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Development of RP-HPLC method for estimation of Olmesartan Medoxomil in tablet dosage forms

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ABSTRACT

Reversed phase high performance liquid chromatographic method was developed and validated for the estimation of Olmesartan medoxomil in bulk and formulation. Selected mobile phase was a combination of phosphate buffer with pH adjusted at 2.8 and acetonitrile (35:65% v/v) and wavelength selected was 250 nm. Retention time of Olmesartan medoxomil was 2.591 min. Linearity of the method was found to be 50-150 µg/ml, with the regression coefficient of 0.9993. Quantification was done by calculating area of the peak and the detection limit and quantitation limit ware 0.02µg/mL and 0.09µg/mL, respectively. There was no significant difference in the intraday and inter day analysis of Olmesartan medoxomil determined for three different concentrations using this method. Present method can be applied for the determination of Olmesartan medoxomil in quality control of formulation without interference of the excipients.

Key words: Olmesartan medoxomil, Reverse phase, HPLC and Tablets.

INTRODUCTION

Olmesartan medoxomil (OMX) is described chemically as the (5-methyl-2-oxo-1,3-dioxol-4-yl) methyl ester of 4-(1-hydroxy-1-methylethyl) -2-propyl-1-{[20-(1H-tetrazol-5-yl)[1,10-biphenyl]-4-yl]methyl}-1H-imidazole-5-carboxylic acid. It is a pro-drug and hydrolyzed to olmesartan during absorption from the gastrointestinal tract. OML is a selective AT1 subtype angiotensin II receptor antagonist [1-4]. Olmesartan medoxomil is not official in any pharmacopoeia. Various analytical methods have been reported in scientific literature for the analysis of OMX alone or in combination with other drugs in pharmaceutical formulations and/or biological fluids including LC-MS-MS [5, 6], HPTLC [7, 8], Spectrophotometry [9] and HPLC [10-12]. Thus, the aim of this study was to develop and validated a fast, simple and cost-effective HPLC method for analysis of OMX from pharmaceutical formulations.

MATERIALS AND METHODS

Materials

A sample of OML, assigned purity 99.72% of pharmaceutical grade was received from Aurobindo Pharma Ltd, Hyderabad, India. OML tablets of strength 20 mg OLMY (Cadila Pharmaceutical Ltd., India) were procured from the local market. HPLC grade acetonitrile were purchased from Merck (Mumbai, India). High purity water was prepared by Millipore milli Q plus purification system. Other solvents and chemicals of analytical grade were purchased from Qualigens (Mumbai, India).

Instrumentation and Chromatographic conditions

The chromatograph system comprised of a Water 2695 binary gradient pump, an inbuilt auto sampler, a column oven and Water 2487 dual wavelength absorbance detector (DAD) was employed throughout the analysis. The data was acquired using Empower-2 software. The column used was XTerra symmetry C_{18} (150×4.6 mm, 3.5µm). The mobile phase consisted of a mixture of phosphate buffer with pH adjusted at 2.8 and acetonitrile (35:65% v/v). The flow rate was set at 0.8 mL/min and a 20µL aliquot was injected into the HPLC column. The eluent was monitored at 250 nm and these conditions the retention time observed for OML was 2.591min.

Standard solutions

The OML was weighed and dissolved in mobile phase at room temperature to obtain a stock solution of 1000µg/mL. Serial dilutions of the stock solution were made for spiking the calibration standards. The calibration curve for OML was prepared at six concentrations range from 50-150 µg/mL.

Sample preparation

To determine the content of OML, twenty tablets were weighed and transferred into a clean and dry motor. Then crushed and mixed well to prepare homogenous mixture. A sample equivalent to 20mg of OML was taken in 50 mL volumetric flask with aid of 25 mL mobile phase and sonicated for 15 min. Then the solution was finally made up to mark with mobile phase. The resulting solution was centrifuged at 3000 rpm/min for 10 mins to get a clear solution. Then supernatant solution was used to get final concentration of 100µg/mL with mobile phase.

Method Validation [13]

The method was validated for linearity, limit of detection (LOD), and quantification (LOQ), system suitability, precision, accuracy, specificity, and robustness in accordance with the ICH guidelines.

RESULTS AND DISCUSSION

The chromatographic conditions were optimized to develop a stability indicating assay method for OML in tablet dosage forms. The basic chromatographic conditions were designed to be simple and reproduce, and were selected after testing the different conditions that affect HPLC analysis, for example column, aqueous and organic components of the mobile phase, proportion of mobile phase components, detection wavelength, diluents and concentration of analyte. The proportion of the mobile phase components was optimized to reduce retention time and enable

good resolution of OML from the degradation products. A detection wavelength of 250 nm was selected. Detection at 250 nm resulted in good response and good linearity (Fig 1).

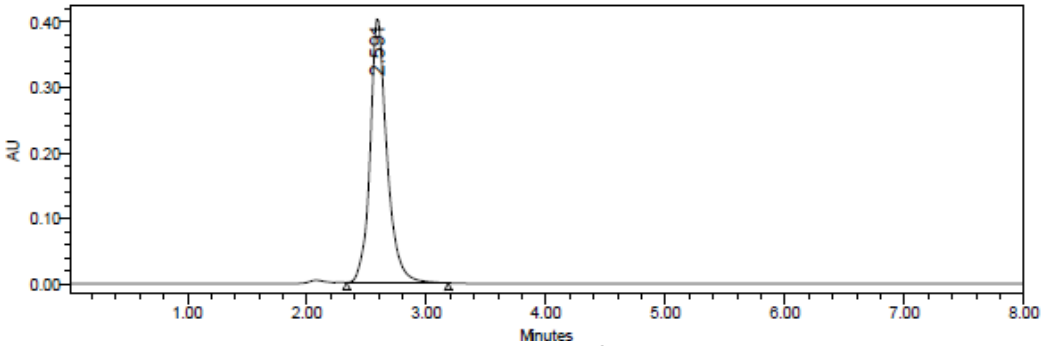

Figure 1: A typical chromatogram of olmesartan medoxomil

The calibration curve was prepared by plotting the peak area of OML against drug concentration (µg/mL) and was linear in the range of 50-150 µg/mL. The data were subjected to least-square linear regression analysis to calculate the calibration equation and correlation coefficient. The regression equation was found as Y=38832X+223152 (r^2 = 0.9993). The results show that there is an excellent correlation between the peak area and the concentration of OML in the range tested. The limit of detection, with a signal to noise ratio of 3:1, was found to be 0.02µg/mL. The limit of quantitation, with a signal to noise ratio of 10:1, was found to be 0.09µg/mL. Results from the linear regression analysis with system suitability data were listed in Table 1.

Table1. Results from regression analysis and system suitability of OML

Parameters	Results
Retention time (min)	2.591
Linear range (µg/mL)	50-150
Limit of detection (µg/mL)	0.02
Limit of quantification (µg/mL)	0.09
Regression line	Y=38832X+223152
Correlation coefficient (r)	0.9993
Theoretical plates	4562
Tailing factor	1.15

The results of intra-day and inter-day precision studies were shown in Table 2. They revealed that % RSD values for intra-day studies ranged between 0.76-1.31% and for inter-day precision between 0.38-1.27percent, which are within the permissible limits of 2.0%. To examine the accuracy of the method, recovery studies were carried out by standard addition method. The results were shown in Table 2. The average percent recoveries obtained as 100.11-100.27%, indicating that the method was accurate.

Table2. Results of recovery studies and precision

Actual Conc. (µg/mL)	% Recovery		Precision			
	Mean±SD	%RSD	Intra-day		Inter-day	
			*Mean±SD	%RSD	*Mean±SD	%RSD
75	100.2±1.1604	1.16	99.72±1.3094	1.31	100.17±1.2752	1.27
100	100.11±1.0476	1.05	100.21±0.7477	0.75	99.5±0.7167	0.72
125	100.27±0.8875	0.89	99.89±0.7605	0.76	100.65±0.3873	0.38

**Concentration (µg/mL)*

The robustness of the method was assessed by assaying test solutions under different analytical conditions deliberately changed from the original conditions. For each different analytical condition the standard solution and test solution were prepared separately. The result obtained from assay of the test solution was not affected by varying the conditions and was in accordance with the true value. System suitability data were also found to be satisfactory during variation of the analytical conditions. The analytical method therefore remained unaffected by slight but deliberate changes in the analytical conditions. During study of the stability of stored solutions of standards and test preparations for assay determination the solutions were found to be stable for up to 48 h. Before each measurement of validation data a system suitability test was performed by measurement of general characteristics such as peak asymmetry, number of theoretical plates and RSD (%) of peak area observed for a standard solution. The values obtained were satisfactory and in accordance with in-house limits.

The proposed method was applied to the analysis of marketed product and the results obtained were given in Table 3. The blank solution was prepared containing the components indicated in tablets except active principle. No interference was observed from the tablet excipients. The results were indicated that the method is suitable for routine analysis of OML in pharmaceutical dosage forms.

Table 3: Analysis of Olmesartan medoxomil in tablets

Tablet Formulation	Label Claim per Tablet (mg)	% Drug found ± SD (n=6)	RSD (%)	SEM
OLMY	20	100.14±0.7456	0.7446	0.3044

CONCLUSION

The results of this study showed that the developed method is simple, cost-effective, precise and accurate. These advantages encourage the application of this method in routine analysis olmesartan medoxomil in pharmaceutical formulations.

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