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Sensitive estimation of olmesartan medoxomil tablets by RP-HPLC method

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Abstract

A simple, selective, rapid, precise and economical reverse phase high pressure liquid chromatographic method has been developed for the estimation of Olmesartan medoxomil from pharmaceutical Tablet dosage form. The method was carried out on a C_{18} (250 mm x 4.6 mm i.d., 5 µ) column with a mobile phase consisting of acetonitrile: 5 mM ammonium acetate (adjusted to pH 4.5 using orthophosphoric acid) (60:40 v/v) at a flow rate of 1.0 ml/min. Detection was carried out at 255 nm. The retention time of Olmesartan medoxomil was 4.9 min. The developed method was validated in terms of accuracy, precision, linearity, limit of detection, limit of quantitation and solution stability.The proposed method can be used for the estimation of these drugs in dosage forms.

Key-Words: Olmesartan medoxomil, Method development and validation, Tablet estimation

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. Only limited methods have been described in the literature for the determination of Olmesartan medoxomilin HPLC, Spectroscopy, biological matrices and LC-MS [5-16]. However, there is no sensitive high performance liquid chromatographic method (HPLC) reported for Olmesartan medoxomilin single dosage form. The present RP-HPLC method was validated following the ICH guidelines (17).

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Material and Methods

Reagents and chemicals

Acetonitrile HPLC grade was procured from Merck KGaA, Germany. Ammonium acetate AR grade were procured from SYSTEMRM, Selangor, Malaysia. Water HPLC grade was obtained from a Milli-QRO water purification system. Reference standards of Olmesartan was received from Aurobindo Pharma Ltd, Hyderabad, India.

Apparatus

HPLC chromatographic separation was performed on a Shimadzu liquid chromatographic system equipped with a LC-20AD solvent delivery system (pump), SPD-20A photo diode array detector, and SIL-20ACHT injector with 50µL loop volume. LC solution version 1.25 was applied for data collecting and processing (Shimadzu, Japan).

Preparation of standard solutions

Standard stock solutions of 1.0 mg/ml Olmesartan medoxomil was prepared separately using a mixture of water and acetonitrile (1:1 v/v). From the standard stock solution, standard solution was prepared to contain 10.0 µg/ml of Olmesartan medoxomil.

Preparation of sample solutions

Twenty tablets, each containing 20.0 mg of Olmesartan medoxomil were weighed and finely powdered; a quantity of powder equivalent to 20.0 mg of Olmesartan medoxomil was weighed and transferred to

a 50 mL volumetric flask with aid of 25 ml mixture solution and sonicated for 15 min. Then the solution was finally made up to mark with mixture solution. The resulting solution was centrifuged at 4000 rpm/min for 7 mins to get a clear solution. Then supernatant solution was used to get final concentration of 100µg/ml.

Assay method

With the optimized chromatographic conditions, a steady baseline was recorded, the mixed standard solution was injected and the chromatogram was recorded. The retention time of Olmesartan medoxomil was found to be 4.9. This procedure was repeated for the sample solution obtained from the formulation. The response factor (peak area ratio of standard peak area and internal standard peak area) of the standard solution and sample solution were calculated. The concentration of the drugs was calculated using following formula:

Concentration of drugs = (Response of the sample/ Response of the standard) x Concentration of standard

Results and Discussion

Estimation of Olmesartan medoxomilin dosage forms

The chromatographic conditions were optimized to develop an assay method for OLM 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. The proportion of the mobile phase components was optimized to reduce run time. The typical chromatogram was presented in Figure 1.

Method validation

Accuracy and precision

The accuracy of the method was determined by recovery experiments. The recovery studies were carried out six times and the percentage recovery and standard deviation of the percentage recovery were calculated and presented in Table 1. From the data obtained, added recoveries of standard drugs were found to be accurate.

The precision of the method was demonstrated by inter day and intra day variation studies. In the intra day studies, six repeated injections of standard and sample solutions were made and the response factor of drug peaks and % CV were calculated and presented in Table 2. In the inter day variation studies, six repeated injections of standard and sample solutions were made for three consecutive days and response factor of drug peaks and percentage % CV were calculated and presented in Table 2. From the data obtained, the developed RP-HPLC method was found to be precise.

Linearity and Range

The linearity of the method was determined at five concentration levels ranging from 10.0 to 80.0 ng/ml for Olmesartan medoxomil. The calibration curve was constructed by plotting response factor against concentration of drugs. The slope and intercept value for calibration curve was $y=8475\times+137.8$ ($R^2=0.999$) for Olmesartan. The results show that an excellent correlation exists between response factor and concentration of drugs within the concentration range indicated above. The calibration curves are shown in Figure. 2.

Limit of Detection and Limit of Quantification

The Limit of Detection (LOD) and Limit of Quantification (LOQ) of the developed method were determined by injecting progressively low concentrations of the standard solutions using the developed RP-HPLC method. The LOD is the smallest concentration of the analyte that gives a measurable response (signal to noise ratio of 3). The LOD for Olmesartan medoxomil was found to be 2 ng/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 was 9 ng/ml Olmesartan, respectively (Table 3).

Solution stability

In order to demonstrate the stability of both standard and sample solutions during analysis, both solutions were analyzed over a period of 5 h at room temperature. The results show that for both solutions, the retention time and peak area of Olmesartan medoxomil remained almost unchanged and no significant degradation within the indicated period, thus indicated that both solutions were stable for at least 5 h, which was sufficient to complete the whole analytical process.

System suitability studies

The column efficiency, resolution and peak asymmetry were calculated for the standard solutions (Table 3). The values obtained demonstrated the suitability of the system for the analysis of this drug combination and the system suitability parameters fall within ± 3 % standard deviation range during routine performance of the method.

Conclusion

In conclusion, the developed method for the estimation of olmesartan is accurate, precise, selective and linear and it can be applicable for the further research ex. pharmacokinetic and Pharmacodynamic studies. The simplicity of the method allows for application in laboratories that lack sophisticated analytical instruments such as LC–MS/MS or GC–MS/MS that

are complicated, costly and time consuming rather than a simple HPLC–UV method. These advantages encourage the application of this method in routine analysis olmesartan medoxomil in pharmaceutical formulations.

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Table 1: Results of analysis of formulation and recovery studies

Drug	Amount mg/ tablet		Amount mg/ tablet	% Recovery*
	Labelled	Found *		
Olmesartan medoxomil	20.0	19.89 ± 1.02	99.210 ± 1.08	99.23 ± 1.41

Table 2: Intraday and interday precision studies of Olmesartan

	Intraday studies (ng/ml)			Interday studies (ng/ml)		
	10	**40**	**80**	**10**	**40**	**80**
Mean	8.8811	39.2903	79.5570	8.8911	39.0903	79.1570
SD	0.13	0.33	0.58	0.09	0.69	0.86
%CV	1.51	0.85	0.73	1.03	1.77	1.08
%Accuracy	88.8	98.2	99.44	88.91	97.72	98.94

Table 3: System suitability studies

S/No.	Parameters	Nebivolol
1.	Theoretical plate/meter	4528
2.	Asymmetric factor	0.89
3.	LOD (ng/ml)	2
4.	LOQ (ng/ml)	9

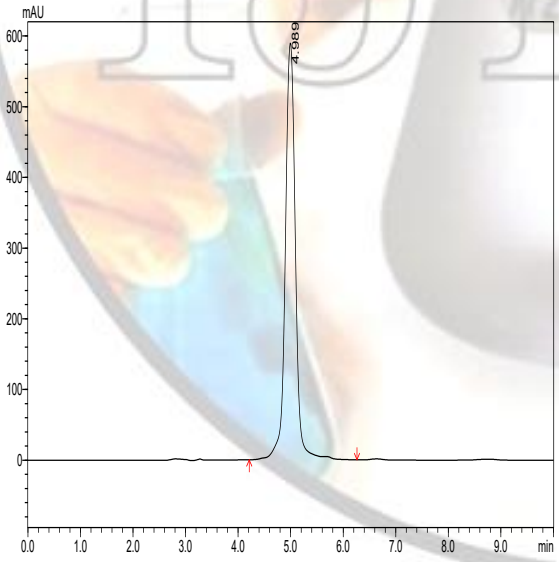

Fig. 1: Typical Chromatogram of Sample Solution

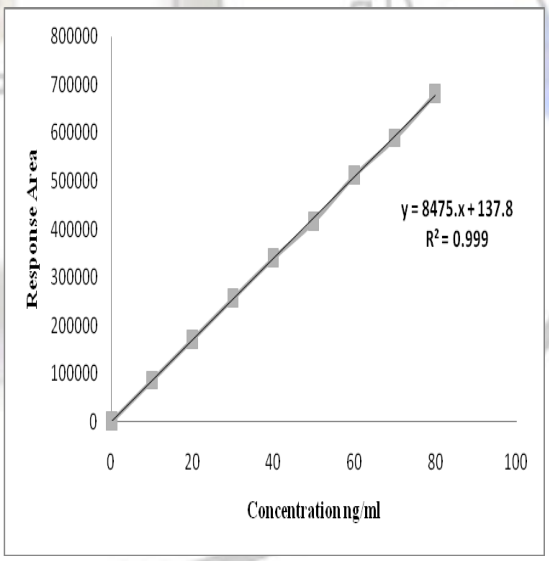

Fig. 2: Calibration Curve of Olmesartan