2)	0.9993	0.9992	0.9999

*Average of six estimations

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.

3.1.3. Accuracy

The validity and reliability of proposed method was 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.#
TEL	80%	99.07±0.63
AML		99.40±0.81
HTZ		99.25±0.77
TEL	100%	99.77±0.80
AML		99.67±0.34
HTZ		99.87±0.65
TEL	120%	99.98±0.73
AML		99.46±0.40
HTZ		99.88±0.57

#Average of three estimations at each level of recovery,

R.S.D: Relative Standard deviation

4. CONCLUSION

The proposed UV spectrophotometric method for simultaneous estimation of AML, TEL & HTZ is accurate and precise. The proposed method is simple, rapid and easy to perform. The developed method is applicable for estimation of AML, TEL & HTZ in pure and combined tablet dosage form in quality control laboratories.

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