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Spectrophotometric simultaneous determination of olmesartan medoxomil and amlodipine besylate in combined tablet dosage form

A.R.Chabukswar[1]*, A.H.Kategaonkar[1], B.S.Kuchekar[1], S.C.Jagdale[1], P.D.Lokhande[2], S.N.Shinde[1]

[1]MAEER'S Maharashtra Institute of Pharmacy, S. No. 124, MIT Campus, Paud Road, Kothrud, Pune - 411 038, (INDIA)

[2]Department of Chemistry, University of Pune, Ganeshkhind Road, Pune - 411 007, (INDIA)

E-mail : anigen18@rediffmail.com

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ABSTRACT

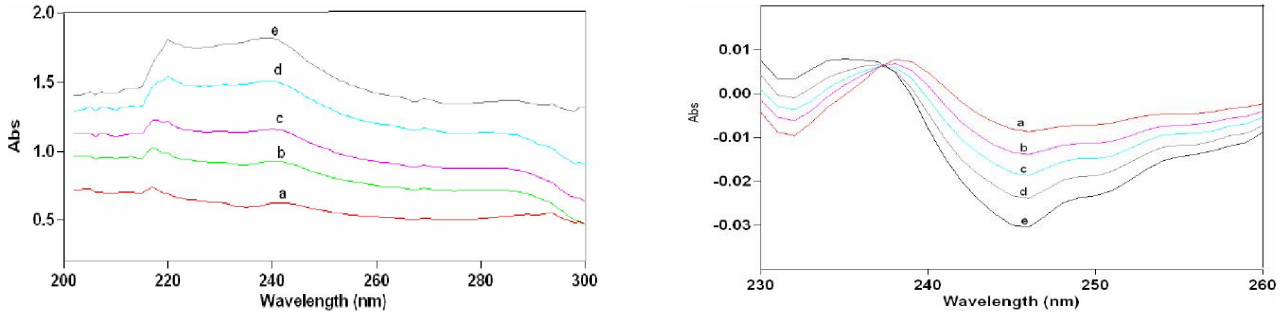
A simple, economical, precise and accurate method for simultaneous determination of Olmesartan medoxomil (OLME) and Amlodipine besylate (AMLO) in combined tablet dosage form has been developed. The method is based on ratio spectra derivative Spectrophotometry. The amplitudes 216.99 nm and 246 nm in the first derivative of the ratio spectra were selected to determine Olmesartan medoxomil and Amlodipine besylate respectively in combined formulation. Beer's law is obeyed in the concentration range of 8-24μg mL^{-1} for OLME and 2-6μg mL^{-1} for AMLO. The % assay for commercial formulation was found to be 100.03±0.717 for OLME and 99.94 ± 0.744 for AMLO. The method was validated with respect to linearity, precision and accuracy.

KEYWORDS

Amlodipine besylate;
Olmesartan medoxomil;
Ratio spectra derivative spectrophotometry.

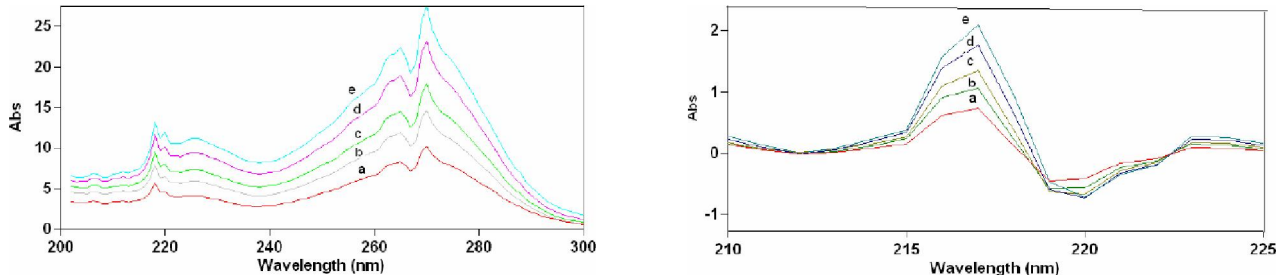
INTRODUCTION

Olmesartan medoxomil is 2,3-dihydroxy-2-butenyl-(1-hydroxy-1-methyl ethyl)-2-propyl-1-[P-(O-1H-tetrazole-5-ylphenyl)benzyl] imidazole-5- carboxylate, cyclic 2,3-carbonate. Olmesartan medoxomil a pro drug, is hydrolyzed to Olmesartan during absorption from the gastrointestinal tract. Olmesartan is a selective AT_1 subtype angiotensin Π receptor antagonist. Amlodipine besylate, is chemically described as 3-ethyl-5-methyl (±)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridine dicarboxylate, monobenzenesulphonate is a long-acting calcium channel blocker. It is official in BP. The literature survey revealed that the many more HPLC and spectroscopic methods of analysis for OLME and AMLO are reported as a single drug formulation. Chromatographic methods for determination of OLME in tablet dosage form[1] as well as spectrophotometric method for OMLE determination in combination with other drugs[2] have been studied. Stability indicating[3] and bioanalytical chromatographic methods[4] for quantification of OLME are also reported. HPTLC[5-7], HPLC[8,9], HPLC MS[10] spectrophotometry[11] methods have also been investigated for determination of amlodipine alone or in combination with other drugs. Literature Survey also revealed that no method is available for simultaneous determination of AMLO and OLME in combined dosage form by ratio spectra derivative spectrophotometry. Hence the aim of the present work was to develop simple, economical, precise and accurate method for simultaneous determination of binary drug formulation. The proposed method was optimized and validated as per the International Conference on Harmonization (ICH) guidelines[12].



(A) (B)

Figure 1 : Ratio spectra (A) and first derivative of the ratio spectra (B) of (a) 2, (b) 3, (c) 4, d) 5 and (e) 6µg mL^{-1} solution of AMLO when 16µg ML-1 solution of OLME is used as divisor. (A)



(A) (B)

Figure 2 : Ratio spectra (A) and first derivative of the ratio spectra (B) of (a) 8, (b) 12, (c) 16, (d) 20 and (e) 24µg mL^{-1} solution of OLME when 4µg mL^{-1} solution of AMLO is used as divisor

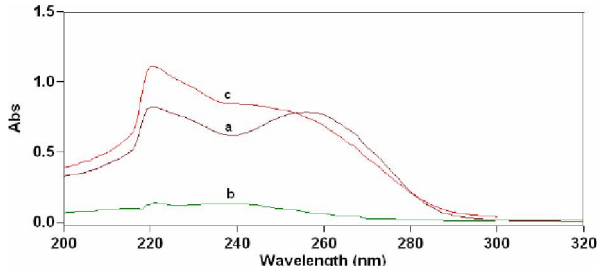


Figure 3 : Overlain zero order absorbance spectra of (a) OLM (16µg/mL) (b) AML (4µg/mL) (c) and their mixture

MATERIALS AND METHODS

Instrumentation

An UV-Visible double beam spectrophotometer (Varian Cary 100) with 10MM matched quartz cells were used for spectrophotometric method. All weighing was done on electronic balance (Model Shimadzu AUW-220D).

Reagents and chemicals

Pure drug sample of AMLO was kindly supplied as a gift sample by Emcure Pharmaceuticals Pvt. Ltd. Pune, India. It was used without further purification. Pure drug sample of OLME was gifted by Sun Pharmaceuticals Pvt. Ltd. Mumbai, India. Tablets were purchased from local market, containing amlodipine besylate 5mg and olmesartan medoxomil 20mg per tablet.

Preparation of standard stock solutions

Standard stock solutions of pure drug containing 100µg mL^{-1} of AMLO and OLME were prepared by dissolving 10mg of pure AMLO and OLME in 50mL of methanol in a 100mL volumetric flask and volume was made up to the mark with methanol separately. The working standard solutions of these drugs were obtained by dilution of the respective stock solution with methanol to produce 10µg mL^{-1} of AMLO and 100µg mL^{-1} of OLME. Beer's law obeyed in the concentration range of 2-6µg mL^{-1} for AMLO and 8-24µg mL^{-1} for OLME.

Preparation of sample stock solution

Twenty tablets were weighed accurately and a quantity of tablet powder equivalent to 20 mg of OMLE (5 mg of AMLO) was weighed and dissolved in the 50mL of methanol with the aid of ultrasonication for 5 min and solution was filtered through Whatman paper No. 41 into a 100mL volumetric flask. Filter paper was washed with methanol, adding washings to the volumetric flask and volume was made up to the mark with methanol, 1.0 ml of this solution was further diluted to

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TABLE 1 : Optical characteristics of the proposed method

Parameter	OLME	AMLO
λ (nm)	216.99	246
Beer's law limit (μgmL^{-1})	8-24	2-6
Molar absorptivity*	4.452×10^3	2.679×10^3
Regression Equation (y = mx + c)		
Slope (m)	0.857	0.0536
Intercept (c)	0.186	-0.0254
Correlation coefficient	0.999	0.996

***obtained from the first derivative ratio spectra**

10 ml with methanol to get required final concentration of OLME (20μg mL^{-1}) and AMLO (5μg mL^{-1}).

Recovery studies

The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to preanalysed sample solution at three different concentration levels (80%, 100 % and 120 %) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 8μg mL^{-1} of OLME and 2μg mL^{-1}of AMLO.

RESULTS AND DISCUSSION

The method involves dividing the spectrum of mixture by the standardized spectra of each of the analyte and deriving the ratio to obtain spectrum that is independent of concentration of analyte used as a divisor. Using appropriate dilutions of standard stock solution, the two solutions were scanned separately. The ratio spectra of different OLME standards at increasing concentrations were obtained by dividing each with the stored spectrum of the standard solution of AMLO (4μg mL^{-1}) as shown in figure 1(A) and the first derivative of these spectra traced, are illustrated in figure 1(B).

Wavelength 216.99nm was selected for the quantification of OLME in OLME + AMLO mixture. The ratio and ratio derivative spectra of the solutions of AMLO at different concentrations were obtained by dividing each with the stored standard spectrum of the OLME (16μg mL^{-1}) (Figure 2(A) and 2(B) respectively).

Wavelength 246 nm was selected for the quantification of AMLO in OLME + AMLO mixture. Measured analytical signals at these wavelengths were proportional to the concentrations of the drugs. The amount of OLME and AMLO in tablets was calculated by using following equations,

TABLE 2 : Results of commercial formulation analysis

Drug	Label claim (mg/tablet)	% of Label estimated? claim *	Standard deviation (±)	Standard error	% R.S.D.
OLME	20	100.03	0.717	0.167	0.718
AMLO	5	99.94	0.744	0.248	0.745

***Average of six determinations**

$$\text{At 216.99nm: } C_{OLME} = \frac{d}{d\lambda}\left[\frac{A_{OLME}}{A_{AMLO}}\right] - \text{Intercept (C)/Slope (m)} \quad (1)$$

$$\text{At 246nm: } C_{AMLO} = \frac{d}{d\lambda}\left[\frac{A_{AMLO}}{A_{OLME}}\right] - \text{Intercept (C)/Slope (m)} \quad (2)$$

Under experimental conditions described, calibration curve, assay of tablets and recovery studies were performed. The zero order overlain spectra are shown in figure 3.

A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient are shown in TABLE 1.

As per the ICH guidelines, the method validation parameters checked were linearity, accuracy and precision. Beer's law obeyed in the concentration range 8-24μg mL^{-1} and 2-6μg mL^{-1} with correlation coefficient of 0.999 and 0.996 for OLME and AMLO respectively. The proposed method was also evaluated by the assay of commercially available tablets containing OLME and AMLO (n = 6). The % assay was found to be 100.03 % for OLME and 99.94 % for AMLO as presented in TABLE 2.

Results of recovery studies are shown in TABLE 3.

R.S.D. is relative standard deviation. For AMLO, the recovery study results ranged from 99.71% to 100.26% with % RSD values ranging from 0.032% to 0.591%. For OLME, the recovery results ranged from 99.76% to 100.1%, with % RSD values ranging from 0.172% to 0.673%. The accuracy and reproducibility is evident from the data as results are close to 100% and standard deviation is low.

CONCLUSION

The validated spectrophotometric method employed here proved to be simple, economical, precise, and

TABLE 3 : Recovery studies of OLME and AMLO

Level of % recovery	Sample (μgmL^{-1})		Standard drug spiked (μgmL^{-1})		% Mean recovery *		Standard deviation		% R.S.D.	
	OLME	AMLO	OLME	AMLO	OLME	AMLO	OLME	AMLO	OLME	AMLO
80	8	2	6.4	1.6	100.1	99.71	0.672	0.108	0.671	0.109
100	8	2	8	2	99.76	99.82	0.673	0.031	0.673	0.032
120	8	2	9.6	2.4	99.79	100.26	0.171	0.593	0.172	0.591

***Average of three determinations**

accurate. The results of the methods are reproducible and thus the developed method can be used as IPQC test and for routine simultaneous determination of OLME and AMLO in tablet dosage form.

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