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SIMULTANEOUS SPECTROPHOTOMETRIC ESTIMATION OF TELMISARTAN AND AMLODIPINE IN TABLET DOSAGE FORM

Angayer Kanchana S, Aruna Ajithadas *, Niraimathi V, Jerad Suresh A
Department of Pharmaceutical Chemistry, College of Pharmacy, Madras Medical College, Chennai-600 003, Tamil Nadu, India.

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ABSTRACT
Four new simple, accurate and precise spectrophotometric methods have been developed for simultaneous determination of telmisartan and amlodipine in pharmaceutical dosage form. Method A involves formation and solving of simultaneous equation using 299nm and 364nm as two wavelengths. Method B involves formation of Q-absorbance equation at 339nm (iso absorptive point) and at 299nm (λ_{max} of telmisartan). Method C involves first order derivative method for simultaneous estimation of these two drugs. Method D involves the AUC for first order derivative spectrum. Both the drugs obey the Beer's law in the range 5-50µg/mL for amlodipine and 5-40µg/mL for telmisartan. The results of analysis have been validated statistically and by recovery studies.

Keywords: *Telmisartan (TEL); Amlodipine (AML); Simultaneous equation; Q-absorbance; Area under curve; Derivative spectrophotometry.*

INTRODUCTION

Telmisartan is 42 -[1,42 -Dimethyl-22 -propyl-[2,62 -bi-1*H*-benzimidazole]-12 -yl)methyl][1,12 -biphenyl]-2-carboxylic acid[1]. Telmisartan is a new angiotensin II receptor antagonist for the treatment of essential hypertension usually given in combination with amlodipine. Amlodipine besylate is 3-Ethyl 5-methyl(4RS)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3-5-dicarboxylate benzenesulphonate[2] and is used as calcium antagonist. The Literature survey of these two drugs revealed that some spectrophotometric, RP-HPLC, HPTLC methods have been developed for estimation of individual drugs and in combination with other drugs and in plasma[3-18]. No method has been developed for the simultaneous estimation of telmisartan and amlodipine in formulations.

EXPERIMENTAL

Instrumentation

All spectral measurements were made on Shimadzu UV-VIS spectrophotometer – 1650 with 1mm matched quartz cells.

Preparation standard stock solution

An accurately weighed quantity of 25mg each of TEL and AML were separately taken in a 50mL volumetric flask, dissolved in ethanol and made up to volume using ethanol to get 500µg/mL respectively.

Preparation of sample solution

The average weight of 20 tablets was determined and finely powdered. The powder equivalent to 40mg of TEL was taken in 50mL volumetric flask and dissolved in 25mL of ethanol, shaken well for 15 minutes and then made up to volume with ethanol. The solution was then filtered through Whatman filter paper No. 41, the first few mL of the filtrate was discarded and remaining solution was used for further analysis.

ASSAY PROCEDURE

Method A: Simultaneous equation method

Aliquots of the standard stock solutions were transferred to a series of 50mL volumetric flask and suitably diluted with distilled water to give varying concentrations ranging from 1-5µg/mL for AML and 8-40ìg/mL for TEL and the solutions were scanned in the spectrum mode from 400-200nm using distilled water as blank. The absorption maximum for AML and TEL are shown in Fig. 1. Two wavelengths selected for formation and solving of simultaneous equation[18] were 299nm and 364nm. The absoptivity coefficient of both drugs was determined at selected wavelengths. A set of two simultaneous equations[19] thus framed were:

$$A_1 = 122.99\ C_1 + 0.68325\ C_2 - I$$

$$A_2 = 9.505\ C_1 + 460.16\ C_2 - II$$

Where, A_1 and A_2 are absorbance of sample solutions at 364nm and 299nm, respectively. C_1 and C_2 are concentration of AML and TEL, respectively in sample solution in g/L. Aliquots of sample solution were diluted suitably and absorbance of the final dilutions was measured at 364nm and 299nm respectively. The concentration of two drugs in sample was calculated using above framed simultaneous equations-I and II. The validity of above framed equation was checked by

***Correspondence :** aruna_anantha@yahoo.com

preparing five mixed standards using pure sample of two drugs, measuring their absorbance at respective wavelengths and calculating concentration of two components. The results of validation studies were found satisfactory.

Method B : Q- absorbance method

Aliquots of the standard stock solution were transferred to a series of 50mL volumetric flask and suitably diluted to give varying concentrations ranging from 1-5µg/mL for AML and 8-40ìg/mL for TEL and the solutions were scanned in the spectrum mode from 400-200nm using distilled water as blank. From the overlain spectra, (Fig. 1) the wavelengths 339nm (isoabsorptive point) and 299nm (λ_{max} of TEL) were selected for formation of Q-absorbance equation[20]. The absorptivity values (A1%, 1cm) of each drug at iso absorptive point were determined. The absorptivity of AML and TEL at 339nm was 76.04 and 10.62 respectively. The concentration of each drug in tablet formulation was determined by substituting the absorbance and absorptivity values in the following equations:

$$C_x = (Q_m - Q_y / Q_x - Q_y) \times A/a_{x1}$$

$$C_y = (Q_m - Q_x / Q_y - Q_x) \times A/a_{y1}$$

where, C_x is the concentration of AML, C_y is the concentration of TEL, Qm is the ratio of absorbance of sample at selected wavelengths, Q_x is the ratio of absorptivity of AML, Q_y is the ratio of absorptivity of TEL, a_{x1} is A(1%, 1 cm) of AML at 339nm, a_{y1} is A(1%, 1cm) of TEL at 339nm.

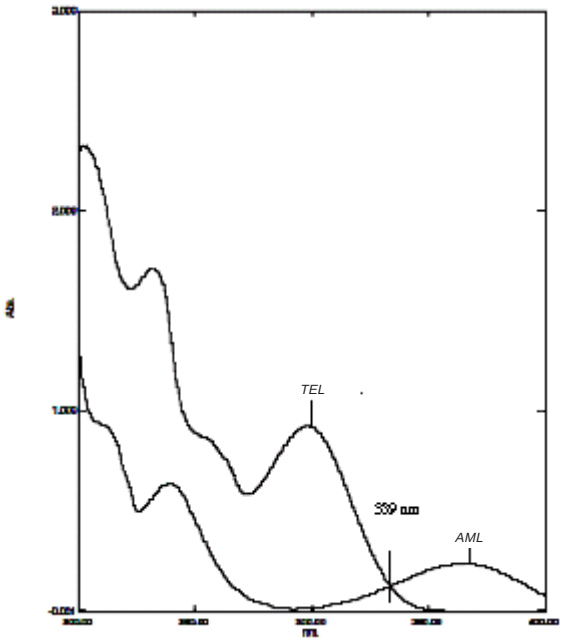

Fig.1. *Overlain spectrum of TEL and AML showing isoabsorptive point*

Method C: First derivative spectrophotometry

Mixed standards of AML and TEL were prepared in the ratio 1:8 of AML and TEL ranging from concentration 0.5-3µg/mL and 4-24µg/mL of AML and TEL respectively and scanned in the range of 200-400nm. Similarly the sample solutions were also scanned. The normal spectra obtained were derivatized for the first order[21]. The overlain spectra of mixed standards of TEL and AML are shown in Fig. 2. The amplitude were measured from 225-240nm for AML and from 282-318 for TEL. The amount of AML and TEL in marketed sample was computed from the calibration curve obtained by plotting the amplitude versus concentration for AML and TEL individually.

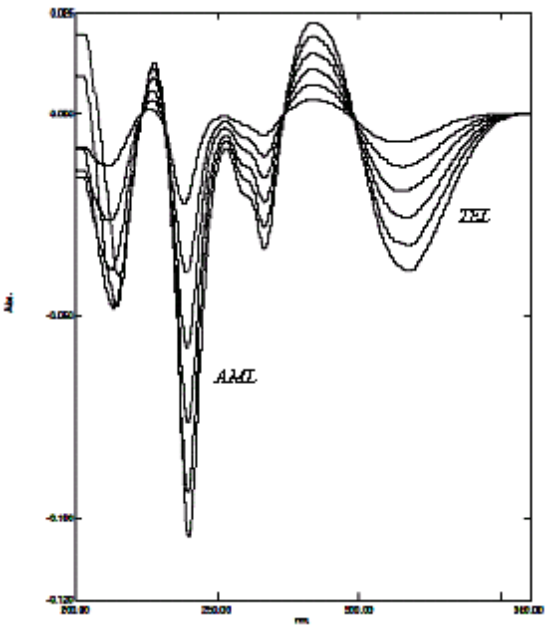

Fig. 2. *Overlain first derivative spectra of mixed standards of TEL and AML*

Method D: AUC for first derivative

The mixed standard solutions of AML and TEL were scanned between 200-400nm using distilled water as blank. The primary spectra so obtained were derivatised for the first order. The area under curve[22] in the first order spectrum between 231.2-253.2nm for AML and 295-354nm for TEL (Fig. 3) were measured by using the inbuilt software. The amount of AML and TEL in marketed sample was computed from the calibration curve obtained by plotting the area versus concentration for AML and TEL individually.

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, recovery experiments were performed by adding known amounts of pure drug to the previously analyzed formulation samples and these samples were reanalyzed by the proposed method.

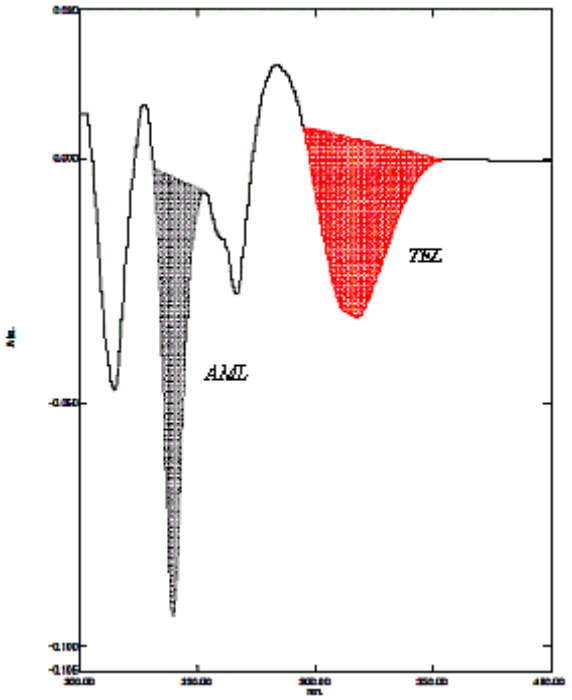

Fig. 3. *AUC of first derivative spectrum of mixed standards of TML and AML*

RESULTS AND DISCUSSION

The optical characteristics such as RSD, regression equation, correlation coefficient, slope and intercept for the two methods were calculated and the results are summarized in Table 1. The amount, % label claim and % of recovery studies obtained by the proposed methods are presented in Table 2. Interference studies revealed that the excipients and additives did not interfere. Hence these methods are most economic, simple, sensitive and accurate and can be used for the simultaneous determination of AML and TEL in pharmaceutical preparations.

Table 1. *Optical characteristics and validation of the proposed methods*

Parameters	Method A		Method B		Method C		Method D	
	AML	TEL	AML	TEL	AML	TEL	AML	TEL
Area/Wave length Range	364	299	364	299	225-240	282-318	231.2-253.2	295-354
Beer's law limit (µg/ml)	5-50	5-40	5-50	5-40	5-50	5-40	5-50	5-40
Linearity Range (µg/ml)	1-5	8-40	1-5	8-40	0.5-3	4-24	0.5-3	4-24
Slope	0.0119	0.0483	0.0119	0.0483	40.4285	5.6984	0.3244	0.0530
Intercept	0.0012	0.0010	0.0012	0.0010	1.5	0.9285	-0.0067	0.0027
Regression Equation (y=mx+c)	0.0119 x+0.0012	0.0483x +0.0010	0.0119x +0.0012	0.0483x +0.0010	40.4285x +1.5	5.6984x +0.9285	0.3244x + (-0.0067)	0.0530x +0.0027
Correlation coefficient	0.9999	0.9997	0.9999	0.9997	0.9997	0.9998	0.9999	0.9999
%RSD	0.1391	0.4859	0.1186	0.2597	0.1407	0.9883	0.9051	0.1727
LOD	0.7880	0.0906	0.2580	0.0906	5.6957	1.1655	0.0613	-0.8180
LOQ	2.2915	0.1917	2.2585	0.1837	16.8728	3.5319	0.1899	2.4789

Table 2. *Results of tablet formulation and recovery studies*

Method	Drug	Label Claim (mg/tablet)	Amount obtained (mg)	% Label claim	% Recovery by the proposed methods
Method A	AML	5.0	4.98	99.6	101.0
	TEL	40.0	41.09	102.7	101.3
Method B	AML	5.0	4.98	99.69	100.9
	TEL	40.0	40.66	101.6	100.3
Method C	AML	5.0	4.94	98.8	100.9
	TEL	40.0	40.50	101.26	99.86
Method D	AML	5.0	4.97	99.4	100.8
	TEL	40.0	39.40	98.5	101.2

** Average of three determinations, ** After spiking the sample*

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