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New RP-HPLC Method for The Determination of Olmesartan Medoxomil in Tablet Dosage Form

Raveendra B.Ganduri[b*], Ramprasad A.Lanka[a], Srinivasu Pamidi[a], Jayachandra R.Peddareddigari[b] and Mustafa Mohammed[b]

[a.] Analytical R&D, Hetero Drugs LTD, Hyderabad, Andhara Pradesh, India.
[b] HITS College of Pharmacy, Bogaram (V), Hyderabad, Andhara Pradesh, India.

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Abstract

A simple rapid, sensitive, accurate, precise and reproducible high performance liquid chromatographic method has been developed to assay Olmesartan medoxomil in tablet dosage form. The HPLC analysis used a reversed phase Hypersil BDS C_8 (250X4.6mm, 5µm) column and a mobile phase constituted of buffer and acetonitrile (55:45 % v/v). The buffer is composed of 3 g of sodium perchlorate and 3 mL of tri ethyl amine in 1000 mL of water and the pH of the solution was adjusted to 3.0 with orthophosphoric acid. The wave length of the detection is 250 nm. The validation data showed that the assay is sensitive, specific and reproducible for the determination of olmesartan in the dosage form. The method is linear from 10 µg mL^{-1} to 120 µg mL^{-1}. The accuracy of the method was found to be 99.54%. Mean inter and intraday assay relative standard deviation (RSD) were less than 1.0%. The proposed method provided an accurate and precise analysis of olmesartan in its pharmaceutical dosage form.

Keywords:

Olmesartan medoxomil; antihypertensive; reversed-phase; validation

1. Introduction

Olmesartan is chemically (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl-4-(1-hydroxy-1methylethyl)-2-propyl-1-[4-[2-(tetrazole-5-yl)phenyl]methylimidazole-5-carboxylate. As a selective and competitive, nonpeptide angiotensin II receptor antagonist, olmesartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II [1-4].

A thorough literature has revealed that several methods were reported for the estimation of olmesartan in biological fluids [5-8].The techniques used include HPLC with mass [5-7], flourimetric [8] detections. The use of LC hyphenated techniques for identification of degradation products in stressed tablets of olmesartan was published in [9].Shinde et al have reported the stability indicating LC method for the determination of olmesartan in bulk drug and in pharmaceutical dosage form [10].Lisiane Bajerski et al developed a stability indicating LC determination of olmesartan medoxomil in tablets [11].Determination of olmesartan medoxomil in tablets by UV-Vis spectrophotometry was published in [12]. Piyush Trivedi et al reported a stability-indicating assay method for estimation of olmesartan medoxomil and its metabolite [13].

* **Corresponding Author**
E-mail: raveendra.ganduri@gmail.com
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Patel CV et al described validated absorption factor spectrophotometric and Reverse-phase High Performance Liquid Chromatography methods for the determination of Ramipril and olmesartan medoxomil in pharmaceutical formulations [14]. The objective of the proposed study was to assay olmesartan in its dosage form. We report the development and validation of a simple HPLC assay with UV detection for the quantitative determination of olmesartan in tablet dosage form.

2. Experimental

2.1 Chemicals and reagents

All the reagents were of analytical-reagent grade unless stated otherwise. Glass-distilled and de-ionized water (Nanopure, Barnsted, USA), HPLC-grade acetonitrile, Sodium per chlorate, diethyl amine and orthophosphoric acid (S.D. Fine Chem., Mumbai, India) were used.

2.2 Instrumentation

The HPLC system was composed of 2695 water alliance system fitted with 2996 PDA detector with empower software. Analytical column used for this method is Hypersil BDS C_8 (250 mm x 4.6 mm) 5µm (Thermo Electron Corporation, Runcorn, UK).

2.3 Buffer preparation

Buffer solution was prepared by dissolving 3 gm of sodium perchlorate and 3 mL of triethyl amine in sufficient quantity of water and made up the volume to 100 mL (pH adjusted to 3.0 with ortho-phosphoric acid).

2.4 Standard Preparation

Olmesartan medoxomil reference substance was accurately weighed (40 mg) and dissolved in a 20 mL quantity of acetonitrile: water (50:50) in a 100 mL volumetric flask and dilute up to the mark and it was further diluted to generate a concentration of 40 µg mL^{-1}.

2.5 Sample Preparation

Twenty tablets of olmesartan (40 mg of olmesartan) were separately weighed and grounded to fine powder. An amount equivalent to 80mg of olmesartan was transferred into a 100 mL volumetric flask and dissolved in 60 mL quantity of methanol: water (50:50) and made up volume to 100mL. Further dilutions were made to generate a concentration of 40 µg mL^{-1}.

2.6 Chromatographic conditions

Before the mobile phase was delivered into the system, buffer and acetonitrile were filtered through 0.45 µm, PVDF membrane filter and degassed using vacuum. The chromatographic conditions used for the analysis were given below.

Column	Hypersil BDS C_8 (250 mm x 4.6 mm) 5µm
Wavelength	250 nm
Injection volume	10 µl
Flow rate	1.0 mL min^{-1}
Column temperature	25^0C
Run time	15 min

2.6 Method validation

Method validation was conducted according to published guidelines [15-16]. Assay performance was evaluated by intraday and inter day (two different days) precision and determined from replicate analysis of samples (40 µg mL^{-1}) in two analytical runs. Analysis of six different sample solutions was performed in the same day for intraday precision. Accuracy of the method was tested by adding a known amount of olmesartan standard (40, 80 and 120 µg mL^{-1}) in three sample solutions. The precision and accuracy were expressed in terms of RSD from mean intra and inter day assays and recovery of the theoretical concentration.

Robustness was tested by analysis of variations in analytical condition. Influence of mobile phase composition and different column brands were evaluated. The chromatographic parameters monitored were peak retention time, tailing factor and theoretical plate number.

3. Results and discussion

Changes in the analytical procedure were tested. Different mobile phases with different proportions of organic modifier (acetonitrile) were tried. The pH value of the mobile phase was checked over a wide range (2.8-3.2). The pH of the aqueous phase was adjusted with orthophosphoricacid. Chromatographic run was evaluated using Hypersil BDS C_8 column.

After selecting the best conditions based on peak performance, the run time of the proposed assay was 15 min with isocratic elution. During injection of a standard and sample solution, the retention times were 6.954 and 6.966 min respectively (Fig.1).

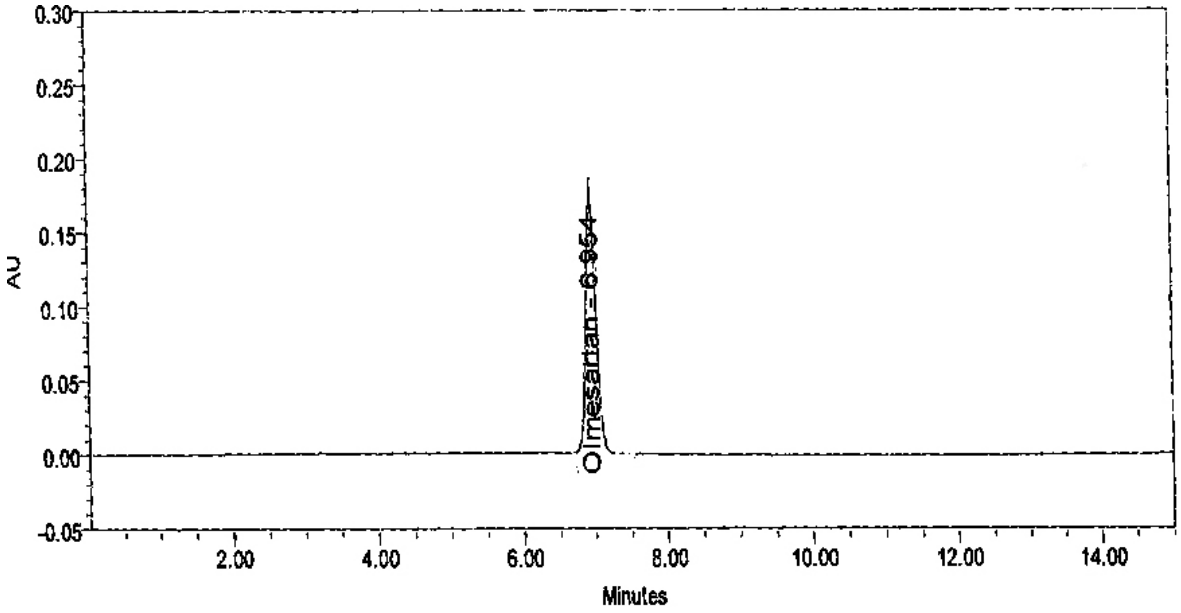
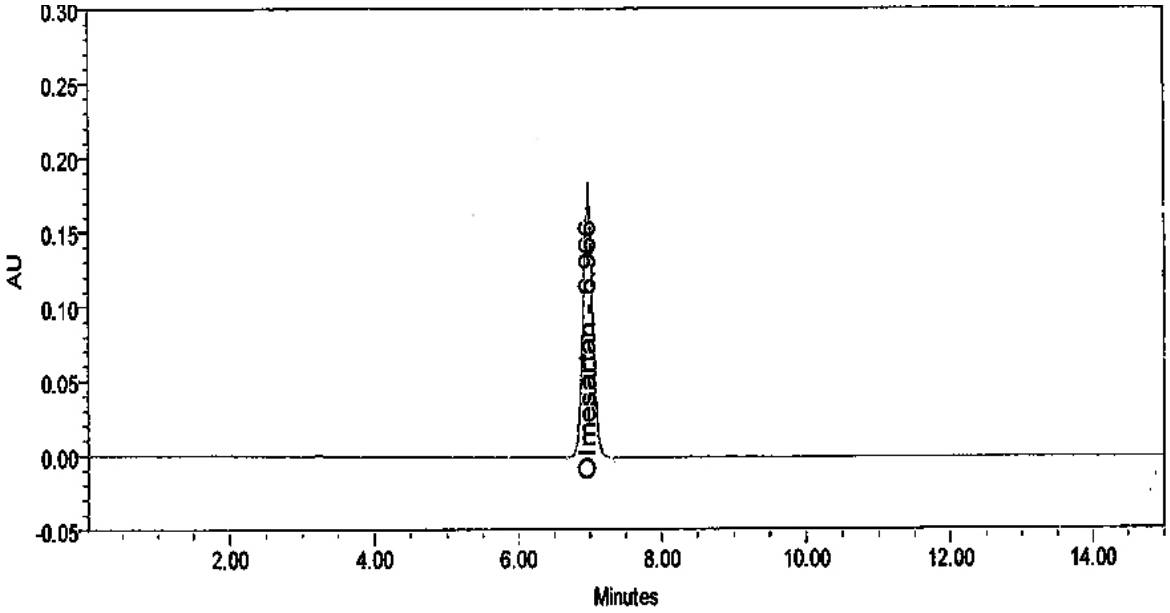


Fig 1. (a) Chromatogram of the standard solution



(b)

Fig 1. (b) Chromatogram of the sample solution

3.1 Interference studies

3.1.1 Excipient interference

All the inactive ingredients namely hydroxyl propyl cellulose, lactose, magnesium stearate, microcrystalline cellulose and titanium dioxide were also tested in the proposed method. No peak was found at the retention time of olmesartan medoxomil when injected in to chromatographic system.

3.1.2 Impurity interference

One of the degradant of olmesartan medoxomil, free olmesartan was injected into the chromatographic system at a level of 0.8 µg mL^{-1}. It had been found that it is not interfering with peak of interest. Forced degradation studies revealed that peak was pure in all the stress conditions. The results were shown in Table 1.

Table 1. Forced Degradation studies

Stress condition	%Assay	%Degradation	Peak purity
Protected sample	99.1	---	0.99724
Water/Reflux-1.0 Hrs	97.3	1.8	0.99902
Acid degradation 0.01N HCl Reflux-1.0 Hrs	97.9	1.2	0.99608
Base degradation 0.01N NaoH Reflux-1.0	96.8	2.3	0.99955
Peroxide degradation 1.5% H_2O_2 Reflux-1.0	97.0	2.1	0.99964
Thermal degradation At 105^0C-24 Hrs	91.2	8.0	0.99586
Photolytic degradation At 254nm-24 Hrs	91.0	8.2	0.99920

3.1 Robustness

Typical variations in analytical conditions were tested. Influence of flow rate, pH, mobile phase composition and filter variability were studied. The results were shown in the Table 2.

Table 2. Robustness study of olmesartan

Robustness Parameter		Tailing factor	Theoretical plate number (n)	RSD (%)
Variation in pH	2.8	1.1	10176	0.08
	3.0 (Optimized)	1.1	13247	0.05
	3.2	1.3	9754	0.10
Mobile phase Composition	50:50	1.3	9568	0.11
	55:45 (Optimized)	1.1	13247	0.05
	60:40	1.3	11053	0.12
Variation in flow rate	0.8 mL min-^{1}	1.2	14560	0.08
	1.0 (Optimized)	1.1	13247	0.05
	1.2	1.0	11221	0.05
Filter variability	Nylon	1.3	15938	0.11
	Centrifuged	1.1	13247	0.05
	PVDF	1.2	14009	0.08

3.2 Linearity

The curve proved to be linear over a concentration range of 10-120 µg mL^{-1} (Fig 2). Standard solution were prepared at seven concentrations (10, 20, 40, 60, 80, 100, 120 µg mL^{-1}) were injected in duplicate. Linear regression of concentration Vs peak area resulted in an average coefficient of determination (R^2) 1.000. The percentage of Y-intercept is 0.150.

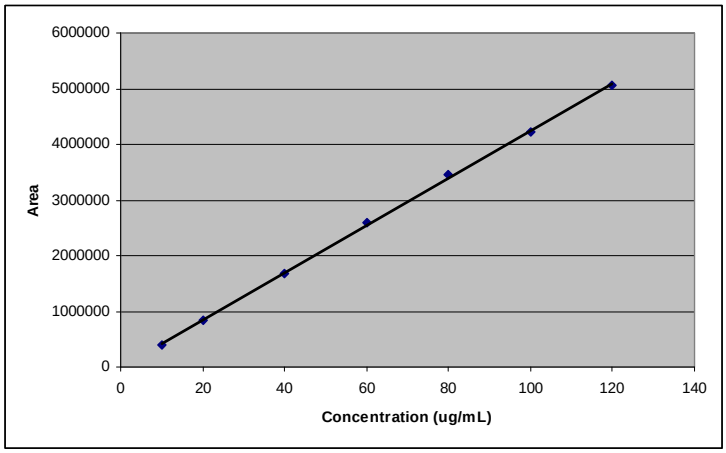


Fig 2. Calibration curve of Olmesartan

3.4 Precision

The intra and inter day precision were estimated from duplicate injection of six sample solutions prepared at 40 µg mL^{-1} of olmesartan analyzed on two different days. Mean and RSD were obtained from calculated olmesartan concentration (Table 3). The results indicate that the method is reproducible.

Table 3. Intra and inter day precision for olmesartan

Sample No	Intraday	Interday
1	99.6	99.2
2	101.2	100.7
3	98.5	99.1
4	100.2	99.5
5	99.1	98.8
6	99.8	100.2
Mean	99.7	99.6
SD	0.93	0.88
RSD (%)	0.93	0.89

3.3 Accuracy

Accuracy was calculated as the percentage recovery of the known added amount of olmesartan reference substance in the sample solutions using three concentration levels covering the specified range (50,100,150 µg mL^{-1}) was added in the sample solutions (40 µg mL^{-1}). The accuracy of the method ranged from 98.7 to 100.3 %, indicating that this assay is reliable (Table 4) and meeting the acceptance criteria 98.0 to 102 %.

Table 4. Accuracy of the analysis of olmesartan

Percent level	Added amount	Found amount	Recovery, %	RSD (%)
50	40.26	40.05	99.46	0.71
100	80.11	79.90	99.73	0.60
150	119.82	119.14	99.43	0.55

4. Conclusion

The HPLC method developed and validated allows a simple and fast quantitative determination of olmesartan from its formulation. A mobile phase composed of solvent A and acetonitrile with a short run time (15 min) and isocratic elution used are advantageous and made the routine analysis easy. Among the significant advantages of this method are simplicity, selectivity, accuracy and precision ensuring that it is suitable for determining the content of olmesartan in tablet dosage form.

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