Original Article

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Simultaneous Estimation of Metaprolol Succinate and Olmesartan Medoxomil from Capsule Dosage Form by First Order Derivative Spectroscopic Method

S. D. Jadhav[*], *S. M. Kumbhar, V. D. Patel, R. M. Panchal and M. S. Bhatia*
[*] *Department of Pharmaceutical Chemistry, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Near Chitranagari, Kolhapur 416013, India.*

Abstact

Metaprolol succinate (MET) and Olmesartan medoxomil (OLM) are used in combination for treatment of hypertension. The present work deals with simple spectrophotometric method development for simultaneous estimation of MET and OLM in capsule formulation (OLSAR-M). The method employed was a first order derivative spectroscopy. For determination of sampling wavelength, 10 µg/ml of each of MET and OLM were scanned on UV-630 double beam spectrophotometer in 200-400 nm range. The sampling wavelengths were 214 nm for OLM where MET showed zero crossing point and 231 nm for MET where OLM showed zero crossing point in first order derivative spectroscopy. For this method, linearity was observed in 10-90 µg/ml for MET and 5-45 µg/ml for OLM. The recovery studies confirmed accuracy of proposed method and low values of standard deviation confirmed precision of method. The method is validated as per ICH guidelines. The proposed method can be optimized further for simultaneous estimation of both drugs from biological fluids, used in pharmacokinetic and bioequivalence studies.

Key words: Derivative Spectroscopy, Metaprolol, Olmesartan, OLSAR-M, ICH.

INTRODUCTION

Various combinations of antihypertensive drugs are available. These combinations of drugs are used in the treatment of hypertension to decrease toxicity profile and improve the tolerability of the therapy[1].

Metaprolol succinate (MEL) is chemically described as 1-[4-(2-methoxyethyl) phenoxy]-3-[(1-methylethyl) amino] propan-2-ol butanedioate (2:1) succinate is a beta-adrenergic blocking agent, which reduces chest pain and lowers high blood pressure. Olmesartan medoxomil (OLM) is (5-methyl-2-oxo-2H-1,3-dioxol-4-yl) methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2H-1,2,3,4-tetrazol-5-yl)phenyl]phenyl}methyl)-1H-imidazole-5carboxyl, medoxomil, used as angiotensin II receptor antagonist[2] (Figure 1). Many spectrophotometric and chromatographic methods were reported for determination of MET[3-10] and OLM[9-16] alone and in combination with other antihypertensive drugs. Till date, dual wavelength method[9] and first order derivative[10] spectrophotometric methods have been developed. But both methods were found to be less sensitive than developed method and estimation of OLM has been carried out at wavelength near 210 nm but methanol has considerable absorbance at this wavelength.

In this communication, we proposed development of a new simple, accurate, precise, and sensitive first order derivative spectroscopic method for simultaneous determination of MET and OLM from their pharmaceutical formulation.

***Corresponding author:** Department of Pharmaceutical Chemistry, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Near Chitranagari, Kolhapur 416013.
Email: swapnil.mpharm@gmail.com

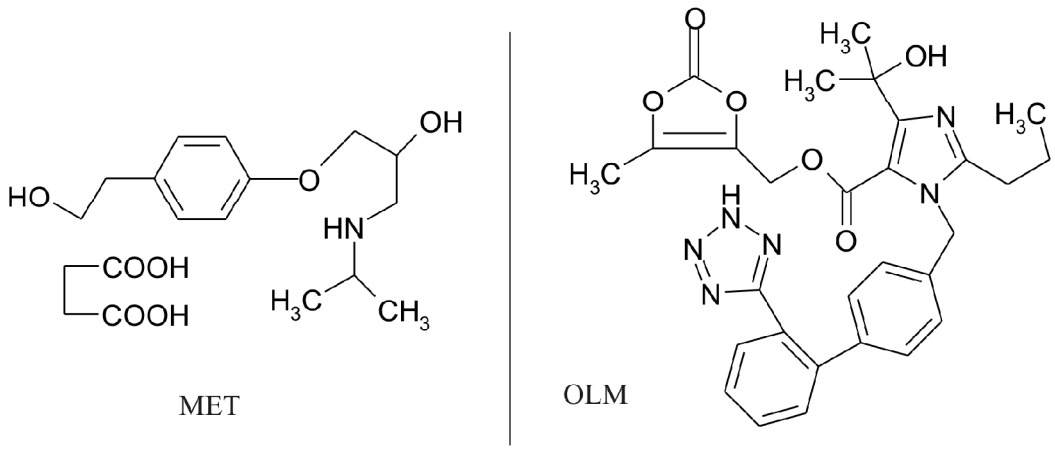

Figure 1. Chemical structure of metaprolol succinate and olmesartan medoxomil

MATERIALS AND METHODS

Materials:

Instrument:

Spectrophotometric analysis was carried out on a JASCO UV-630 double beam spectrophotometer using a 1 cm quartz cell. The instrument settings were zero order and first derivative mode and band width of 2.0 nm in the range of 200–400 nm.

Reagents and chemicals:

Metaprolol succinate and Olmesartan medoxomil were supplied by CIPLA India Pvt. Ltd. Goa. All solvents were spectrophotometric grade were obtained from SD fine chemicals. Water was purified by glass distillation apparatus in laboratory.

Method:

Linearity Study:

Stock solutions were prepared separately in water: methanol (20:80) to obtain 100 µg/ml of both drugs. The nine working mixed standard were prepared by dilution of stock solution in same solvent system in concentration range 5-45 µg/ml of OLM and 10-90 µg/ml for MET. MET and OLM were initially scanned for determining sampling wavelength in range 200-400 nm. Sampling wavelengths were 214 nm for OLM where MET showed zero crossing point and 231 nm for MET where OLM showed zero crossing point in first order derivative mode (Figure 2). The nine solutions of each drug were scanned in wavelength range f 200-400 nm in zero order derivative modes. These spectra were then processed to first order derivative mode by software. The absorbance values of both drugs were recorded at respective wavelength in first order derivative mode. The calibration graphs were constructed for MET and OLM. The calibration curve data will be useful for quantitative estimation of both drugs at respective wavelength.

Assay of Capsule Formulation:

Twenty capsules of OLSAR-M (MET-50 mg and OLM-20 mg) were weighted individually and average weight of capsule was calculated. Content of twenty capsules were mixed together and powder equivalent to 20 mg of OLM taken, dissolved in 60 ml of solvent system. This solution was then filtered through Whatman filter paper No. 41. The volume was made up to 100 ml with solvent system and sonicated for 10 minutes. To 1 ml of this stock solution was diluted to 10 ml to get concentration equal to 20 µg/ml of OLM and 50 µg/ml of MET. This solution is scanned on UV-630 system in range 200-400 nm using solvent system as blank. The spectra obtained were processed to first order derivative mode and absorbances were noted at respective wavelengths. The concentrations of MET and OLM were calculated from regression equations generated from calibration graph. The results of marketed formulation (OLSAR-M) analysis are reported in Table 1.

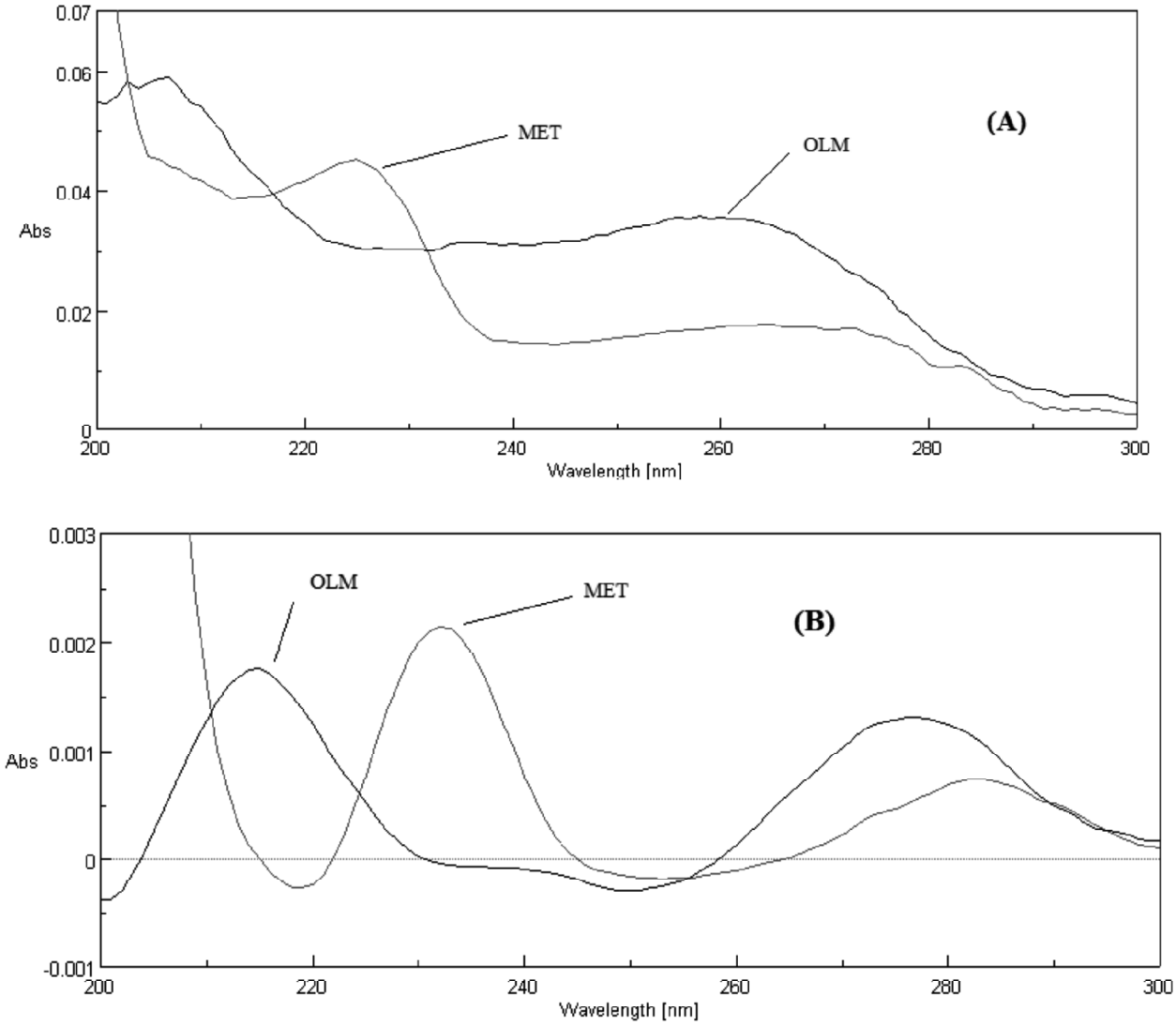

Figure 2. Overlain spectra of MET and OLM in zero (A) and first (B) order derivative mode

Table 1. Results of capsule (OLSAR-M) analysis and recovery study

Drug	Label Claim (mg/Capsule)	%Label Claim Estimated Mean[a]± SD[b]	Amount Added (mg)	% Recovery Estimated Mean[a]± SD[b]
		99.25±1.257	40	99.76±1.266
MET	50	101.91±1.965	50	100.87±1.186
		98.78±1.032	60	99.92±1.601
		98.21±1.034	16	98.04±0.9143
OLM	20	98.75±1.289	20	99.84±0.7453
		99.31±1.712	24	99.55±0.9560

a: Average of three determinations b: Standard deviation.

RESULTS AND DISCUSSION

After thorough literature survey, it has been observed that no method was reported for simultaneous estimation of OLM and MET. Hence, we proposed to develop analytical method for simultaneous estimation of OLM and MET from their capsule dosage form.

The overlain spectra of MET and OLM in zero order mode indicated that there is no specific wavelength at which estimation of either of both drug is possible at any wavelength. Hence individual spectrum of MET and OLM were processed by software to first order derivative mode and overlain spectrum was recorded. After observing overlain spectrum, 214 nm was selected as wavelength of analysis for OLM as no interference of MET was observed at this wavelength. Similarly, 231 nm was selected as a wavelength of analysis.

The quantification of individual drug is carried out by using calibration curve data i.e. slope and intercept values. The concentrations of drugs calculated using linear regression equation $a = A + B \times C$ where a is absorbance of drug, A is intercept, B is slope and C is concentration of drug.

The developed method was validated by following ICH Q2B (R1) guidelines[17]. The following parameters were studied for validation.

Accuracy:

Recovery studies were performed by standard addition method at three levels i.e., 80%, 100% and 120%. Known amounts of pure MET and OLM were added to pre-analyzed sample of marketed formulation and they were subjected to analysis by the proposed method. Results of recovery studies are shown in Table 1. The results of recovery studies were found to be in range of 98.04 to 100.87 with standard deviation value of 1.601.

Precision:

Precision study was performed to find out intra-day and inter-day variations. The results of precision studies are reported in Table 2 and values of standard deviation less than 2% indicates high degree of precision.

Limit of Detection (LOD) and Limit of Quantitation (LOQ):

The LOD and LOQ were separately determined based on the calibration curves.

Table 2. Results of Precision Studies

Analyte	Precision		Amount of Pure Drug Added in mg	% concentration Found (Mean[a] ± SD[b])
MET	Intra-Day	T1	40	99.04 ±1.2422
		T2	50	99.55 ± 0.5152
		T3	60	99.60 ±0.6613
	Inter-Day	D1	-	1001.11±0.6739
		D2	-	100.02±0.9637
		D3	-	100.04 ± 1.2422
OLM	Intra-Day	T1	16	98.33 ± 1.1558
		T2	20	99.40 ± 1.2844
		T3	24	98.56± 1.4750
	Inter-Day	D1	-	98.75±1.2897
		D2	-	99.31±1.71258
		D3	-	99.59 ± 0.27678

a: Average of three determinations b: Standard deviation.

The standard deviation of the y-intercepts (σ) and slope of the regression lines (S) were used. These values were calculated using following formula

$$LOD = 3.3 \times \sigma / S \qquad LOQ = 10 \times \sigma / S$$

The limit of quantitation and limit of detection were found to be 0.187ng/mL

and 0.065 ng/mL for OLM and 0.157 ng/mL and 0.050 ng/mL for MET respectively. These low LOD and LOQ indicate that very small quantities of analyte can be estimated by this method.

Robustness:

The robustness of method was studied by changing composition of solvent system. The results of robustness studies are reported in Table 3.

Table 3. Result of robustness and ruggedness study

Parameter	Modification	% Recovery Mean[b] ± SD[c]	
		MET	OLM
Robustness Study			
Solvent System Ratio (Water: Methanol)	15:85	99.91±1.9658	99.21 ± 1.0107
	18:82	98.78±1.0328	100.39 ± 0.3644
	20:80[a]	99.59 ±0.5015	98.21±1.0346
	22:78	99.72 ± 0.5042	98.75±1.2897
	25:75	99.87 ± 0.8311	99.31±1.71258
Ruggedness Study			
Instrument	UV-530	100.09±0.73	100.39±0.37
	UV-630	100.10 ± 0.87	100.68 ± 0.94
Analyst	I	99.72 ± 0.50	99.31 ± 0.32
	II	99.45 ± 0.51	99.37 ± 1.10

a: Optimized parameter for developed method b: Mean of three readings

c: Standard deviation

Ruggedness:

The ruggedness study was carried out by using different instruments and analyst. The results are as shown in Table 3.

CONCLUSION

The results of analysis and various validation parameters indicated that developed method is simple, accurate, precise and sensitive method simultaneous determination of MET and OLM from their pharmaceutical formulation. The optimization of developed method will lead to estimation of MET and OLM from biological fluids.

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