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Absorption Correction Method for Simultaneous Estimation of Metoprolol Succinate and Olmesartan Medoxomil in Combined Tablet Dosage Form

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ABSTRACT:

A new, simple, precise, accurate and sensitive UV - Spectrophotometric absorption correction method has been developed for simultaneous determination of Metoprolol Succinate and Olmesartan Medoxomil in combined tablet dosage form. Methanol was used as solvent. Absorbance correction method was based on the property of additivity of absorbances. The two wavelengths on Olmesartan medoxomil curve were found out where it showed same absorbance, which were 233 and 244 nm. At 244 nm, Olmesartan Medoxomil showed some absorbance while Metoprolol Succinate showed zero absorbance. Both the drugs gave absorbance at 233 nm. The method involved solving of an equation based on measurement of absorbance at two wavelengths 233 and 244 nm. The determinations were made at 233 nm for Metoprolol Succinate and Olmesartan Medoxomil and 244 nm for Olmesartan Medoxomil over the concentration range of 5-25 µg/ml for Metoprolol and 4-20 µg/ml for Olmesartan medoxomil with mean recovery of 99.81 ± 0.45 and 99.45 ± 0.406 % for Metoprolol Succinate and Olmesartan Medoxomil, respectively by absorbance correction method. This method was found to be simple, sensitive, accurate, precise, reproducible and economical and can be applicable for the simultaneous determination of METOPROLOL and OLMESARTAN in combined dosage form.

KEY WORDS: Metoprolol Succinate, Olmesartan Medoxomil, Absorbance correction method, Validation, Combined dosage form

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INTRODUCTION:

Metoprolol Succinate (METO) is chemically (RS)-1-isopropylamino-3-p-(2-methoxyethyl) phenoxypropan-2-ol(2R,3R)-Succinate^[1], is a cardio selective β -blocker, used in the treatment of hypertension, angina pectoris, arrhythmia, myocardial infarction and heart failure^[2]. It is official in Indian Pharmacopoeia (IP), British Pharmacopoeia (BP) and United States Pharmacopoeia (USP). IP^[3], BP^[4] and USP^[5] describe potentiometric method for its estimation. Various methods like UV spectrophotometry^[6], RP-HPLC^[7], validated HPLC method for estimation of Metoprolol in human plasma^[8], spectrophotometric method for simultaneous determination of METO with other drug^[9] and RP-HPLC method for simultaneous determination of METO with other drug^[10] are reported in literature for estimation of METO in pharmaceutical dosage forms as well as in biological fluids. Olmesartan medoxomil (OLME) is chemically (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-5-carboxylate^[11], is a angiotensin II receptor antagonist for the treatment of hypertension^[12]. Olmesartan medoxomil is not official in any pharmacopoeia. Various methods like spectrophotometric^[13] and HPLC method for simultaneous estimation of OLME with other drug^[14], and RPHPLC method for simultaneous estimation of OLME with other drug^[15] for the determination of OLME are reported in literature for estimation of OLME in pharmaceutical dosage forms as well as in biological fluids. The combined dosage forms of METO and OLME are available in the market for the treatment of hypertension. Literature

survey reveals the simple spectroscopic method^[16] for determination of METO and OLME in combined dosage form based on simultaneous equation method using methanol as a solvent. The present manuscript describes alternative simple, sensitive, accurate, precise, reproducible, and economical absorbance correction method for simultaneous estimation of METO and OLME in combined dosage form.

MATERIALS AND METHODS

Apparatus:

A shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. A Reptech electronic weighing analytical balance based on EMFC technology and a Toshcon ultrasonic bath (Toshniwal process instrument pvt ltd.) was used in the study.

Reagents and Materials:

METO and OLME bulk powder was kindly gifted by Alpha laboratories, Baroda, Gujarat, India. The commercial fixed dose combination Olmax M 25 was procured from the local market. All other chemicals used were of analytical grade. Methanol (AR grade) was purchased from Finar Chemicals Ltd, Ahmedabad India. Caliberated glasswares were employed throughout the work.

Methodology

Absorbance spectrum of pure OLME was scanned in the spectrum basic mode. Using the cursor function, the absorbance corresponding to 244 nm (wavelength λ_1 , the wavelength of minimum absorbance for OLME) was noted from spectrum. Then the cursor function was moved along with peak curve until the absorbance equal to that of absorbance at 244 nm was found. The wavelength obtain corresponding to this absorbance value was 233 nm (λ_2). The absorbance of various dilutions of OLME in methanol was measured at 244 nm. Absorbance spectrum of pure METO was also scanned in the spectrum basic mode. METO showed some absorbance value at 233 nm (λ_2) while it does not show any absorbance value at 244 nm. The absorbance value at 244 nm is due to OLME only in the combined mixture of both drugs. Wavelength λ_1 (244 nm) was selected for the measurement of OLME.

Preparation of standard stock solutions

An accurately weighed quantity of METO (50 mg) and OLME (40 mg) were transferred to a 50 ml volumetric flask and dissolved and diluted to the mark with methanol to obtain a standard solution having concentration of METO (1000 $\mu\text{g/ml}$) and OLME (800 $\mu\text{g/ml}$). Accurately measured 10 ml of the above solution was transferred to 100ml of volumetric flask and diluted to the mark with methanol to obtain a solution having concentration 100 $\mu\text{g/ml}$ of METO and 80 $\mu\text{g/ml}$ of OLME.

Preparation of sample solution

Ten Tablets were weighed and powdered. The powder equivalent to 25 mg of METO and 20 mg of OLME was transferred to a 50 ml volumetric flask. Methanol was added to it and sonicated for 20 min. The solution was filtered through Whatman filter paper No. 41 and the volume was adjusted up to the mark with methanol. The above solution was suitably diluted with methanol to get a final concentration of 10 $\mu\text{g/ml}$ of METO and 8 $\mu\text{g/ml}$ of OLME.

Method Validation

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines^[17].

Linearity (Calibration curve)

Calibration curves were plotted over a concentration range of 5-25 $\mu\text{g/ml}$ for METO and 4-20 $\mu\text{g/ml}$ for OLME. Accurately measured mixed standard working solutions of METO and OLME (2.5, 5.0, 7.5, 10.0 and 12.5ml) were transferred to a series of 50 ml of volumetric flasks and diluted to the mark with methanol and absorbances were measured at 244 nm and 233 nm for both the drugs. The calibration curves were constructed by plotting absorbance at 244 nm versus concentrations for OLME and absorbance difference ($A_{233} - A_{244}$) concentration for METO.

Accuracy (% Recovery)

The accuracy of the methods was determined by calculating recoveries of METO and OLME by the standard addition method. Known amounts of standard solutions of METO (8, 10, 12 $\mu\text{g/ml}$ for METO) and OLME (6.4, 8, 9.6 $\mu\text{g/ml}$ for OLME) were added to prequantified sample solutions of tablet dosage form. The amounts of METO and OLME were estimated by applying obtained values ($n = 6$) to the regression equation of the calibration curve.

Method Precision (% Repeatability)

The precision of the instruments was checked by repeatedly injecting ($n = 6$) standard solutions METO and OLME (10 and 8 $\mu\text{g/ml}$ respectively) without changing the parameter for the absorbance correction method.

Intermediate Precision (Reproducibility)

The intraday and interday precisions of the proposed methods were determined by estimating the corresponding responses 3 times on the same day and on 3 different days over a period of one week for 3 different concentration of standard solutions of METO (5, 10, 15, 20 and 25 $\mu\text{g/ml}$) and OLME (4, 8, 12, 16, 20 $\mu\text{g/ml}$). The results were reported in terms of relative standard deviation (% RSD).

Limit of detection and Limit of quantification:

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived by calculating the signal-to-noise ratio (S/N) using the following equations designated by International Conference on Harmonization (ICH) guidelines.

$$\text{LOD} = 3.3 \times \sigma/S$$

$$\text{LOQ} = 10 \times \sigma/S$$

Where, σ = the standard deviation of the response and S = slope of the calibration curve.

Analysis METO and OLME in combined dosage forms

Pharmaceutical formulation of METO and OLME was purchased from local pharmacy. The responses of formulations were measured at 244 nm and 233 nm for OLME and METO, respectively by absorbance correction method as described above. The amounts of METO and OLME present in sample solution were determined by fitting the responses into the regression equation for METO and OLME in the method.

RESULTS AND DISCUSSION

Absorbance correction method^[18]

The utility of dual wavelength data processing program is its ability to calculate unknown concentration of component of interest in a mixture containing an interfering component. For elimination of the effects of an interfering component, two specific wavelengths are chosen.

1. First wavelength λ_1 at which minimum absorbance of OLME was observed and there was no interference of METO at this wavelength (244 nm).

2. Second wavelength λ_2 was the wavelengths at which the absorbance of OLME was same as at λ_1 , and also METO gives some absorbance at this wavelength (233.0 nm). In this proposed method the absorbance of METO alone in a mixture of METO and OLME was determined using dual wavelength data processing program. To remove the interference of OLME to the absorbance at 233.0 nm (λ_2), the wavelength of minimum absorbance for OLME, another wavelength 244 nm (λ_1) was found out at which the absorbance of METO was zero. This was confirmed by measuring the absorbance of various dilution of OLME in methanol at 233.0 nm and 244 nm. The absorbance at these two wavelengths was found to be equal. These two selected wavelengths were employed to determine the concentration of METO from the mixture of METO and OLME (Figure 1). The difference in absorbance at these two wavelengths ($A_{233.0} - A_{244}$) cancels out the contribution of absorbance of OLME in mixture.

Validation data of the proposed methods

Linearity - Linear correlation was obtained between absorbance and concentration of METO and OLME in the range of 5-25 & 4-20 $\mu\text{g/ml}$ respectively. The linearity of the calibration curves was validated by the high value of

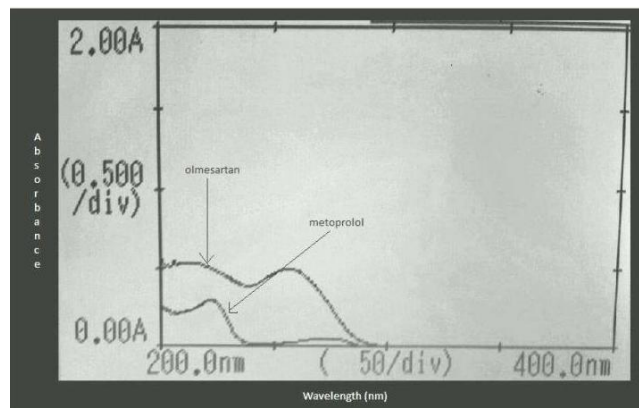


Figure 1: Overlay of Metoprolol Succinate and Olmesartan Medoxomil

Table. 1 Regression analysis data and summary of validation parameters for the proposed absorbance correction method

Parameters	Absorbance Correction Method	
	METO	OLME
Concentration range ($\mu\text{g/ml}$)	5-25	4-20
Slope	0.0082	0.0354
Intercept	0.0076	0.0215
Correlation Coefficient (r^2)	0.9997	0.9993
LOD ($\mu\text{g/ml}$)	0.79	0.21
LOQ ($\mu\text{g/ml}$)	2.38	0.64
Accuracy (% recovery, n = 6)	99.81 \pm 0.45	99.45 \pm 0.40
Repeatability (%RSD, n = 6)	1.11	0.58
Precision (% RSD)		
Interday (n = 6)	0.68 - 2.61	0.27 - 1.57
Intraday (n = 6)	0.28 - 2.08	0.14 - 1.23

correlation coefficients of regression (Table 1).

Accuracy - The recovery experiments were carried out by the standard addition method. The mean recovery obtained was 99.81 \pm 0.45 and 99.45 \pm 0.40 % for METO and OLME, respectively (Table 1). The high values indicate that the method is accurate.

Method precision - The % RSD values for METO and OLME were found to be 1.11 and 0.58 (Table 1). The low values of RSD indicate the proposed method is repeatable.

Intermediate precision - The low RSD values of interday (0.68 - 2.61 % and 0.27 - 1.57 %) and intraday (0.28 - 2.08 % and 0.14 - 1.23 %) variations for METO and OLME, respectively reveal that the proposed method is precise (Table 1).

LOD and LOQ - LOD for METO and OLME were found to be 0.79 $\mu\text{g/ml}$ and 0.21 $\mu\text{g/ml}$, respectively. LOQ for METO and OLME were found to be 2.38 $\mu\text{g/ml}$ and 0.64 $\mu\text{g/ml}$, respectively (Table 1). These data show that the method is sensitive for the determination of METO and OLME.

Assay of the pharmaceutical formulation

The proposed validated methods were successfully applied to determine METO and OLME in their combined dosage form.

The results obtained for METO and OLME were comparable with the corresponding labelled amounts (Table 2).

CONCLUSION

The results of the analysis of pharmaceutical formulation by the proposed method are highly reproducible and reliable and are in good agreement with the label claim of the drug. The additives usually present in the pharmaceutical formulations of the assayed samples did not interfere with determination of METO and OLME. The methods can be routinely used for the analysis of the METO and OLME in combined dosage form.

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