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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETRIC AND RP-HPLC METHOD FOR ESTIMATION OF OLMESARTAN MEDOXOMIL IN TABLET DOSAGE FORM

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ABSTRACT

Two simple and sensitive spectrophotometric and RP-HPLC methods are described for the determination of Olmesartan Medoxomil. The first method Spectrophotometry was based on the standard curve. Olmesartan Medoxomil exhibits λmax at 258 nm. Quantitative estimation of Olmesartan Medoxomil was carried out the standard calibration curve at 258 nm. The second method, high-performance liquid chromatographic method was developed for the determination of Olmesartan Medoxomil using Acetonitrile: Methanol (50:50, v/v) and pH adjust 4.0 with glacial acetic acid as the mobile phase and measuring the response at λmax 256 nm. The analysis was performed on a Lichrocart C18 (250 X 4.0 mm), 5-µm column. The method was found to be accurate, with linearity ranging from 2 to24 for spectrophotometry and 5 to30 for HPLC with a correlation coefficient (r2) 0.9994 and 0.9996 respectively. Precision mean % assay was found to be 99.09 for spectrophotometry and 99.53 for HPLC, The mean % recovery was found to be 99.5 -107.01 for spectrophotometry and 100.6-106.9 for HPLC

KEY WORDS

Spectrophotometric, RP-HPLC, Olmesartan Medoxomil, Tablet

INTRODUCTION

Olmesartan Medoxomil fixed dose combination tablet contain Olmesartan Medoxomil as antihypertensive agent.Olmesartan Medoxomil is chemically 2,3-dihydroxy-2-butenyl 4-(l-hydroxy-l-methylethyl)-2-propyl-l-[7-(o-lH-tetrazol-5-ylphenyl)benzyl]imidazole-carboxylate, cyclic 2,3-carbonate or (5-methyl-2-oxo~l,3-dioxolen-4-yl)rnethyl 4-(l -hydroxy-l-methylethyl)-2-propyl-1-{4-[2-(tetrazolyl)phenyl]phenyl}methylimidazole-5-carboxylate and has a empirical formula of $C_{29}H_{30}N_6O_6$[1]. Olmesartan Medoxomil blocks the vasoconstrictor effect of angiotensin II by selectively blocking the binding of angiotensin II to the AT I receptor in vascular muscle. Its action is therefore independent of the pathway of angiotensin II synthesis. Several chromatographic

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methods are reported for estimation of Olmesartan Medoxomil from pharmaceutical formulations [2-10] and biological fluid [11], yet not official in any of the pharmacopoeia. Developed spectrophoto metric and HPLC methods are simple methods of analysis of Olmesartan Medoxomil from marketed tablet formulations. The developed methods were found to be rapid, accurate, reproducible and economical. These methods can be used successfully for quality control testing of the drugs from combined tablet dosage form. The non-availability of UV-Spectrophotometry method and HPLC method until now for the analysis of this component made it worthwhile objective to pursue the present research work. Therefore, in the proposed work, a successful attempt has been made to develop analytical method with due consideration of accuracy, sensitivity, rapidity, economy.

EXPERIMENTAL

Reagents and chemicals

Olmesartan Medoxomil were kindly provided by mecleods pharmaceutical Limited, (India). Methanol and acetonitrile were of HPLC grade and purchased from Merck Ltd, New Delhi, India. Water used was of HPLC grade water from Merck Ltd, New Delhi, India. Olmesartan Medoxomil tablets. - Claimed to contain 20 mg of the drug. was procured from Macleods Pharmaceutical Ltd., (India)

Instrumentation

A thermospectronic model of Elico India SL-159 UV/VIS Spectrophotometer with 1cm. matched quartz cells was used for spectrophotometric method. The HPLC system (Merk, Hitachi) consisted of a L-7110 pump, a U.V.Visible detector, a Lichrocart C18 (250 X 4.0 mm), 5µm) column, a Lichrocart, HPLC guard cartridge system and a winchrom software.

Chromatographic conditions

The chromatographic analysis was performed at ambient temperature on a RP-C18 analytical column with a mobile phase composed of Acetonitrile: Methanol (50:50v/v) (pH 4.0, adjusted with glaciel acetic acid) and was isocratically eluted at a flow rate of 1 mL min-1. A small sample volume of 20 µL was used for each sample run, being injected into the HPLC system. The chromatogram was monitored with UV detection at a wavelength of 256 nm.

Method 1 Spectrophotometry

Using the spectra of Olmesartan Medoxomil in mobile phase (Acetonitrile: water 80:20 v/v), the wavelength maxima of drug 258.0 was selected sampling wavelengths for this method. The spectral data from these scan was used to determine the concentration of drug in the sample solution.

Preparation of Standard Stock Solution

10 mg of Olmesartan Medoxomil was weighed accurately and transferred to a 10ml volumetric flask, and the volume was adjusted to the mark with the mobile phase acetonitrile: water (80:20 v/v), to give a stock solution of 1000ppm.

Preparation of Working Standard Solution

From stock solutions of Olmesartan Medoxomil 1 ml was taken and 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, 2.4 ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with mobile phase, gives standard drug solution of 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24 µg/ ml concentration.

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Preparation of the Calibration Curves of the Drug

Each of the standard drug solutions were injected 3 times and the mean absorbance of drug was calculated and plotted against the concentration of the drug. The regression equation was found out by using this curve and the calibration curve was obtained.

Analysis of Tablet formulation

Twenty tablets were accurately weighed and finely powered. Tablet powder equivalent to 10 mg of Olmesartan Medoxomil was taken in 10 ml of volumetric flask; resultant solution was filtered through Whatmann filter paper and finally volume made up to mark with same solvent. 1 ml of filtrate was taken in 10 ml volumetric flask and volume was made up to 10 ml with mobile phase to obtain concentration of 100µg/ml. Further 0.1 ml of this solution was taken and diluted up to 10 ml obtain final concentration of 10µg/ml of Olmesartan Medoxomil. The resulting solution was again filtered using Whatmann filter paper no.41 and then sonicated for 10 min. Finally diluted sample was taken and absorbance was measured by using spectrophotometer at 258 nm. Concentration of Olmesartan Medoxomil was found out by using regression equation.

Method 2 RP-HPLC Method

HPLC method was developed using a Lichrocart C-18 column with 250x 4 mm i.d. and 5-µm particle size column. Mobile phase selected for this method contained Methanol and acetonitrile was taken in same proportion and pH was adjusted to 4 with glacial acetic acid was filtered through 0.2-micron membrane filter. Flow rate employed was 1.0 ml/min. Detection of eluent was carried out at 257 nm.

Preparation of Standard Stock Solution

10mg of Olmesartan Medoxomil was weighed accurately and transferred to a 10ml volumetric flask, and the volume was adjusted to the mark with the mobile phase (acetonitrile: methanol 50:50 v/v, pH-4 with Glacial Acetic Acid) to give a stock solution of 1000ppm.

Preparation of Working Standard Solution

From stock solutions of Olmesartan Medoxomil 1 ml was taken and diluted up to 10 ml. from this solution 0.5, 1.0, 1.5, 2.0, 2.5, 3.0ml solutions were transferred to 10ml volumetric flasks and make up the volume up to 10 ml with mobile phase, gives standard drug solution of 5, 10, 25, 30µg/ ml concentration.

Preparation of the Calibration Curve of the Drug

Each of the standard drug solutions were injected 3 times and the mean peak area of drug was calculated and plotted against the concentration of the drug. The regression equation was found out by using this curve.

Analysis of Tablet formulation

Sample Preparation Twenty tablets were accurately weighed and finely powered. Tablet powder equivalent to 10 mg of Olmesartan Medoxomil was taken in 10 ml of volumetric flask; resultant solution was filtered through Whatmann filter paper and finally volume made up to mark with same solvent. 1 ml of filtrate was taken in 10 ml volumetric flask and volume was made up to 10 ml with mobile phase to obtain concentration of 100µg/ml. Further 0.1 ml of this solution was taken and diluted up to 10 ml obtain final concentration of 10µg/ml of Olmesartan Medoxomil. The resulting solution was again filtered using Whatmann filter paper no.41 and then sonicated for 10 min.

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A reverse phase C-18 column equilibrated with mobile phase methanol: acetonitrile (50:50, v/v; pH 4) was used. pH adjusted by using glacial acetic acid up to 4. Mobile phase was filtered through Whatmann filter paper and degassed. Mobile phase flow rate was maintained at 1 ml/min and effluents were monitored at 256 nm. The sample was injected using a 20 µl fixed loop, and the total run time was 10 min. The sample solution was chromatographed and a concentration of Olmesartan Medoxomil in Tablet samples was found out using regression. A typical chromatogram shown in Fig 1

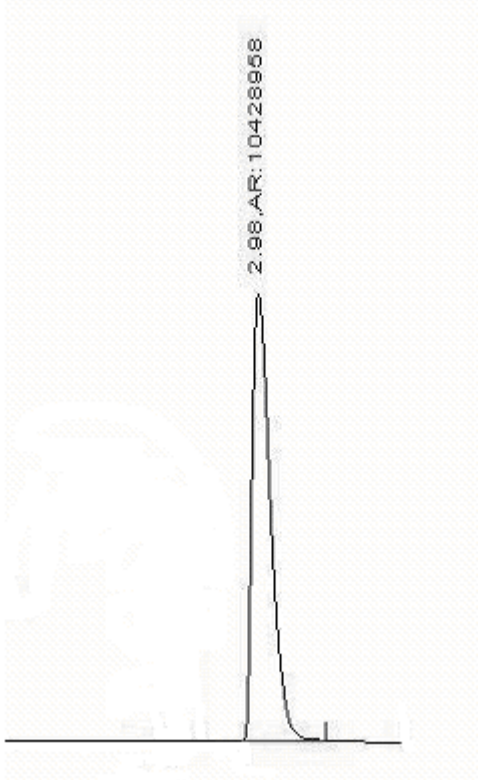

Figure 1
HPLC chromatogram of Olmesartan Medoxomil

RESULT

The % purity for the tablet formulation was found 99.09% for spectrophotometry and for HPLC 99.53%. At the chromatographic conditions selected for the system suitability parameters for HPLC are the theoretical plates (n) is 17500, capacity factor (k) is 1.42 x 10^{-3}, asymmetry (T) is 1.09. The retention time for Olmesartan Medoxomil is 3.0±0.5 min. (Fig. 2) respectively. The correlation coefficient for the linearity of the HPLC method was 0.9996 (Table 1) respectively. The % recovery for Olmesartan Medoxomil was found 99.5-101.9% respectively (Table 2) and was well within the acceptance limit. . The RSD for precision data of repeatability found was 0.036% and for intermediate precision was found for day to day 0.165% and analyst to analyst 0.019% and samples was analyzed in replicates (n = 3) (Table 3). The RSD for robustness data in changed condition was found 0.083%, which was within the limit (Table 3). For the spectrophotometric method the correlation coefficient for the linearity was 0.9994 (Table 1). The % recovery for Olmesartan Medoxomil was 100.6-106.9% respectively (Table 2) and was well within the acceptance limit. The RSD for precision data of repeatability found was 0.034% and for intermediate precision was found for day to day 0.083% and analyst to analyst 0.037% and samples was analyzed in replicates (n = 3) (Table 3). The RSD for robustness data in changed condition was found 0.021%, which was within the limit (Table 3). Standard and sample solution stability was evaluated at room temperature for 48 hr. The result of RSD demonstrates that stability testing of Olmesartan Medoxomil was found below 2.0% within the acceptance range. It showed that both standard and sample solution was stable up to 48 hr at room temperature for UV and HPLC.

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Table 1

Characteristics of the analytical method derived from the standard calibration curve

Spectrophotometry				
Compound	Linearity range µg/ml	Correlation co-efficient (r^2)	slope	intercept
Olmesartan Medoxomil	2 to24	0.9994	0.0134	0.0613
HPLC				
Olmesartan Medoxomil	5 to30	0.9996	79477	687433

Table 2

Method accuracy

Spectrophotometry				
Level	**Drug added** (mg)	**drug recovered** (mg)	**% Assay** Mean ± SD	**% RSD** Mean ± SD
80%	8	7.96	99.5±0.006	0.0130
100%	10	9.96	99.6±0.0009	0.0125
120%	12	12.23	101.9±0.060	0.0004
HPLC				
80%	8	8.27	103.3±0.107	0.0130
100%	10	10.06	100.6±0.085	0.0125
120%	12	12.83	106.9±0.004	0.0004

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Table 3
Method precision and robustness

Parameters For precision		% RSD (Spectrophotometry)		% RSD (HPLC)	
Repeatability		0.036		0.074	
Intermediate precision	Day to day	0.165		0.083	
	Analyst to analyst	0.019		0.037	
Parameters For robustness		% RSD (Spectrophotometry)		% RSD (HPLC)	
		Normal condition	Changed condition	Normal condition	Changed condition
		0.041	0.083	0.010	0.021

DISCUSSION

Spectrophotometry method

The proposed analytical method is simple, accurate and reproducible Olmesartan Medoxomil showed max at 258 nm, standard calibration curve method was tried for estimation in formulation.

HPLC Method

Considering the efficiency of HPLC, attempt has been made to develop simple, accurate, precise, rapid and economic method for simultaneous estimation of and olmesartan medoxomil in a tablet dosage form. Thus method described enables to the quantification olmesartan medoxomil. The advantages lie in the simplicity of sample preparation and the low costs of reagents used. Experimental results were indicative of satisfactory precision and reproducibility. Hence, these method can be used for analysis of solid dosage form in quality control department.

CONCLUSION

The methods described for the determination of Olmesartan Medoxomil in marketed tablet formulations can successfully employed for the determination of Olmesartan Medoxomil in marketed tablet formulations for routine analysis in quality control laboratories.

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