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Validated Spectrophotometric Method for Estimation of Olmesartan Medoxomil in Pharmaceutical Formulation

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Abstract

A simple, sensitive and accurate spectrophotometric method has been developed for the deterrmination of Olmesartan Medoxomil in raw material and tablets. The λ_{max} of Olmesartan Medoxomil was found to be 256 nm. The linear dynamic response was found to be in the concentration range of 4-14 µg/mL and coefficient of correlation was found to be 0.9993. The %RSD value was below 2.0 for intraday and interday precision indicated that the method was highly precise. The LOD and LOQ were found to be 0.105 and 0.3045 µg/mL respectively which revealed that method was highly sensitive. The percentage recovery value was higher than 100 %, indicating the accuracy of the method and absence of interference of the excipients present in the formulation. The proposed method was simple, fast, accurate, precise and reproducible and hence can be applied for routine quality control analysis of Olmesartan Medoxomil in bulk and pharmaceutical formulations.

Key words: Olmesartan Medoxomil, Spectroscopy, Estimation, Validation

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Introduction

Olmesartan Medoxomil is the member of angiotensin receptor blocker approved by the Food and Drug Administration (FDA) for the treatment of hypertension [1, 2, 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-tetrazol-5-yl)phenyl]phenyl}methyl)-1H-imidazole-5-carboxylate (Figure 1) . Key structural elements of Olmesartan Medoxomil include a hydroxy alkyl substituent at the imidazole 4- position and a hydrolysable ester at the imidazole 5- position. Inter and Intramolecular hydrogen bonding involving these groups may contribute to the potentiation of antagonistic activity. After the oral administration, Olmesartan Medoxomil is de-esterified in the intestinal tract to produce the active metabolite Olmesartan and this active Olmesartan acts by blocking the binding of angiotensin II to the AT_1 receptors in vascular muscle; it is therefore independent of angiotensin II synthesis pathways, unlike ACE inhibitors [4]. By blocking binding rather than synthesis of angiotensin II, olmesartan inhibits the negative regulatory feedback on renin secretion. As a result of this blockage, olmesartan reduces vasoconstriction and the secretion of aldosterone. This lowers blood pressure by producing vasodilation, and decreasing peripheral resistance [5]. Olmesartan Medoxomil is a white to light yellowish-white powder or crystalline powder with a formula of $C_{29}H_{30}N_6O_6$ (MW 558.59). It is practically insoluble in water and sparingly soluble in methanol.

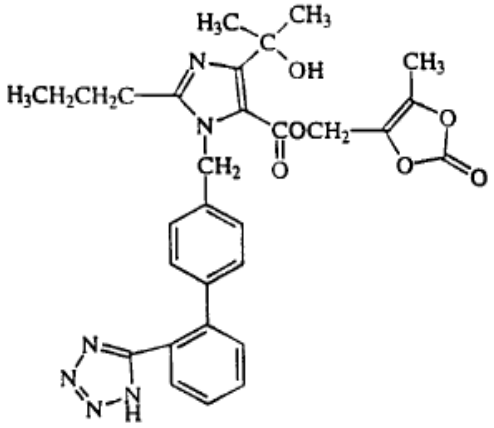

Figure 1: Olmesartan Medoxomil

Literature survey reveals that Olmesartan Medoxomil can be estimated by HPLC and HPTLC methods individually or in combination with other drugs[6,7,8] . However very few spectrophotometric methods were reported for quantitation of Olmesartan Medoxomil in tablet dosage forms in the literature[9]. The objective of the present investigations was to develop a simple, accurate and sensitive spectrophotometric method for estimation of Olmesartan Medoxomil in tablet dosage form.

Materials and Methods

Chemicals & Reagents: Standard Olmesartan Medoxomil was receieved as a gift sample from ACI Pharmaceuticals Ltd Dhaka, Bangladesh. And the commercially available Olmesartan Medoxomil tablets claimed to contain 10 mg of active ingredients were procured from local market. Analytical grade methanol was used as solvent.

Instruments: UV-Visible double beam spectrophotometer (UV-1601 PC SHIMADZU Limited, Japan), micropipette of variable volume 10-1000 µL and Digital electric balance.

Selection of wavelength : In order to ascertain the wavelength of maximum absorption (λ_{max}) of the drug, different solutions of the drugs (4 µg/ml to 14 µg/ml) in methanol were scanned using spectrophotometer within the wavelength region of 200 – 380 nm against methanol as blank. The resulting spectra were shown in Figure 2 and the absorption curve showed characteristic absorption maxima at 256 nm for Olmesartan Medoxomil.

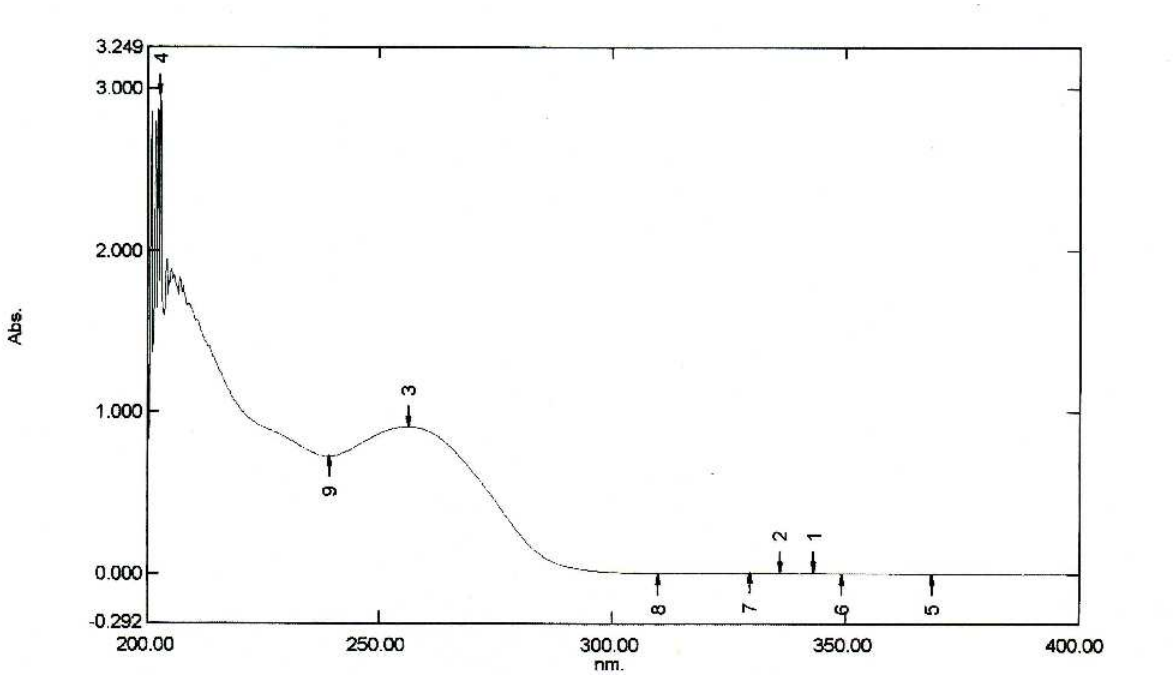

Figure 2: UV spectrum of Olmesartan medoxomil in methanol

Preparation of standard solution for calibration curve: 10 mg Standard Olmesartan Medoxomil was accurately weighed and transferred to 100 ml volumetric flask and was dissolved properly and diluted up to the mark with methanol to produce a stock solution of 100 µg/ml. Appropriate amounts of this stock solution were diluted with the same solvent, which yield concentrations of 4µg/mL, 6µg/mL, 8µg/mL 10µg/mL, 12µg/mL and 14µg/mL and were used for the construction of calibration curve.

Preparation of sample solution: Twenty tablets each claimed to 10 mg of Olmesartan Medoxomil were weighed accurately and powdered. A quantity equivalent to 10mg of Olmesartan Medoxomil was weighed accurately and transferred to a 100 mL volumetric flask. Then 40mL methanol was added to it and the mixture was sonicated for 5 minutes for a complete solution of drug and then the volume was diluted up to the mark with the same solvent. The resulting solution was filtered through Whatman filter paper. The solution obtained was diluted with the same solvent so as to obtain a concentration in the range of linearity as previously discussed for the pure drug and absorbance was recorded at 256 nm against methanol as blank.

Result and Discussion

The proposed method was validated according to International Conference on Harmonization (ICH) guidelines [10].

Linearity: The linearity of this method was determined at six concentration levels ranging from 4µg/mL- 14µg/mL. The plot of absorbance vs respective concentration (Fig 3) of Olmesartan Medoxomil was found to be linear in the range of 4µg/mL- 14µg/mL. Beer's law was found to be obeyed over this concentration range. The regression equation was found to be Y = 0.0425 x + 0.0099 and the correlation coefficient (R) of the standard curve was found to be 0.9993 (Table 1).

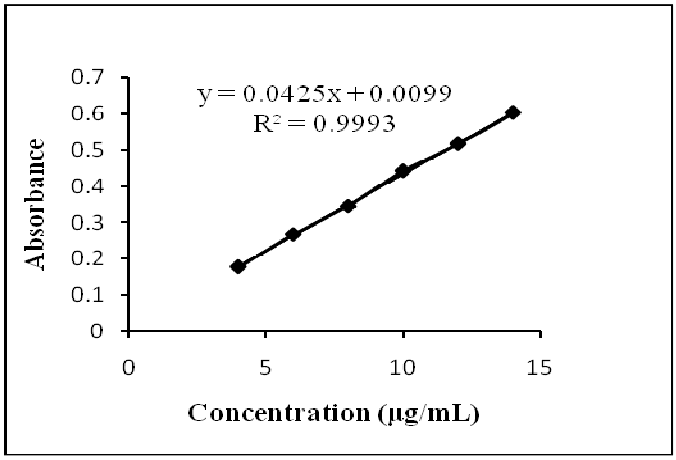

Figure 3: Standard curve

Precision: The precision is a measure of the ability of the method to generate reproducible results. The precision of the assay was determined by repeatability (intra-day) and intermediate precision (inter-day) and reported as % RSD. For this, 10 µg/mL of the solution was measured three times in a day and the same was repeated in next three days and then the % RS D was calculated. The precision (measurements of intra-day and inter-day) results showed (Table 1)

good reproducibility with percent relative standard deviation (% RSD) was below 2.0%. This indicated that method was highly precise.

Recovery studies (Accuracy): Recovery studies were performed to judge the accuracy of the method. The studies were carried out by adding a known quantity of pure drug to the pre-analyzed formulation and the proposed method was followed. From the amount of drug found, the percentage recovery was calculated. Recovery study was carried out at three levels 80%, 100% and 120% for the formulation concentration of 6µg/mL. The percentage recovery value (Table 2) was found to be higher than 100%, indicated that the accuracy of the method and absence of interference of the excipients present in the formulation.

Sensitivity: Limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equation given in ICH guidelines [10]. The LOD and LOQ for Olmesartan Medoxomil were found to be 0.105µg/mL and 0.3045 µg/mL respectively (Table 1), this demonstrated that the method was highly sensitive.

Table 1: Validation parameters

Parameters	Result	
Absorption maxima(nm)	256	
Linearity range (µg/mL)	4 to 14	
Standard Regression equation	Y = 0.0425x + 0.0099	
Correlation coefficient	0.9993	
LOD (µg/mL)	0.105	
LOQ (µg/mL)	0.3045	
Precision (at10 µg/mL)	Intraday (%RSD)	Interday (%RSD)
	0.119	0.260

Table 2: Recovery study

Level of Addition (%)	Formulation (µg/mL)	Addition of pure drug (µg/mL)	% Recovery of pure drug	Recovery (%) ± S.D.
80	6	4	100.33	
100	6	6	100.65	100.48±0.161
120	6	8	100.45	

Table 3: Determination of active ingrediemt in tablets

Sample	Label claimed	Amount found	% Labeled Claim*
Olmesartan Medoxomil	10 mg/Tab	10.42.±0.132	100.40

(* Average of three determinations)

Stability: The stability of the solutions (both standard and sample) was checked by measuring the absorbance over a period of 24 h at room temperature (unstressed condition) and at 105℃ (stressed condition). It was observed that for both solutions, the absorbance and spectrum of Olmesartan Medoxomil remained almost similar in both stressed and unstressed condition within this indicated period with no significant degradation of Olmesartan Medoxomil which demonstrated that the proposed method was highly stable.

Conclusion

From the above discussion it is clear that the proposed method was simple, sensitive, stable and reliable with good precision and accuracy. The proposed method was also applied for the assay of Olmesartan Medoxomil in tablet formulation (in triplicate) and the results are shown in Table 3. The results obtained were in good agreement with the label claims. Hence, this method can be used for the routine determination of Olmesartan Medoxomil in pure sample and in tablet formulations.

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