Original Article

Development and validation of the simultaneous UV spectrophotometric method for estimation of metoprolol succinate and olmesartan medoxomil in the tablet dosage form

Abstract

Introduction: A simple, rapid, accurate, precise, and economical UV spectrophotometric method for the simultaneous determination of metoprolol succinate (METO) and olmesartan medoxomil (OLME) in a combined tablet dosage form using the simultaneous equation method has been developed. **Materials and Methods:** The method is based on the simultaneous equations for analysis of both the drugs using distilled water as a solvent. METO has absorbance maxima at 221 nm and OLME has absorbance maxima at 257 nm in distilled water. **Results:** The linearity was obtained in the concentration range of 5–25 μg/ml and 4–20 μg/ml for METO and OLME, respectively. The concentrations of the drugs were determined by using the simultaneous equations method. The mean recovery was 100.90 ± 1.76 and 100.26 ± 0.71 for METO and OLME, respectively. **Conclusion:** The method was found to be simple, accurate, and precise and was applicable for the simultaneous determination of METO and OLME in the pharmaceutical tablet dosage form. The results of analysis have been validated statistically and by recovery studies.

Key words: Distilled water, metoprolol succinate, olmesartan medoxomil, recovery, simultaneous equations, validation

Bindi N. Vora, Rajesh R. Parmar, Pratik P. Nayak, Dushyant A. Shah

APMC College of Pharmaceutical Education and Research, College Campus, Motipura, Himmatnagar 383 001, India

Address for correspondence:
Ms. Bindi N. Vora,
A-102 Siddharth Flats,
Near Trupti Jain Derasar,
Kalanala, Bhavanagar,
Gujarat 364 001, India.
E-mail: bindi.vora1989@gmail.com

Access this article online

Website: www.phmethods.org

DOI: 10.4103/2229-4708.97724

Quick response code

INTRODUCTION

Metoprolol succinate (METO) is chemically known as (*RS*)-1-isopropylamino-3-*p*-(2-methoxyethyl) phenoxypropan-2-ol(2*R*,3*R*)-succinate,[1] is a cardio-selective β-blocker, used in the treatment of hypertension, angina pectoris, arrhythmia, myocardial infraction, 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 the potentiometric method for its estimation. Various methods such as UV spectrophotometry,[6] RP-HPLC,[7] and validated HPLC for estimation of metoprolol in human plasma,[8] the spectrophotometric method for simultaneous determination of METO with other drugs[9] and the RP-HPLC method for simultaneous determination of METO with other drugs[10] are reported in the literature for estimation of METO in pharmaceutical dosage forms as well as in biological fluids. Olmesartan medoxomil (OLME) is chemically known as (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,[11] is a angiotensin II receptor antagonist for the treatment of hypertension.[12] OLME is not official in any pharmacopoeia. Various methods such as spectrophotometry[13] and HPLC for simultaneous estimation of OLME with other drugs,[14] and the RPHPLC method for simultaneous estimation of OLME with other drugs[15] for the determination of OLME are reported in the 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. A literature survey reveals the simple spectroscopic methods[16] for determination of METO and OLME in combined dosage forms based on the simultaneous equation method using methanol as a solvent. No literature surveys have been revealed for spectroscopic methods using water as a solvent. This review article describes a simple, accurate, precise, rapid, and economic spectrophotometric method based on the simultaneous equations for simultaneous estimation of METO and OLME in tablet dosage forms using distilled water as a solvent.

MATERIALS AND METHODS

Apparatus

A Shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer with a spectral width of 2 nm, a 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 powders were 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. Distilled water and calibrated glasswares were employed throughout the work.

Preparation of standard stock solutions

An accurately weighed quantity of METO (50 mg) and OLME (50 mg) was transferred to a separate 50 ml volumetric flask and dissolved and diluted to the mark with distilled water using 10 ml methanol to obtain standard solution having concentration of METO (1000 μg/ml) and OLME (1000 μg/ml). Accurately measured 10 ml of both the solutions were transferred into a 100 ml of volumetric flask and diluted to the mark with distilled water to obtain solution having concentration a of 100 μg/ml of METO and OLME.

Methods

The standard solutions of METO (10 μg/ml) and OLME (10 μg/ml) were scanned separately in the UV range of 200–400 nm to determine the λ_{max} of both the drugs. The λ_{max} values of METO and OLME were found to be 221 nm and 257 nm, respectively. Five standard solutions having concentrations 5, 10, 15, 20, and 25 μg/ml for METO and 4, 8, 12, 16, and 20 μg/ml for OLME were prepared in distilled water using the solutions having a concentration of 100 μg/ml. The absorbance of resulting solutions was measured at 221 nm and 257 nm, and the calibration curves were plotted at these wavelengths. The absorptivity coefficients of these two drugs were determined using the calibration curve equations. The concentration of METO and OLME in the sample solution was determined by solving the respective simultaneous equations generated by using absorptivity coefficients and absorbance values of METO and OLME at these wavelengths.

Validation of the proposed method

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

Linearity (calibration curve)

The calibration curves were plotted over a concentration range of 5–30 μg/ml and 4–20 μg/ml for METO and OLME, respectively. Accurately measured standard solutions of METO (5, 10, 15, 20, and 25 ml) and OLME (4, 8, 12, 16, and 20 ml) were transferred to a series of 100 ml of volumetric flasks and diluted to the mark with distilled water. The absorbances of the solutions were measured at 221 and 257 nm against distilled water as blank. The calibration curves were constructed by plotting absorbances *versus* concentrations and the regression equations were calculated.

Method precision (repeatability)

The precision of the instrument was checked by repeated scanning and measurement of absorbance of solutions (n = 6) for METO and OLME (10 μg/ml for both METO and OLME) without changing the parameter of the proposed spectrophotometry method.

Intermediate precision (reproducibility)

The intra-day and inter-day precision of the proposed method was determined by analyzing the corresponding responses three times on the same day and on three different days three different concentrations of standard solutions of METO and OLME.

Accuracy (recovery study)

The accuracy of the method was determined by calculating recovery of METO and OLME by the

standard addition method. Known amounts of standard solutions of METO and OLME were added at 80, 100, and 120% level to prequantified sample solutions of METO and OLME (10 μg/ml for METO and 8 μg/ml for OLME). The amounts of METO and OLME were estimated by applying obtained values to the respective regression line equations. The experiment was repeated for five times.

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.

$$LOD = 3.3 \times \sigma/S$$

$$LOQ = 10 \times \sigma/S$$

where σ is the standard deviation of the response and S is the slope of the calibration curve.

Analysis of METO and OLME in a combined tablet dosage form

Ten tablets were weighed and powdered. The powder equivalent to 25 mg of METO and 20 mg of OLME was transferred into a 50 ml volumetric flask. Methanol (10 ml) was added to it and sonicated for 20min. The solution was filtered through Wattman filter paper No. 41, and the volume was adjusted up to the mark with distilled water. The above solution was suitably diluted with distilled water to get a final concentration of 10 μg/ml of METO and 8 μg/ml of OLME. The absorbances of the tablet sample solution, i.e. A1 and A2 were recorded at 221 nm and 257 nm and ratios of absorbance were calculated, i.e. A2/A1. Relative concentration of two drugs in the sample solution was calculated using respective simultaneous equations generated by using absorptivity coefficients and absorbance values of METO and OLME at these wavelengths.

RESULTS AND DISCUSSION

In this method, two wavelengths were used for the analysis of the drugs. Further, 221 nm (λ_{max} of METO) and 257 nm (λ_{max} of OLME) are the wavelengths at which calibration curves were prepared for both the drugs. The criteria for obtaining maximum precision[18] by this method were calculated and found to be outside the range 0.1–2. Once the absorptivity values are determined, very little time is required for analysis, as would require determination of absorbances of the sample solution at two selected wavelengths and few simple calculations. The standard solutions of METO and OLME were scanned separately in the UV range, and zero-order spectra for METO and OLME were recorded [Figure 1]. Maximum absorbance was obtained at 221 nm and 257 nm for METO and OLME, respectively. Linear correlation was obtained between absorbances and concentrations of METO and OLME in the concentration ranges of 5–25 μg/ml and 4–20 μg/ml for both drugs, respectively. The linearity of the calibration curve was validated by the high values of correlation coefficient of regression. LOD and LOQ values for METO were found to be 0.30 and 0.90 μg/ml and 2.22 and 6.74 μg/ml at 221 and 257 nm, respectively. LOD and LOQ values for OLME were found to be 0.16 and 0.47 μg/ml and 0.19 and 0.57 μg/ml at 221 and 257 nm, respectively. These data show that the method is sensitive for the determination of METO and OLME. All the regression analysis data and the summary of validation parameters for the proposed method are reported in Table 1. The recovery experiment was performed by the standard addition method. The mean recoveries were 100.90 ± 1.780 and 100.26 ± 0.721 for METO and

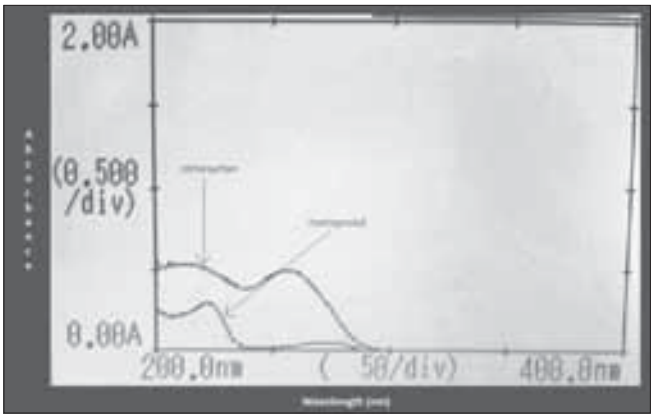

Figure 1: Overlay of metoprolol succinate and olmesartan medoxomil.

Table 1: Regression analysis data and summary of validation parameter of the calibration curves

Parameters	METO		OLME	
Wavelength (nm)	221	257	221	257
Beer's law limit (μg /ml)	5–25	5–25	4–20	4–20
Regression equation	y = 0.017x +	y = 0.0020x –	y = 0.038x +0.068	y = 0.035x – 0.020
($y = a + bc$)	0.050	0.0066	0.038	0.035
Slope (b)	0.017	0.0020	0.068	0.020
Intercept (a)	0.050	0.0066	0.999	0.9993
Correlation coefficient (r^2)	0.9991	0.9996	0.16	0.19
LOD (μg/ml)	0.30	2.22	0.47	0.57
LOQ (μg /ml)	0.90	6.74		

OLME, respectively, which indicates the accuracy of the proposed method [Table 2]. The proposed validated method was 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 3]. The relative standard deviation (RSD) values for assay of METO and OLME were found to be 1.37 and 0.81, respectively. The RSD was less than 2%, which indicates that the proposed method is repeatable [Table 4].

CONCLUSION

No interference of the excipients with the absorbance of interest appeared; hence the proposed method is applicable for the routine simultaneous estimation of METO and OLME in pharmaceutical tablet dosage forms.

The proposed spectrophotometric method was found to be simple, sensitive, accurate, and precise for simultaneous determination of METO and OLME in the tablet dosage form. The method utilizes easily available and low cost solvent like distilled water for analysis of METO and OLME. Hence, the method was also found to be economical for the estimation of METO and OLME from tablets.

Table 2: Results of the recovery studies

Level of recovery %	Amount of pure drug added (µg/ml)		Simultaneous equation method % recovery	
	METO	OLME	METO	OLME
80	8	6.4	98.91	100.02
100	10	8	102.34	101.07
120	12	9.6	101.45	99.69
Mean % recovery			100.90	100.26
SD			1.780	0.721
CV			1.760	0.719

SD = Standard deviation; CV = coefficient of variance

Table 3: Results of analysis of tablet formulation

Drugs	Simultaneous equation method, % ± SD (*n* = 6)
METO	99.62 ± 1.36
OLME	97.52 ± 0.79

n, Number of replicates

Table 4: Results of intermediate precisions

Day	% Label claim estimated (mean ± %RSD)	
	METO	OLME
Intra-day	99.23 ± 1.20	97.91 ± 1.05
Inter-day	99.01 ± 1.20	97.81 ± 0.72

ACKNOWLEDGMENTS

The authors are thankful to Alpha Laboratories, Baroda, Gujarat, India for providing gift samples of METO and OLME for research. The authors are highly thankful to APMC College of Pharmaceutical Education and Research, Himmatnagar, Gujarat, India, for providing all the facilities to carry out the work.

REFERENCES

1. Maryadele, O'Neil J. The Merck Index: An Encyclopedia of chemicals, drugs and biologicals. 14th ed. Whitehouse Station, New Jersey: Merck and Co., Inc.; 2006. p. 1060.
2. Sweetman S. The Martindale: The Complete Drug Reference. 35th ed. London, UK: Pharmaceutical Press; 2007. p. 1201.
3. Indian Pharmacopoeia. Vol. II. The Controller Publication. Govt of India. New Delhi; 2010. p. 1681.
4. British Pharmacopoeia. Vol. 2. London: The British Pharmacopoeia Commission; 2010. p. 1419.
5. The United State Pharmacopoeia. USP 28, NF 23. Rockville, MD: United State Pharmacopoeial Convention, Inc.; 2005. p.1279.
6. Badulescu M, Balalau D. UV-Vis Spectrophotometric Assay of metoprolol and Method Validation. Farmacia 2008;6:363-70.
7. Prasada Rao MM, Rahaman SA, Prasad YR, Reddy PG. RP-HPLC method of simultaneous estimation of amlodipine besylate and metoprolol in combined dosage form. Int J Pharm Res Dev 2010;2:69-76.
8. Aqil M, Ali A, Ahad A, Sultana Y, Najmi AK, Saha N. A validated HPLC method for estimation of metoprolol in human plasma. Acta Chromatogr 2007;19:130-40.
9. Sureshkumar K, Ravikumar R, Rajasekaran A, Ravichandran V. Simultaneous Spectrophotometric determination of metoprolol tartarate and ramipril. Digest J Nano Bio 2010;5:173-6.
10. Rao MM, Rahaman SA, Prasad YR, Reddy PG. RP-HPLC method of simultaneous estimation of amlodipine besylate and metoprolol in combined dosage form. Int J Pharm Res Dev 2010;2:69-76.
11. Maryadele, O'Neil J. The Merck Index: An Encyclopedia of chemicals, drugs and biologicals. 14th ed. Whitehouse Station, New Jersey: Merck and Co., Inc.; 2006. p. 1178.
12. Sweetman SC. The Martindale: The Complete Drug Reference. 35th ed. London, UK: Pharmaceutical Press; 2007. p. 1224.
13. Dhabale PN, Bhagade SR. Simultaneous UV spectrophotometric methods for estimation of amlodipine besilate and olmesartan medoxomil in tablet dosage form. J Chem Pharm Res 2011;3:650-6.
14. Wankhede SB, Wadkar SB, Raka KC, Chitlange SS. Simultaneous estimation of amlodipine besylate and olmesartan medoxomil in pharmaceutical dosage form. Indian J Pharm Sci 2009;71:563-7.
15. Patil PS, More HN, Pishwikar SA. RP HPLC method for simultaneous estimation of amlodipine besylate and olmesartan medoxomil from tablet. Indian J Pharm Sci 2011;3:146-9.
16. Vacchani KH, Patel SA. Development and validation of spectrophotometric method for simultaneous estimation of metoprolol succinate and olmesartan proxetil in tablet. J Appl Pharm Sci 2011;1:112-5.
17. ICH, Q2 (R1) Validation of Analytical Procedure: Text and Methodology, International Conference on Harmonization, Geneva, Switzerland; 2005.
18. Beckett AH, Stenlake JB. Practice Pharmaceutical Chemistry. 4th ed, Part II. New Delhi: CBS Publisher; 1997. p. 285-8.

How to cite this article: Vora BN, Parmar RR, Nayak PP, Shah DA. Development and validation of the simultaneous UV spectrophotometric method for estimation of metoprolol succinate and olmesartan medoxomil in the tablet dosage form. Pharm Methods 2012;3:44-7.
Source of Support: Nil, **Conflict of Interest:** None declared.