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Simultaneous estimation of Olmesartan Medoximil and Metaprolol Tartarate by RP-HPLC method

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ABSTRACT

A simple, specific, accurate, and precise RP-HPLC method was developed and validated for the estimation of Olmesartan Medoximil, Metaprolol Tartarate in bulk drug and pharmaceutical dosage forms. A Xterra C18 column having 150 mm x 4.6 mm, 5 µm in isocratic mode, with mobile phase containing Phosphate buffer (pH 2.8 with Ortho phosphoric acid) : Acetonitrile [35 : 65, v / v] was used. The flow rate was 0.5 ml / min and effluents were monitored at 284 nm. Chromatogram showed peak at a retention time of 3.654 ± 0.008 min for Olmesartan Medoximil and 5.167 ± 0.008 min for Metaprolol Tartarate. The method was validated for system suitability, linearity, precision, accuracy, specificity, ruggedness, robustness, LOD and LOQ. Recovery of Olmesartan Medoximil, Metaprolol Tartarate was found to be in the range of 99.22 - 100.11 % and showing linearity in the range of 10-50 µg / ml. The LOD and LOQ for estimation of Olmesartan Medoximil and Metaprolol Tartarate were found to be 0.003 µg / ml, 0.09 µg / ml, and 0.012µg / ml , 0.3 µg / ml respectively. Proposed method can be successfully applied for the quantitative determination of Olmesartan Medoximil and Metaprolol Tartarate in bulk drug and pharmaceutical dosage forms.

Keywords: Olmesartan Medoximil, Metaprolol Tartarate, RP-HPLC, Xterra.

INTRODUCTION

[1]-[4] Olmesartan Medoxomil (OM) is chemically (5-methyl-2-oxo-2H-1, 3-dioxol-4-yl)methyl4-(2-hydroxy propan-2-yl)-2-propyl-1-({4-[2-(2H-1,2,3,4-tetrazol-5yl) phenyl]phenyl}methyl)-1Himidazole-5-carboxylate, is angiotensin II receptor antagonist used for the treatment of hypertension. Olmesartan Medoxomil is not official in any pharmacopiea.

Metaprolol Tartarate (MT) is chemically (RS) -1-(Isopropyl amino)-3-[4-(2-methoxyethyl) Phenoxy] propan-2-ol tartarate, is a cardio selective β-blocker, used in the treatment of hypertension, angina pectoris, arrhythmia, myocardial infarction and heart failure. IP, BP and USP describe potentiometric method for its estimation.

[5]-[7] The combined dosage forms of Olmesartan Medoxomil and Metaprolol Tartarate are available in the market for the treatment of hypertension. Literature survey reveals that simple spectroscopic methods, HPTLC, LC-forced degradation studies are available for determination of MT and OM either individually or in combination with other drugs. But there is no single method for simultaneous estimation of Olmesartan Medoximil and Metaprolol Tartarate by RP-HPLC method. Hence there is a need to develop a new method and to extend it for quantitative determination. The present manuscript describes simple, sensitive, accurate, precise, rapid and economic RP-HPLC method for the simultaneous estimation of Olmesartan Medoxomil and Metaprolol Tartarate in pharmaceutical tablet dosage forms.

MATERIALS AND METHODS

Olmesartan Medoximil and Metaprolol Tartarate were obtained from Ranbaxy pharmaceuticals. Tablets containing 0.02 gm of Olmesartan Medoximiland 0.05 gm of Metaprolol Tartarate were used. The HPLC grade acetonitrile was obtained from Qualigens Fine Chemicals Ltd., Mumbai and Water obtained from Thomas Baker Chemicals Ltd., Mumbai. [8-12]

Preparation of Mobile phase

The HPLC grade Acetonitrile was mixed with Phosphate buffer of pH 2.8 (pH adjusted with orthophosphoric acid) in the ratio 65: 35 and degassed in ultrasonic water bath for about 5 minutes and filtered through 0.45 µ filter under vacuum filtration.

Preparation of standard solution

0.01 gm of Olmesartan Medoximil and 0.01 gm of Metaprolol Tartarate working standards were accurately weighed and transferred into a 100ml clean dry volumetric flask and about 70ml of diluent was added and sonicated until it was dissolved completely and the volume was made up to the mark with the same solvent (stock solution). Further 1.2ml of Olmesartan Medoximil and 3ml of Metaprolol Tartarate was pippeted from the above stock solution into a 10ml volumetric flask and diluted up to the mark with diluent.

Sample preparation

10 Tablets of Olmesartan Medoximil and Metaprolol Tartarate were weighed and powdered in glass mortar. The powder equivalent to the amount of active ingredient present in 10 tablets (0.1568 gm) was transferred into a 100 ml clean dry volumetric flask, 70 ml of diluent was added to it and was shaken by mechanical stirrer and sonicated for about 30 minutes by shaking at intervals of five minutes each and was diluted up to the mark with diluent and allowed to stand until the residue settles before taking an aliquot for further dilution (stock solution). 0.6ml of upper clear solution was transferred to a 10 ml volumetric flask and diluted with diluent up to the mark and the solution was filtered through 0.45 µm filter before injecting into HPLC system.

Selection of wavelength

100µg/mL solution of Olmesartan Medoximil and 100µg/mL solution Metaprolol Tartarate was prepared using methanol as solvent. The above mentioned solutions were scanned individually from 190 to 400 nm in UV-Visible spectrophotometer. The optimal response for the overlain spectrum of Olmesartan Medoximil and Metaprolol Tartarate was obtained at 284 nm. Hence the complete method was processed at the wavelength of 284nm.

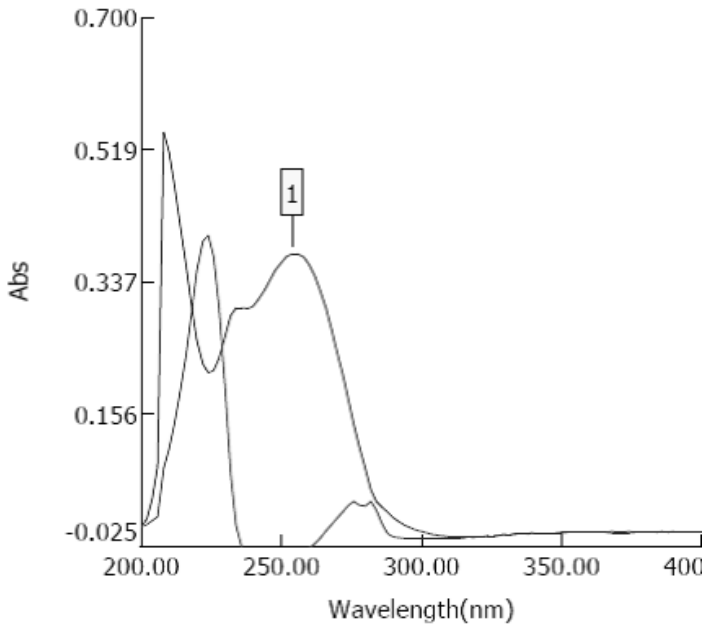

Fig.No.1: Overlain UVspectrum of Olmesartan and Metaprolol

RESULTS AND DISCUSSION

A new reverse-phase, isocratic, liquid chromatographic method with UV detection at 284 nm was developed for the quantitative determination of Olmesartan Medoximil and Metaprolol Tartarate in pharmaceutical dosage forms. The chromatographic method was performed on Xterra C18 column (150mm x 4.6mm, 5µm) with an isocratic mobile phase of Phosphate buffer (pH 2.8 with Ortho phosphoric acid) : Acetonitrile[35 : 65, v / v] with a flow rate of 0.5 ml/min was used. The resulting chromatogram exhibited a retention time of 3.654 ± 0.008 min for Olmesartan Medoximil and 5.167 ± 0.008 min for Metaprolol Tartarate. The above method was optimized with a view to develop an assay method for Olmesartan Medoximil and Metaprolol Tartarate.

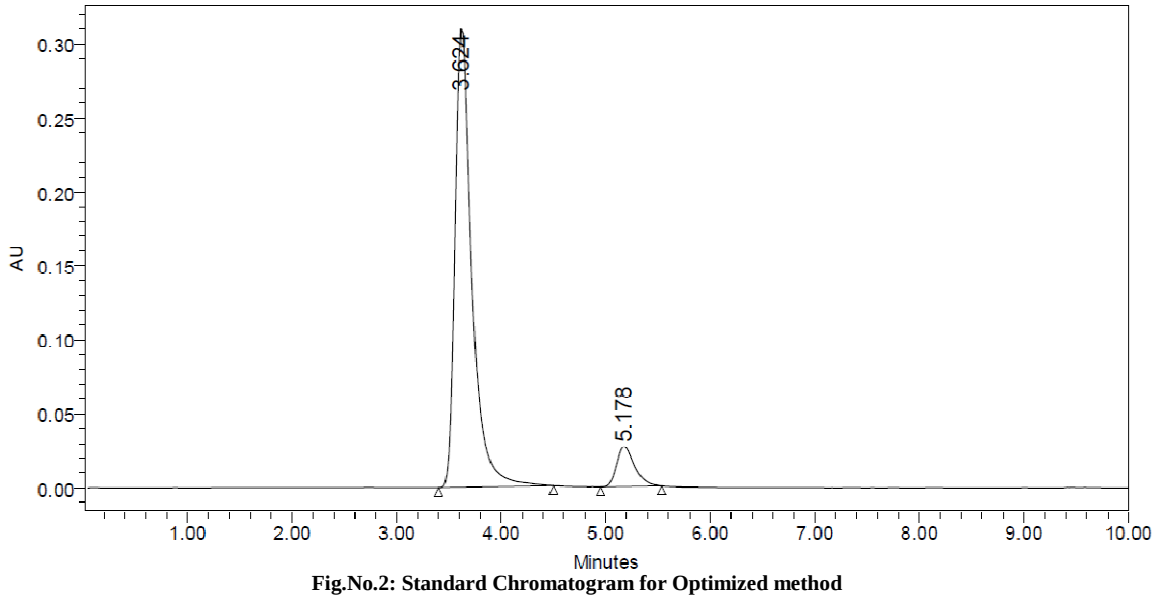

Fig.No.2: Standard Chromatogram for Optimized method

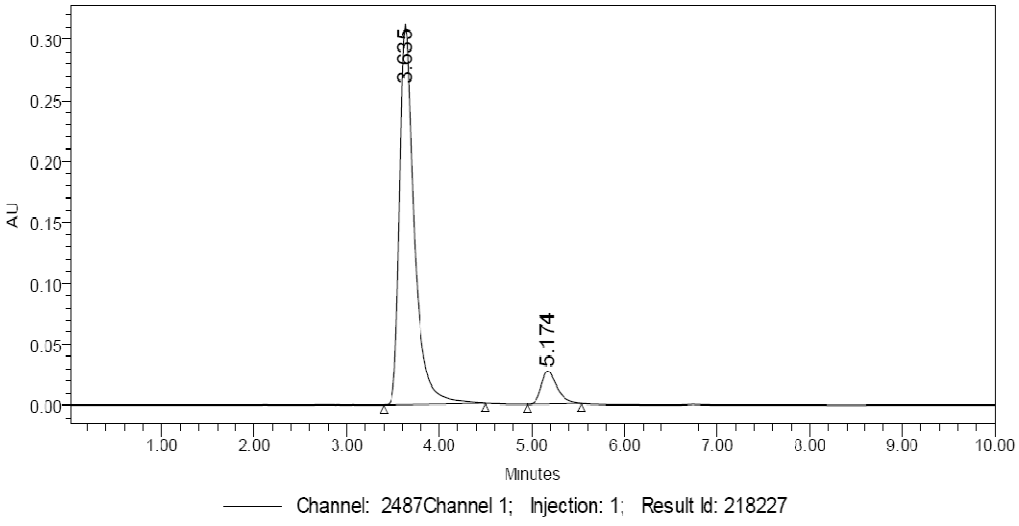

Fig.No.3: Sample Chromatogram for Optimized method

Validation of the method

The accuracy of a method was determined by recovery experiments. A known quantity of the pure drug was added to the pre-analysed sample formulation as 50%,100% and 150% levels. The recovery studies were carried out 3 times of each level and the percentage recovery and mean of the percentage recovery were calculated. From the data obtained, it was observed that the recoveries of standard drugs were found to be accurate and within the specified limits. The precision of the method was determined by repeatability and intermediate precision. The area of drug

peaks and percentage relative standard deviation were calculated. The results revealed that the developed method was found to be reproducible in nature. The standard drug solutions in varying concentrations ranging from 50-150% of the targeted level of the assay concentration were examined by the assay procedure. Olmesartan Medoximil and Metaprolol Tartarate were found to be linear in the range of 10-150µg/ml.

The slope, intercept and correlation coefficient values were also calculated. The correlation coefficient of Olmesartan Medoximil and Metaprolol Tartarate was found to be 0.995 and 0.997 respectively. The calibration curves were plotted as peak area Vs concentration of the standard solutions. The calibration graph shows that linear response was obtained over the range of concentrations used in the assay procedure. These data demonstrates that the methods have adequate sensitivity over the concentration of the analytes. The range demonstrates that the method is linear outside the limits of expected use. The LOD and LOQ of the developed method were determined by analyzing progressively low concentration of the standard solutions using the developed methods. The LOD is the smallest concentration of the analyte that gives a measurable response (signal to noise ratio of 3.3). LOD of Olmesartan Medoximil and Metaprolol Tartarate were found to be 0.003 µg / ml, 0.09 µg / ml respectively. The LOQ is the smallest concentration of the analyte, which gives response that can be accurately quantified (signal to noise ratio of 10). The LOQ of Olmesartan Medoximil and Metaprolol Tartarate were found to be 0.012µg / ml, 0.3 µg / ml respectively. The system suitability studies were performed for the standard solutions. The values obtained demonstrated the suitability of the system for the analysis of the above drug combination. From the above experimental data results and parameters it was concluded that the developed RP-HPLC method is simple, economical, rapid, precise and accurate. Hence these methods can be used for routine analysis of Olmesartan Medoximil and Metaprolol Tartarate in combined tablet dosage forms.

Table no.1: Validation Parameters

Parameters	Olmesartan	Metaprolol
Accuracy	%Recovery 99..4%	%Recovery 99.13%
System Precision	%RSD 1.3	%RSD 1.3
Method Precision	%RSD 0.46	%RSD 0.45
Linearity	r^2=0.999	r^2=0.999
Range	60-100mg/ml	96-160mg/ml
LOD	2.96	3.0
LOQ	9.96	10.0

CONCLUSION

The method was validated for system suitability, linearity, precision, accuracy, specificity, ruggedness, robustness, LOD and LOQ. As there was no interference due to excipients and mobile phase, the method was found to be specific. The method was robust and rugged as observed from insignificant variation in the results of analysis by changes in flow rate and mobile phase composition separately and analysis being performed by different analysts. Good agreement was seen in the assay results of pharmaceutical formulation by developed method. Hence it can be concluded that the proposed method was a good approach for obtaining reliable results and found to be suitable for the routine analysis of Olmesartan Medoximil and Metaprolol Tartarate in bulk drug and pharmaceutical dosage formulations.

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