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Der Pharma Chemica, 2012, 4 (2):725-730
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Simultaneous spectrophotometric estimation of amlodipine besylate and telmisartan in tablet dosage form

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ABSTRACT

Two simple, rapid, precise and accurate spectrophotometric methods have been developed for determination of Amlodipine Besylate (AMB) and Telmisartan (TEL) by simultaneous equation method and first order derivative method in combined dosage form. The simultaneous equation method is based on measurement of absorbance at 367 nm and 292 nm as two wavelengths selected for quantification of AMB and TEL. The second method is first order derivative based on the measurement of absorbance at 270nm and 295nm as two wavelength selected as for quantification of AMB and TEL. Both methods obeyed Beer's law in the concentration range of 20-100 µg/ml for AMB and 5-30 µg/ml for TEL. The proposed methods were validated and can be used for analysis of combined dosage tablet formulation containing AMB and TEL.

Key Words: Amlodipine Besylate (AMB) and Telmisartan (TEL), Simultaneous equation method, first order derivative.

INTRODUCTION

Amlodipine besylate (AMB), 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[1]. Literature survey reveals several spectroscopic[2-6], HPLC [9-13]and HPTLC[14-16] methods for the estimation of AMB individually as well as in combination with other drugs.

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[24]. Literature survey reveals UV spectroscopic [18], HPLC [14-15]and HPTLC[19-21] methods for the estimation of TEL individually as well as in combination with other drugs.

A combination of TEL and AMB has been reported to show substantial and sustained 24 hour blood pressure (BP) reduction and is well-tolerated in a range of patients with hypertension and at risk of cardiovascular (CV) events. AMB and TEL are available in combined tablet dosage form for the treatment of hypertension. Not a single UV or HPLC method is reported so far for the simultaneous analysis of AMB and TEL in their combined dosage form. So a need was felt to develop new methods to analyze these drugs simultaneously. A successful attempt has been made to estimate the two drugs simultaneously by UV spectrophotometric analysis. In this article simple, rapid, accurate, reproducible and economical methods have been described for the simultaneous determination of AMB and TEL in tablet formulations using simultaneous equation method and first order derivative method.

MATERIALS AND METHODS

Instrumentation:
A Shimadzu UV/Visible spectrophotometer, model 1700 (Japan), spectral bandwidth of 2 nm and wavelength accuracy of ± 0.5 nm, with automatic wavelength correction was employed. A Shimadzu electronic analytical balance (AX-200) was used for weighing the samples.

Reagents and Chemicals:
Pure samples of Amlodipine besylate (Micro labs ltd. India), and Telmisartan (Glenmark Pharmaceuticals Ltd., India) were used in the proposed spectrophotometric analysis. Telma-AM (Glenmark Pharmaceuticals Ltd., Solan, India) was used as a pharmaceutical dosage form labeled to contain 5 mg AMB and 40 mg of TEL per tablet. All chemicals and reagents used are of analytical reagent grade.

Preparation of Standard Stock Solution:
Standard stock solutions (100 µg/ml) of AMB and TEL were prepared by dissolving separately 10 mg of each drug in 20 ml of glacial acetic acid and volume was made up to 100 ml with distilled water. The working standard solutions of these drugs were obtained by dilution of the respective stock solution with distilled water.

Preparation of Sample Stock Solutions:
Twenty tablets were weighed and crushed to a fine powder. An accurately weighed powder sample equivalent to 40 mg of TEL was transferred to a 100 ml volumetric flask and dissolved in 20 ml of glacial acetic acid. After the immediate dissolution, the volume was made up to the mark with the distilled water, and was then filtered through Whatmann filter paper No.41. The solution was suitably diluted with distilled water to obtain sample solutions containing AMB and TEL in the concentrations ratio of 1:8 µg/ml respectively as in the tablet formulation.

Simultaneous equation method:
For the simultaneous equation method, aliquots of AMB and TEL (10 µg/ml) were scanned in the range of 200-400 nm. Then 367nm and 292nm were selected as the two sampling wavelengths for AMB and TEL respectively. Fig.1 represents the overlain UV spectra of AMB and TEL. AMB and TEL exhibited linearity in the range of 20-100 µg/ml and 5-30 µg/ml respectively at their respective selected wavelengths. Calibration curves for AMB and TEL are shown in Fig.2 and Fig.3. Coefficients of correlation were found to be 0.999 and 0.994 for AMB and TEL respectively. The optical characteristics and regression values for the calibration curves are presented in Table 1. For simultaneous estimation of AMB and TEL, mixed standards containing AMB and TEL in a concentration ratio of 1:8 were prepared by appropriate dilution of the standard stock solutions with distilled water. The absorbances of the mixed standard solutions were measured at the selected wavelengths.

The two equations were constructed based upon the fact that at $\lambda_1$and λ_2 the absorbance of the mixture is the sum of individual absorbances of AMB and TEL.

At λ_1, $A_1 = ax_1bc_x + ay_1 bc_y$…… (1)
At λ_2, $A_2 = ax_2bc_x + ay_2bc_y$…… (2)

Where, A_1 and A_2 are absorbances of mixture at 292 nm and 367nm respectively.
λ_1 and λ_2 are wavelengths of TEL and AMB respectively,
ax_1 and ax_2 are absorptivity of TEL at λ_1 and λ_2,
ay_1 and ay_2 are absorptivity of AMB at λ_1 and λ_2 respectively,
c_x and c_y are concentration of TEL and AMB respectively.

First order derivative method:
AMB and TEL (10 µg/ml) were scanned separately in a wavelength range of 200-400 nm against distilled water as a blank. The first derivative spectra were obtained by instrumental electronic differentiation in the range of 200 to 400 nm. A signal at 270 nm of first order derivative spectrum was selected for quantification of AMB where no interference due to TEL was observed and similarly a signal at 295 nm was selected for quantification of TEL, where AMB did not interfere with the estimation of TEL. A first order derivative overlain spectrum of AMB and TEL is shown in Fig. 4.

RESULTS AND DISCUSSION

Under the experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. The developed methods were validated as per ICH guidelines for linearity, repeatability, LOD, LOQ as

shown in Table 1. The mean % content of AMB and TEL in tablet formulation by the simultaneous equation method was found to be 99.80 and 98.18 respectively and for first order derivative method it was found to be 99.35 and 99.07 respectively as shown in Table 2. The mean % recoveries of AMB and TEL were found to be 99.162 % and 100.88 % respectively by simultaneous equation method and 99.37% and 99.99% respectively for first order derivative method as shown in Table 3.

Table 1: Optical Characteristics and Validation Parameters of AMB and TEL

Parameter	Amlodipine Besylate		Telmisartan	
	Method I	**Method II**	**Method I**	**Method II**
λ_{max} (nm)	367	270	292	295
Beer's law range (µg/ml)	20-100	20-100	5-30	5-30
Precision (%RSD)	0.2760	0.8194	0.2103	0.0521
LOD (µg/ml)	0.1597	0.1845	0.2177	0.0745
LOQ (µg/ml)	0.4840	0.559	0.6596	0.2373
Regression Equation: Y=mx+C				
Slope	0.011	0.0004	0.07	0.0007
Intercept	0.001	0.0002	0.097	0.0009
Regression Coefficient (r^2)	0.999	0.999	0.994	0.997

Table 2: Analysis of Pharmaceutical Dosage Form

Drug	Method	Label Claim (mg/tab)	Amount Found (%)	S.D.*	% R.S.D
AMB	I	5	99.80	0.0041	0.2760
	II		99.35	0.00671	0.671
TEL	I	40	98.18	0.3241	0.2103
	II		99.07	0.0075	0.0947

**S.D.= Standard Deviation, Mean of six estimations*

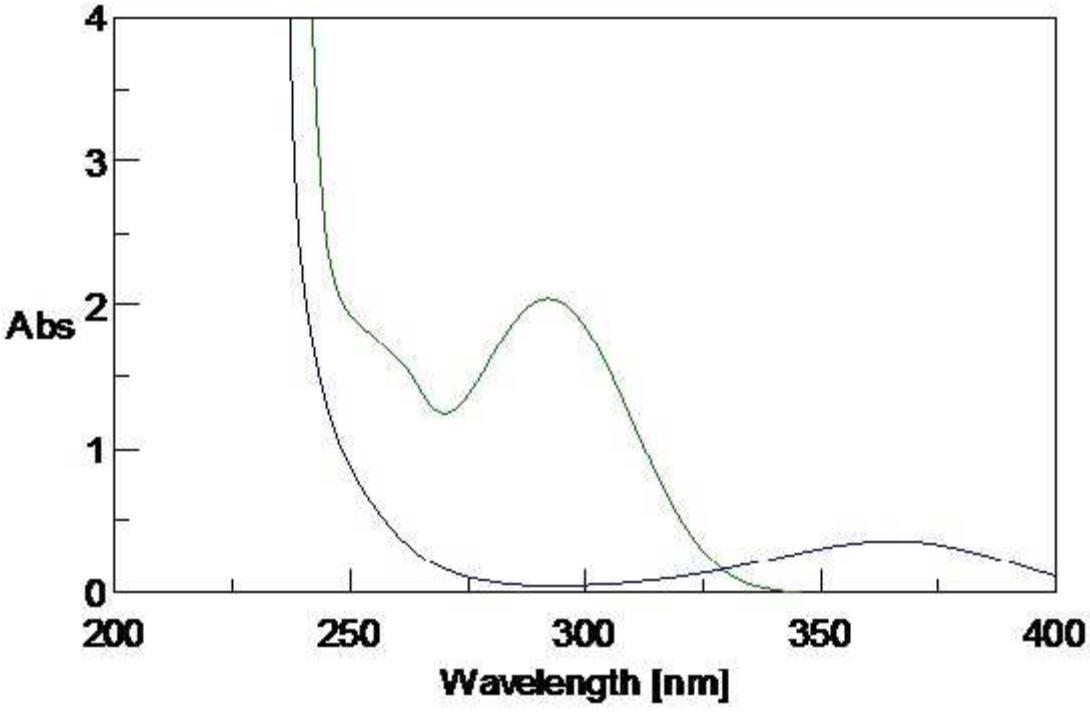

Fig:1 Overlain spectra of Amlodipine Besylate (20 µg/ml) and Telmisartan (20 µg/ml)

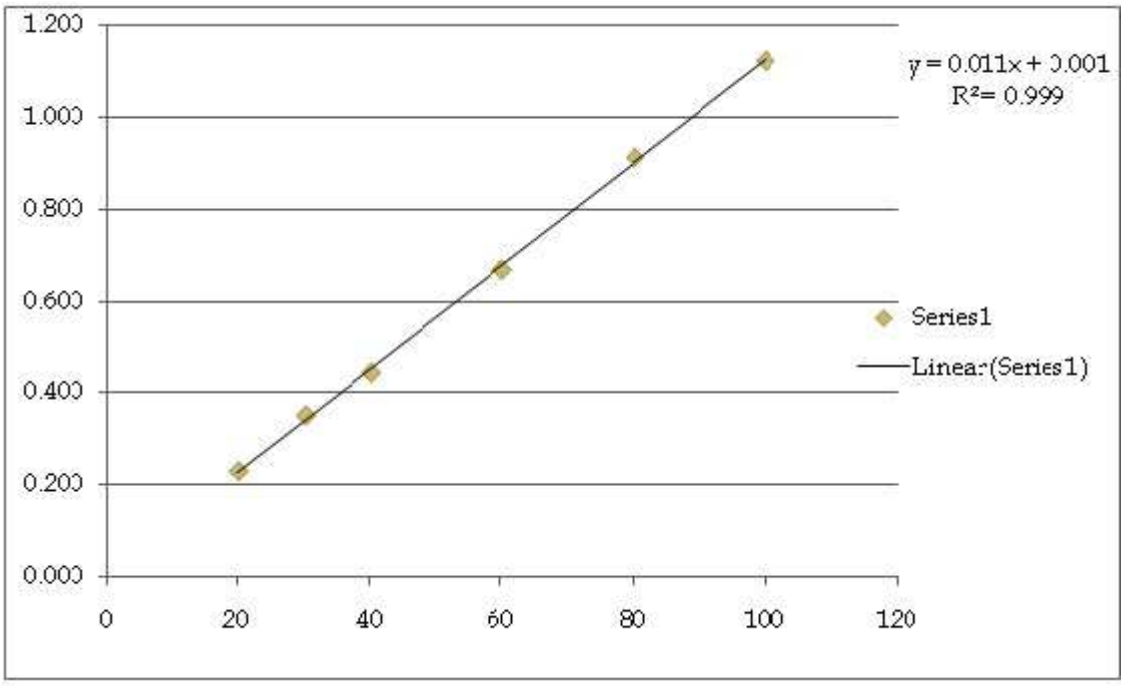

Fig.2: Calibration curve of Amlodipine Besylate (AMB)

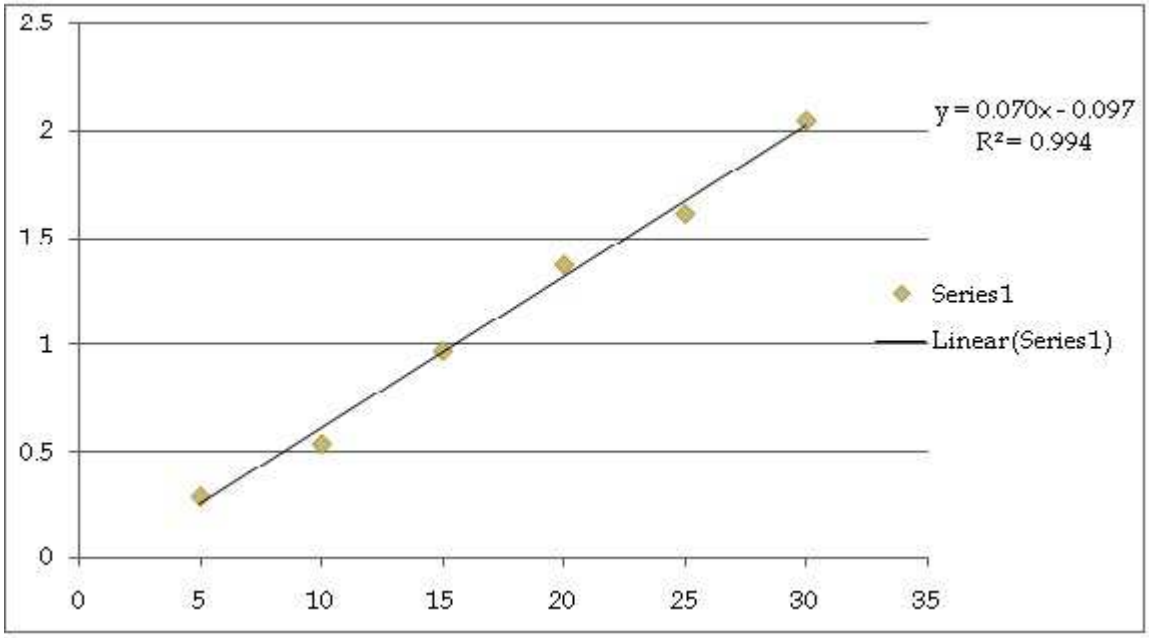

Fig.3: Calibration curve of Telmisartan (TEL)

Table 3: Statistical Analysis of Recovery Studies

Level of recovery (%)	Method	%Recovery**		% R.S.D	
		AMB	TEL	AMB	TEL
80	I	98.50	101.08	1.31	0.05466
	II	99.89	99.98	0.5911	0.3713
100	I	98.50	101.08	1.31	0.04371
	II	99.13	99.99	0.0721	0.0985
120	I	98.33	101.54	0.3002	0.36542
	II	99.12	100.01	0.527	0.1314

***Mean of three estimations*

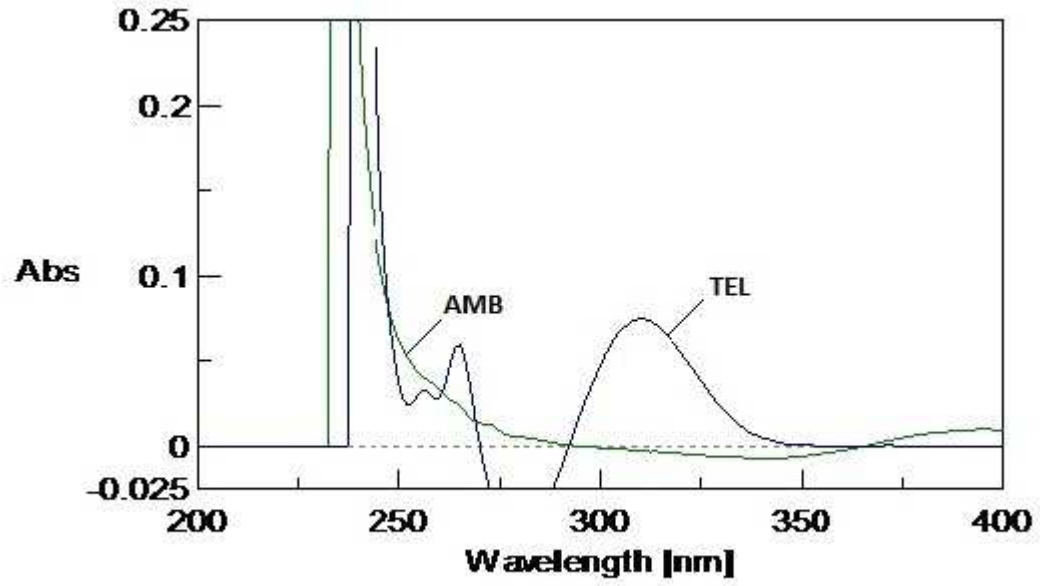

Fig4: First order derivative overlain spectra of AMB and TEL

CONCLUSION

Two simple, rapid, precise and accurate spectrophotometric methods have been developed for simultaneous estimation of AMB and TEL by using simultaneous equation and first order derivative method. The standard deviation and RSD were found to be low, indicating high degree of precision of the methods. The % recovery was found to be occurred within a range of 98-102% indicating high degree of accuracy of the proposed method. The developed methods can be employed for the routine estimation of AMB and TEL in both bulk and tablet dosage form.

Acknowledgements
The authors express their gratitude to the Principal, Pad. Dr.V.V.P.F's College of pharmacy, Vilad ghat, Ahmednagar (MH) India, for providing necessary facilities, and Glenmark Pharmaceuticals,India, for generous gift samples of pure Amlodipine besylate (AMB) and Telmisartan (TEL).

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