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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS DETERMINATION OF OLMESARTAN MEDOXOMIL AND METOPROLOL SUCCINATE IN PHARMACEUTICAL PREPARATIONS

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ABSTRACT

Simple, accurate, and reproducible two UV-spectrophotometric methods have been developed for simultaneous estimation of Olmesartan Medoxomil (OLME) and Metoprolol Succinate (METO) in tablet dosage form. The first UV- Spectrophotometric method was a determination using the Area Under Curve method and the second UV method was a determination using the Multi-Component mode method at 256.5 nm and 222.0 nm over the concentration range 5-30 µg/mL and 5-30 µg/mL for OLME and METO respectively. Both UV-spectrophotometric methods were statistically validated and can be used for analysis of combined dose tablet formulation containing OLME and METO.

Keywords: Olmesartan Medoxomil, Metoprolol Succinate, Area under curve method and Multicomponent mode method

INTRODUCTION

OLME is chemically (5-methyl-2-oxo-2*H*-1,3-dioxol-4-yl)methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2*H*-1,2,3,4-tetrazol-5-yl) phenyl] phenyl}methyl)-1*H*-imidazole-5-carboxylate, and METO is chemically (*RS*)-1-(Isopropylamino)-3-[4-(2-methoxyethyl) Phenoxy] propan-2-ol succinate[1]. OLME is a angiotensin II receptor antagonist for the treatment of hypertension [2].

OLME is not official in any pharmacopoeia. Various methods like HPTLC[3], spectrophotometric and HPLC method for simultaneous estimation of OLME with other drug[4], HPTLC method for simultaneous estimation of OLME with other drug[5], RP HPLC method for simultaneous estimation of OLME with other drug[6], stability-indicating LC method[7] for the determination of OLME and UV method for OLME and METO[8, 9] are reported in literature for estimation of OLME in pharmaceutical dosage forms as well as in biological fluids. METO is a cardioselective β-blocker, used in the treatment of hypertension, angina pectoris, arrhythmia, myocardial infarction and heart failure [10].

It is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). IP [11], BP [12] and USP [13] describe potentiometric method for its estimation. Various methods like UV spectrophotometry [14],RP-HPLC[15],validated HPLC method for estimation of METO in human plasma[16],spectrophotometric method for simultaneous determination of METO with other drug[17] and RP-HPLC method for simultaneous determination of METO with other drug [18] are reported in literature for estimation of METO in pharmaceutical dosage forms as well as in biological fluids.

The proposed method were optimized and validated as per ICH guidelines [19]. The combined dosage

forms of OLME and METO are available in the market for the treatment of hypertension.

MATERIALS AND METHODS

Chemicals and Reagents: OLME and METO pure drug were kindly gifted by Ravoos Laboratories (Pvt.) Ltd, Hyderabad. Combination Tablet product brand name RASOTAN BETA 25 containing 20 mg OLME and 25 mg METO manufactured by Windlas Biotech Limited, Dehradun and marketed by Emcure Pharmaceuticals was purchased from the local market. Methanol was purchased from Merck specialities Pvt. Ltd. Double distilled water used in all experiments was obtained from Milli-Q System (Millipore).

Instrumentation and analytical conditions: The UV methods were performed on a Double-beam Shimadzu UV-Visible spectrophotometer, 1700, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1 cm matched quartz cells was used to measure absorbance of solution. The method is based upon determination of OLME at 256.5 nm and METO at 222.0 nm.

Preparation of standard solutions: Standard stock solution of OLME and METO were prepared by transferring accurately weighed OLME (10 mg) and METO (10 mg) to a 100 mL volumetric flask separately, dissolved and diluted to a mark with methanol to obtain a standard solution of OLME (100 µg/mL) and METO (100 µg/mL). From these solutions 8 mL of OLME and 10 mL of METO standard stock solutions were mixed in a 10 mL volumetric flask and made up the volume with distilled water, to get the concentration of 80 µg/mL of OLME and 100 µg/mL of METO.

Preparation of the sample solutions: Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 20 mg of OLME and 25 mg of METO were transferred to 100 mL volumetric flask; diluted to a mark with methanol and sonicated for 20 min. The resulting solution was filtered through Whatmann filter paper and filtrate was appropriately diluted with distilled water to get concentration of 80 µg/mL of OLME and 100 µg/mL of METO.

Method Validation [19]

Linearity: The calibration curve for UV method was obtained with concentrations of the standard solutions 5-30 µg/mL for both drugs. The solutions were prepared in triplicate. Linearity was evaluated by regression analysis, which was calculated by the least square regression method.

Precision: Precision of UV method was checked by analyzing the samples at three different time intervals of the same day (intraday precision) as well as on different days (interday precision).

Accuracy: To check the degree of accuracy of UV method, recovery studies were performed in triplicate by standard addition method at 80%, 100% and 120%.

Limit of detection and limit of quantitation: LOD, LOQ of UV method were calculated by using the values of slopes and intercepts of the calibration curves for both the drugs.

RESULT AND DISCUSSION

The proposed UV methods, allows a rapid and accurate quantitation of OLME and METO in tablet preparation without any time consuming sample preparation (Table 3). Moreover, the spectrophotometric methods involve simple instrumentation compared with other instrumental techniques. Wavelengths selected for analysis are 256.5 nm (λ_{max} of OLME) and 222.0 nm (λ_{max} of METO). Calibration curves were constructed in the concentration range of 5-30 µg/mL for both drugs.

Beer's law was obeyed over this concentration range, and the coefficient of regression for both the drugs was found to be nearer to 1 (Table 1).

The accuracy of proposed method were determined (Table 4), indicating an agreement between the true value and found value. Precision was calculated as interday and intraday variations for both the drugs. Percent relative standard deviations for estimation of OLME and METO under intraday and interday variations were found to be less than 2 (Table 2).

CONCLUSION

The two proposed methods based on the spectrophotometry were developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are low, indicating high degree of precision of the methods. The results of the recovery studies performed show the high degree of accuracy for the proposed methods. Hence, it can be concluded that the developed spectrophotometric methods are accurate, precise and selective and can be employed successfully for the estimation of OLME and METO in tablet dosage form.

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Table 1: Validation data of OLME and METO

Parameters	OLME		METO	
	Method I	Method II	Method I	Method II
Working wavelengths	256.5	256.5	222.0	222.0
Beer-Lamberts Law range (µg/mL)	5-30	5-30	5-30	5-30
LOD (µg/mL)*	0.2216	0.2216	0.7347	0.7347
LOQ (µg/mL)*	0.6715	0.6715	2.2265	2.2265
Regression Values:				
I. Slope*	0.460	0.460	0.309	0.309
II. Regression coefficient(r^2)*	0.998	0.998	0.997	0.997

**Denotes average of three estimations, Where, Method-I – Area Under Curve method, Method-II- Multi-Component mode method.*

Table 2: Intra-day and Inter-day Precision

Precision*	OLME		METO	
	Method I	Method II	Method I	Method II
Interday (%RSD)	0.6734	0.8015	1.3957	0.7330
Intraday (%RSD)	1.4682	0.7071	1.5076	0.8399

**Denotes average of six estimations, Where, Method-I – Area Under Curve method, Method-II- Multi-Component mode method.*

Table 3: Results of simultaneous estimation of tablet formulation

Methods	Tablet content	Label claim (mg/tab)	Amount found (mg/tab)	Label claim* (%)	(%) RSD	SE
I	OLME	20	19.99	99.97	1.6585	0.6767
	METO	25	24.97	99.87	1.9535	0.7965
II	OLME	20	20.13	100.67	0.5883	0.2418
	METO	25	25.09	100.36	0.4508	0.1847

**Denotes average of six estimations. Where, Method-I – Area Under Curve method, Method-II- Multi-Component mode method, SE- Standard error of mean.*

Table 4: Result for recovery studies

Level of % recovery	Methods	% Recovery *		%RSD		SE	
		OLME	METO	OLME	METO	OLME	METO
80	I	99.57	101.03	0.0614	0.1361	0.0353	0.0794
	II	100.42	100.41	0.9170	0.4328	0.5317	0.2504
100	I	100.63	98.72	0.1448	0.4079	0.0841	0.2325
	II	100.32	100.18	0.3241	0.2905	0.1877	0.1680
120	I	100.14	100.96	0.0251	0.0396	0.0145	0.0231
	II	100.71	100.31	0.6220	0.3057	0.3617	0.1770

**Denotes average of three estimations. Where, Method-I – Area Under Curve method, Method-II- Multi-Component mode method, SE- Standard error of mean.*

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