ORIGINAL ARTICLE

Validated Ultraviolet Spectrophotometric Method for Simultaneous Estimation of Olmesartan Medoxomil in Marketed Formulation

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Abstract

Aim: The goal of the present study is to provide a new, straightforward, and verified UV spectrophotometric technique for estimating Olmesartan Medoxomil in commercial formulations like Olmesar 20 and Olmecip 20 (Maclodes Pharmaceutical Ltd.). **Materials and Methods:** Olmesartan Medoxomil is the member of angiotensin receptor blocker approved by the Food and Drug Administration for the treatment of hypertension. In oral administration, olmesartan medoxomil undergoes intestinal de-esterification to form the active metabolite Olmesartan, which inhibits the binding of angiotensin-I (AT-I) to angiotensin-II (AT-II) receptors in vascular muscle. **Results and Discussion:** Validation of created analytical techniques in accordance with Intracerebral hemorrhage scale recommendations. In a 10 ml volumetric flask, tablet powder corresponding to 10 mg of olmesartan medoxomil was added. For linearity, accuracy, precision, and robustness, 12 distinct concentrations (ranging from 2 to 24 µg/ml) were formed and the calibration plot was condensed. Statistical analysis shows that these approaches are reliable and specific for estimating olmesartan medoxomil in commercially available tablet formulations. **Conclusion:** The method outlined for determining olmesartan medoxomil in marketed tablet formulations may be effectively used for routine analysis in quality control laboratories.

Key words: Accuracy, linearity, medoxomil, olmesartan, precision, robustness, validation

INTRODUCTION

Olmesartan Medoxomil is the member of angiotensin receptor blocker approved by the Food and Drug Administration for the treatment of hypertension.[1-3] Chemically, it is (5-methyl$_2$-oxo-2H-1,3-dioxol-4-yl)methyl 4-(2-hydroxypropan-2-yl)-2-propyl-1-({4-[2-(2H-1,2,3,4-tetrazol5-yl) phenyl]phenyl}methyl)-1H-imidazole-5-carboxylate [Figure 1]. A hydroxy alkyl substituent at the imidazole fourth position and a hydrolysable ester at the imidazole fifth position are important structural components of olmesartan medoxomil. These groups may form inter and intramolecular hydrogen bonds that might enhance antagonistic action. Following oral administration, Olmesartan medoxomil undergoes intestinal de-esterification to form the active metabolite Olmesartan, which inhibits the binding of angiotensin-I (AT-I) to angiotensin-II (AT-II) receptors in vascular muscle. Unlike Angiotensin-converting enzyme inhibitors, Olmesartan is not dependent on AT-II synthesis pathways. Olmesartan decreases the adverse regulatory feedback on renin secretion through preventing binding rather than production of AT-II. Olmesartan lessens vasoconstriction and aldosterone secretion as a result of this obstruction. By causing vasodilation and reducing peripheral resistance, this reduces blood pressure.[2] Olmesartan medoxomil has the chemical formula $C_{29}H_{30}N_6O_6$ [Figure 1] and is available as a white to light yellowish-white powder or crystalline powder (MW 558.59). It barely dissolves in methanol and is nearly insoluble in water.

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According to a review of the literature, olmesartan medoxomil may be measured using high-performance liquid chromatography and high-performance thin layer chromatography techniques alone or in combination with other medications.[3-7] To quantify olmesartan medoxomil in tablet dosage forms, however, only few spectrophotometric techniques have been published in the literature.[8-11] The goal of the present study is to provide a new, straightforward, and verified ultraviolet (UV) spectrophotometric technique for estimating olmesartan medoxomil in commercial formulations such as Olmesar 20 and Olmecip 20 (Maclodes Pharmaceutical Ltd.).

MATERIALS AND METHODS

Olmesartan medoxomil's operational requirements were acquired as gift samples from Macleods Pharmaceutical Ltd. in Himachal Pradesh, India, and were included in a commercial formulation that included 20 mg of the drug. All of the chemicals came from Merck Chemical Ltd. in India and were of analytical quality. Validation of created analytical techniques in accordance with intracerebral hemorrhage (ICH) scale recommendations.

Apparatus

An ELico India SL-159 UV/VIS spectrophotometer with a 1 cm matched quartz cell was utilized for the spectrophotometric study. This particular model is thermospectronic.

Preparation of standard stock solution

To create a stock solution of 1000 ppm, 10 mg of olmesartan medoxomil was properly weighed and placed to a 10 ml volumetric flask. The volume was then adjusted to the mark with the mobile phase (acetonitrile: water [80:20 v/v]).

Development of a practical standard solution

1 ml of the olmesartan medoxomil stock solution was collected, and it was diluted up to 10 ml. From this solution, 0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.2, and 2.4 ml solutions were transferred to 10 ml volumetric flasks and made up the volume to 10 ml with mobile phase, giving standard drug solution of 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24 µg/ml concentration.

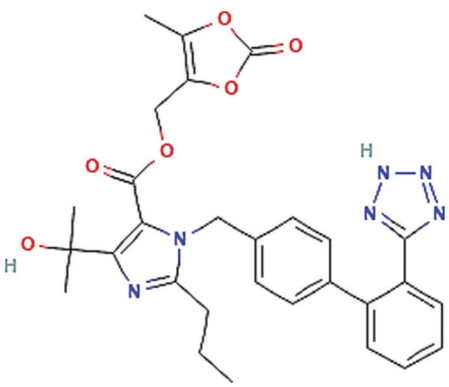

Figure 1: Structure of olmesartan medoxomil

Preparation of the calibration curves of the drug

After sampling each of the standard drug solutions 3 times, the mean peak area of the drug was computed [Table 1], and it was then plotted against the drug's concentration. This curve was used to determine the regression equation. It was possible to acquire the calibration curve [Figure 2] and a typical chromatogram [Figure 3].

Preparation of analysis of tablet formulation

The weight and fineness of 20 pills were exact. In a 10 ml volumetric flask, tablet powder corresponding to 10 mg of olmesartan medoxomil was added. The resulting solution was then filtered using Whatman filter paper before the volume was adjusted to the mark with the same solvent. To produce a concentration of 100 µg/ml, 10 ml of mobile phase was added to 1 ml of filtrate in a 10 ml volumetric flask. Olmesartan medoxomil had a final concentration of 10 µg/ml after being diluted by an additional 0.1 ml of this solution up to 10 ml. The resultant mixture was once again filtered using Whatman filter paper no. 41 before being sonicated for 10 min. The final step was taking a diluted sample and measuring absorbance at 258 nm with a spectrophotometer. Olmesartan medoxomil concentration was determined using a regression equation, and the results are reported in Table 2.

Validation

Linearity

The capacity of an analytical process to produce results that are (within a certain range) directly proportional to the analyte concentration in the sample is known as linearity. After analyzing 12 distinct concentrations (ranging from 2 to 24 µg/ml), the calibration plot was condensed [Table 1]. For each concentration, the absorbance was measured three times, and the mean was computed. Figure 4 provides the regression equation and curve's correlation coefficient.

Accuracy

To verify the accuracy of the established approach, recovery tests were carried out.[12-15] A specific concentration of the

Table 1: Assay of olmesartan medoxomilin dosage forms

Brand name	Olmesartan medoxomil	
	Label claim in mg	% Purity on mean value
Olmesar 20	20 mg	99.09
Olmecep 20	20mg	99.30

reference medication (80%, 100%, or 120% of the pre-measured sample solution) was then added, and the recovery was analyzed. The results are displayed in Table 3.

Precision

Repeatability

To verify the accuracy of the established approach, recovery tests were carried out. A specific concentration of the reference medication (80%, 100%, or 120% of the pre-measured sample solution) was then added, and the recovery was analyzed. The results are displayed in Table 3. Intermediate precision

Intermediate precision

Day-to-day and analyst to analyst

The variance in laboratories, such as various days, analyzers, and equipment, indicates the intermediate precision. The standard dilution was made, and three replicates of each dilution were examined using each of the devised procedures by a separate analyst. The data are shown in Tables 4 and 5, which includes the results of the statistical analysis approach.

Robustness

To test the method's ability to stay unaffected, purposeful minor modifications were performed in accordance with ICH standards by changing the pH and/or concentration of the mobile phase. Acetonitrile: water (70:30 v/v) was employed as the mobile phase instead of the original ratio of acetonitrile: water (80:20 v/v) [Table 6].

Table 2: Recovery study for accuracy of olmesartan medoxomil

Concentration of drug in sample (µg/ml)	10	10	10
Standard drug soln. added (µg/ml)	8	10	12
Amt. Recovered Replicate 1	7.965	9.960	12.342
Amt. Recovered Replicate 2	7.960	9.978	12.250
Amt. Recovered Replicate 3	7.955	9.963	12.110
Mean	7.960	9.967	12.234
SD	0.005	0.009	0.116
%RSD	0.0006	0.0009	0.0095

SD: Standard deviation, RSD: Relative standard deviation.

RESULTS AND DISCUSSION

Solubility study

Olmesartan medoxomil's solubility in various solvents and mixtures is shown in Table 7. For the approach development, acetonitrile and water were chosen since they are often used and are readily available.

UV method

Preparation of the calibration curves of the drug

The results of scanning pure olmesartan medoxomil in the UV range (200–400 nm) are shown in Figure 2. The greatest value, which was determined to be 258 nm, was chosen for technique improvement, and regression was found to be 0.9994 at this wavelength.

The standard curve of pure olmesartan medoxomil is depicted in Table 8 and Figure 3. A regression equation was derived from this standard curve with an R^2 value of 0.9994, indicating that the regression equation is linear.

Assay of tablet formulation

The examination of two distinct commercial tablet formulations is shown in Table 1, and the RSD of the average of three determinations was determined to be below 1. The estimate of olmesartan medoxomil from its tablet dose form may thus be done using that approach.[16]

Validation parameter of UV method

Accuracy

Table 2 displays the olmesartan medoxomil recovery data after typical medication addition. RSD and the mean percentage recovery recovered were both determined to be under one.

Table 3: Repeatability for olmesartan medoxomil

Concentration of drug in sample µg/ml	2	4	6	8	10	12
Replicate 1	2.12	3.95	5.98	8.12	10.22	12.23
Replicate 2	2.05	3.98	5.96	8.10	10.24	12.22
Replicate 3	2.10	3.99	5.99	8.05	10.10	12.12
Mean	2.09	3.97	5.97	8.09	10.18	12.19
SD	0.036	0.020	0.015	0.036	0.075	0.060

SD: Standard deviation

Table 4: Intermediate precision for olmesartan medoxomil

Concentration of drug in sample μg/ml	2	4	6	8	10	12
Replicate 1	1.98	3.99	5.97	7.96	9.98	11.98
Replicate 2	1.96	3.98	5.98	7.97	9.97	11.96
Replicate 3	1.97	3.95	5.97	7.99	9.98	11.97
Mean	1.97	3.97	5.97	7.97	9.97	11.97
SD	0.010	0.020	0.005	0.015	0.005	0.010
%RSD	0.0050	0.0052	0.0009	0.0019	0.0005	0.0008

SD: Standard deviation, RSD: Relative standard deviation

Table 5: Robustness study for olmesartan medoxomil

Standard concentration (μg/ml)	6	12	18
Replicate 1	5.95	11.98	17.98
Replicate 2	5.98	11.97	17.96
Replicate 3	5.96	11.96	17.97
Mean	5.96	11.97	17.97
SD	0.015	0.010	0.010
%RSD	0.0025	0.0008	0.0005

SD: Standard deviation, RSD: Relative standard deviation

Table 6: Optical parameter

Parameters	Observation
λ max	536 nm
Beer's law limit (μg/mL)	2–24 μg/mL
Regression equation*	AUC=0.0134 Conc. + 0.0134
Correlation Coefficient (r^2)	0.9996
Molar Absorptivity (L mol^{-1} cm^{-1})	3.267×10^5
Sandell's sensitivity μg/mL – 0.001 absorbance unit	0.0170

Table 7: Solubility of olmesartan medoxomil

Solvent	Solubility
Water	Insoluble
0.1 N HCl	Insoluble
0.1 N NaoH	Soluble
Methanol	Freely soluble
Acetonitrile	Freely soluble
80% Acetonitrile	Soluble
50% Acetonitrile	Sparingly soluble
Ethanol	Soluble
Acetate buffer pH 3.7	Soluble
Phosphate buffer pH 7.4	Soluble

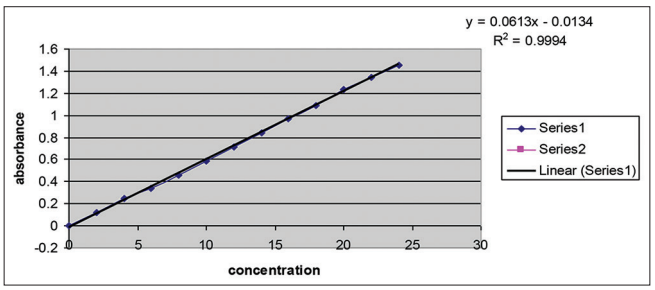

Figure 2: Standard calibration curve of pure olmesartan medoxomil

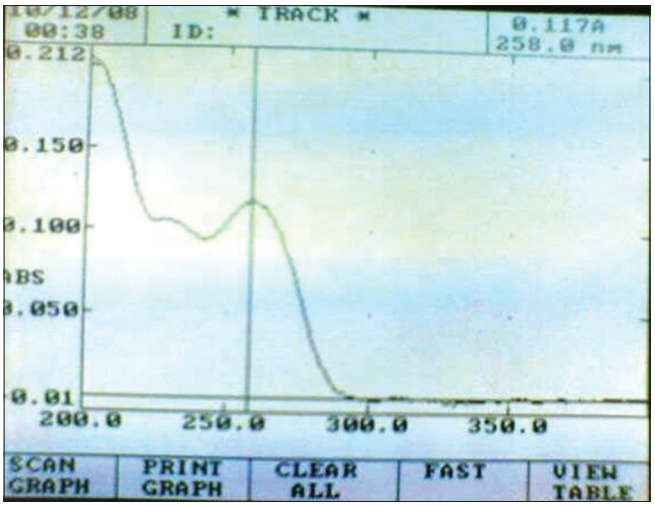

Figure 3: Ultraviolet spectra of pure olmesartan medoxomil

Precision

Repeatability

Table 3 displays the repeatability data for commercial tablet formulations. When both formulations were analyzed, S.D. and R.S.D. were shown to be within the acceptable range.

Intermediate precision

Day-to-day and analyst to analyst

Intermediate accuracy is shown in Tables 4 and 9. It was discovered that the precision's mean value was below 1.

Table 8: Linearity of olmesartan medoxomil

Rep.	0	2	4	6	8	10	12	14	16	18	20	22	24
1	0	0.125	0.201	0.321	0.457	0.539	0.625	0.786	0.889	0.996	1.121	1.297	1.502
2	0	0.150	0.236	0.339	0.483	0.593	0.732	0.807	0.936	1.103	1.231	1.411	1.457
3	0	0.076	0.295	0.366	0.434	0.626	0.785	0.909	1.091	1.171	1.338	1.333	1.491
Mean	0	0.117	0.244	0.342	0.458	0.586	0.714	0.834	0.972	1.090	1.230	1.347	1.450
S.D.	00	0.037	0.047	0.022	0.024	0.043	0.081	0.065	0.105	0.088	0.108	0.058	0.024
R.S.D%	000	0.321	0.194	0.663	0.053	0.074	0.114	0.078	0.108	0.080	0.088	0.043	0.015

Table 9: Result of intermediate precision for olmesartan medoxomil

Concentration of drug in sample µg/ml	2	4	6	8	10	12
Replicate 1	1.99	3.98	6.99	8.97	9.96	11.98
Replicate 2	1.98	3.97	6.97	8.99	9.97	11.97
Replicate 3	1.97	3.96	6.97	8.98	9.98	11.96
Mean	1.98	3.97	6.97	8.98	9.970	11.97
SD	0.010	0.010	0.011	0.010	0.010	0.010
%RSD	0.0050	0.0025	0.1655	0.0011	0.001	0.0008

SD: Standard deviation, RSD: Relative standard deviation

Robustness

Table 5 displays the findings of the robustness research, and it was discovered that the results for the mobile phase had seen very little change and were unaffected.

Optical parameter

Purified olmesartan medoxomil's optical properties as determined by spectrophotometry are shown in Table 6. Molar absorptivity (L mol^{-1} cm^{-1}), Beer's law limit (µg/ml), regression equation, correlation coefficient (r^2), and Sandell's sensitivity were computed.

CONCLUSION

Calculating the proportion of a medicine in a formulation using analytical methods is a crucial aspect of quality control. When it comes to a variety of disorders including hypertension, the treatment of diabetic complications, the management of diabetic nephropathy, etc., olmesartan medoxomil is crucial to maintaining human health. Here, analytical methods are crucial for estimating the amount of medication present in commercial formulations. In the present study, analytical techniques for estimating olmesartan in commercially available tablet formulations were established. Statistical analysis shows that these approaches are reliable and specific for estimating olmesartan medoxomil in commercially available tablet formulations. The method outlined for determining olmesartan medoxomil in marketed tablet formulations may be effectively used for routine analysis in quality control laboratories.

DECLARATIONS

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Ethics approval

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets of research were collected from experiments and analysis of variables during present study. These datasets are available from the corresponding author on reasonable request.

Authors' contributions

KD designed and optimizes the study and developed the methodology. PS, SJ, and KD performed the experiments, collection of data, and interpretation data. PS and KD wrote the manuscript. VJ and PS contributed to manuscript revision and provided supervision. All authors read and approved the final manuscript.

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