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Research Article

DEVELOPMENT AND VALIDATION OF A NOVEL SPECTROPHOTOMETRIC ANALYTICAL METHOD FOR THE DETERMINATION OF OLMESARTAN MEDOXOMIL IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Simple, sensitive, specific and economic spectrophotometric method was developed and validated for quantification of olmesartan medoxomil pharmaceutical formulations. The absorption maximum in ethanol solvent was found to be 257.8. Linearity was obtained in the concentration range 5 to 30µg/mL for olmesartan medoxomil with a correlation coefficient of 0.9982. The precision (intra-day and inter-day) of me thod was found within limits. The result of the analysis was validated statistically and recovery studies confirmed the accuracy and precision of the proposed method. The developed methods were applied successfully to the determination of this drug in various pharmaceutical formulations.

Keywords: Olmesartan medoxomil, Ethanol, UV-Visible spectrophotometric method, Validation

INTRODUCTION

Olmesartan medoxomil was approved by the US Food and Drug Administration (FDA) in April 2002 (Benicar®, Daiichi Sankyo) for the treatment of hypertension. Chemically it is known as 2,3-dihydroxy-2-butyl 4-[1-hydroxy-1-methylethy]-2-propyl-1-[p(o-1H-tetrazol-5-ylphenyl) benzyl] imida-zole-5-carboxylate, cyclic 2,3-carboxylatate[1] and its structure (fig. 1). It belongs to the category of Angiotensin II receptor blockers. It is a prodrug and is rapidly de-esterifies during absorption to form olmesartan, the active metabolite[2-3]. Olmesartan is more effective than other angiotensin II receptor blockers (candesartan,irbesartan, losartan and valsartan) tested at their recommended doses, in terms of reduction in cuff or 24-h ambulatory blood pressure, in patients with essential hypertension. These differences in blood pressure reduction may be clinically relevant and have important long-term implication[4].

UV method is commonly employed method for routine analysis since it is economical and easy to perform. Literature reports reveal that olmesartan medoxomil can be estimated by RPLC-HPLC[5], RP-HPLC[6], LC-MS[7] and HPLC[8] methods individually or in combination with other drugs.

Parambi and coworkers[9] developed a UV spectrophotometric method for the estimation of olmesartan medoxomil in pharmaceutical dosage form. The method utilizes tetrahydrofuran (THF) as a solvent. THF has been categorized as a class 2 solvent (solvent to be limited in use) as per ICH and it is reported to be hazardous by OSHA communication definition[10]. Vapors from THF have been reported to cause nausea, dizziness, headache or blackout which restricts its use for analysis. Moreover, it is also reported to be a severe skin irritant and affects central nervous system. Repeated and prolong exposure of this solvent may cause liver damage or dermatitis by defatting the skin. Thus, it is desirable to develop alternate spectrophotometric methods of analysis that utilize commonly acceptable solvents.

Thus, an attempt was made to develop a simple, safer, precise, accurate and economical method for the estimation of olmesartan medoxomil by using ethanol as a solvent system. Ethanol is categorized as ICH class 3 solvent (solvents with low toxic potential). So ethanol can be used safely for determination of olmesartan medoxomil in various formulations.

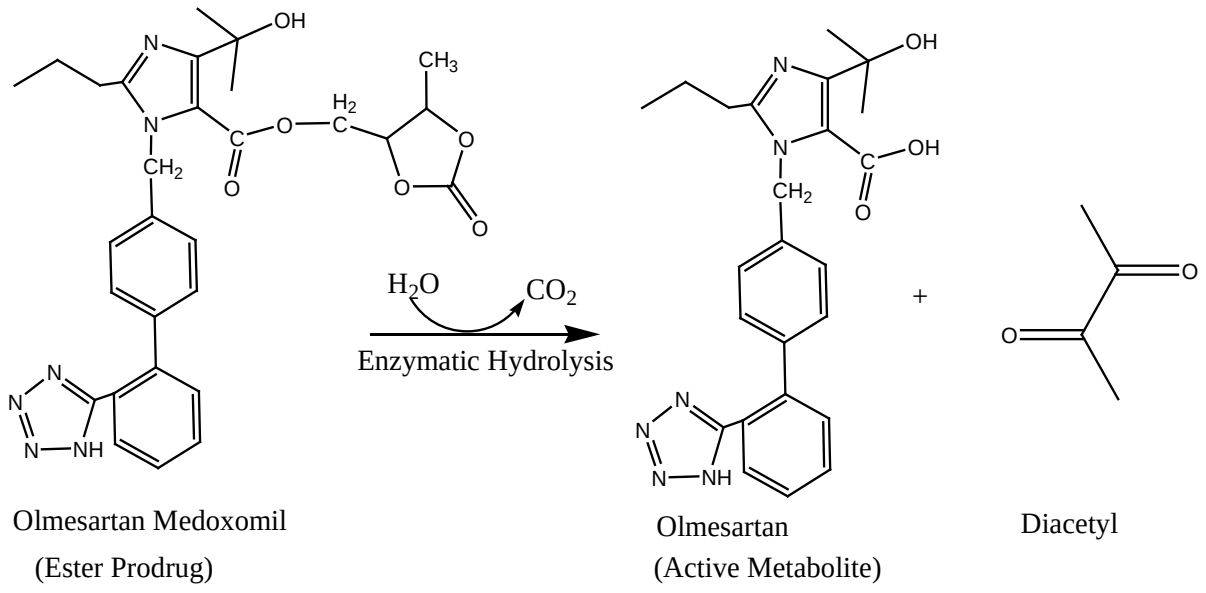

Fig. 1: Conversion of Olmesartan medoxomil to Olmesartan

MATERIALS AND METHODS

Instruments

A double beam UV-visible spectrophotometer (1700, Pharmaspace, Shimadzu, Kyoto, Japan) connected to a computer loaded with spectra manager software UV probe was employed with a pair a 1 cm quartz cells for all analytical work. All weights were taken on digital electronic balance (Sansui electronic, Tokyo, Japan).

Materials

Pure drug, olmesartan medoxomil as a gift sample by Sun Pharmaceuticals Pvt. Ltd. India, tablet formulations containing olmesartan medoxomil of brand name OLSAR of Unichem, India and PINOM of Lupin laboratories Ltd. India was purchased from local pharmacy shop and laboratory prepared nanoemulsion formulation containing olmesartan medoxomil as therapeutic agent.

Solvent

Ethanol (95 %) was provided by Sd fine chemicals ltd. Mumbai, India was used as the solvent.

Preparation of standard solution

Standard stock solution of olmesartan medoxomil was prepared by dissolving 10 mg of drug in 10mL volumetric flask using ethanol as solvent. Stock solutions of 1000 µg/ml were obtained in this manner. From this stock solution, working standard solution of concentration 100µg/ml was prepared by appropriate dilutions. Working standard solution was scanned in the entire UV range to determine the λmax. The λmax of olmesartan medoxomil was found to be 257.8 nm (fig. 2).

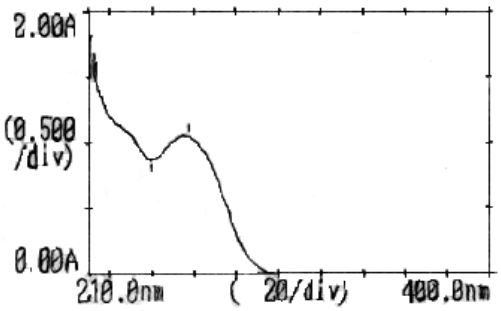

Fig. 2: Absorption maxima of olmesartan medoxomil

Calibration curve

Six standard dilutions of drug were prepared having concentrations of 5-30 µg/ml. The absorbance of the standard solution was measured at 257.8 nm and calibration curve was plotted (fig. 3). The correlation coefficient of the drug was determined using calibration curve.

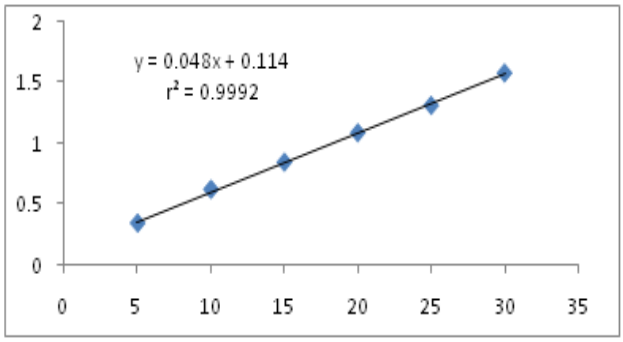

Fig. 3: Calibration curve in ethanol (95 %)

Various statistical parameters are derived from the calibration curve and summarized in table1.

Table 1: Statistical parameters

Parameter	Values
Correlation coefficient (r^2)	0.999
Slope	0.048
Intercept	0.114
Coefficient of determination (r)	0.999
Standard deviation	0.347

Preparation of sample solution

Sample preparation for tablet formulations

Sample solution containing the drug was prepared by dissolving 20 mg powder in 10mL volumetric flask using ethanol to give stock solutions of 1000 µg/ml. From this stock solution, working standard solution of 100 µg/ml concentration was prepared by appropriate dilution. Six standard dilutions of concentrations of 5, 10, 15, 20, 25 and 30 µg/ml was prepared from working standard solution. The absorbance of this sample solution was measured at 257.8 nm and drug concentration was determined using proposed analytical methods.

Estimation of drug in marketed formulation

Ten tablets of each brand were weighed and crushed to a fine powder separately. An accurately weighed powder sample equivalent to 4 mg of olmesartan was transferred to a 10 ml volumetric flask, dissolved in 5 ml ethanol, shaken for 10 min and the volume was made up to the mark with ethanol. The solution was then filtered through Whatman filter paper no. 41.

The solution was further diluted to get different concentrations in the range of 5-30 µg/ml. Absorbances of the sample solution were recorded at 257.8 nm, and concentration of drug in the sample was determined[11]. The analysis procedure was repeated three times with the formulation and result is shown in table 2.

Table 2: Result of tablet analysis

Brand name	Label claim (mg)	Estimated amount of drug (mg)	% Label claim	Standard deviation
OLSAR	20	19.440	97.200	0.31
PINOM	20	19.665	98.579	0.17

Table 3: Result of Nanoemulsion analysis

Formulation code	S_{mix} ratio	Composition of nanoemulsion			Added amount of drug (mg)	Estimated amount of drug (mg)	% Recovery
		% oil	% S_{mix}	% water			
F1	1:0	10	15	75	10	9.266	92.666
F2	2:1	10	15	75	10	8.940	89.400
F3	3:1	10	15	75	10	9.577	95.770
F4	4:1	10	15	75	10	9.560	95.600
F5	4:1	10	35	55	10	8.624	86.244

Estimation of drug in nanoemulsion formulation

Sample preparation of nanoemulsion containing drug was done by taking 1mL nanoemulsion in a 10 ml volumetric flask and shaken vigorously with ethanol for 10 minutes. Volume was made up to 10 ml with the same solvent. Absorbance of the sample was measured at 257.8 nm and drug concentration was determined using UV-Visible spectrophotometer as shown in table 3.

Method validation

The method was validated with parameters like linearity and range, precision, accuracy, repeatability, limit of detection and limit of quantification[12].

Linearity and range

The linearity for olmesartan medoxomil was determined at six concentration levels, ranging from 5-30µ/ml using working standards.

Accuracy

The accuracy of the proposed methods, recovery studies were carried out by adding a known amount of drug to the preanalyzed tablet powder and percentage recoveries were calculated. The percentage recovery for the tablet formulation was more than 98 and less than 102. The results of recovery studies were satisfactory.

Precision

The reproducibility of the proposed method were determined by performing the analysis of tablet and nanoemulsion formulation at different time intervals on the same day (intraday precision) and on three different days (inter-day precision).The results of intra-day and inter-day precisions were expressed in %RSD (percentage relative standard deviation). The %RSD for intra-day and intraday precision was found less than 2 established the analytical method to be précised.

Recovery studies

The accuracy of the proposed methods was checked by recovery study, by addition of standard drug solution to preanalysed sample solution at different concentration levels within the range of linearity as shown in the table 4 and 5 for nanoemulsion as well as tablet formulations.

Table 4: % Recovery data for Nanoemulsion formulation

Formulation code	Amount of drug in NE♦ (mg)	Amount of pure drug added (mg)	Total estimated amount (mg)	% RSD	% Recovery
FI	10	5	14.072	0.84	96.120
F2	10	10	18.817	0.99	98.770
F3	10	15	24.314	1.32	100.900
F4	10	10	19.343	1.08	97.830
F5	10	10	18.498	0.67	98.736

♦Nanoemulsion

Table 5: % Recovery data for Tablet formulation

Brand name	Label claim (mg)	Amount of pure drug added (mg)	Total estimated amount (mg)	% RSD	% Recovery
OLSAR	20	20	39.085	0.78	98.225
PINOM	20	20	39.348	0.97	98.415

Limit of detection and limit of quantification[13]

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the assessable result. LOD was calculated using the following formula

$$LOD = 3.3\frac{\sigma}{S}$$

Where, S = slope of calibration curve, σ = standard deviation of the response

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a result that can be accurately quantified. LOQ was calculated using the following formula

$$LOQ = 10\frac{\sigma}{S}$$

Where, S = slope of calibration curve, σ = standard deviation of the response.

RESULTS AND DISCUSSION

The objective of this study was to develop an efficient method for the detection of olmesartan medoxomil in various formulations by using a safer solvent by UV-Visible spectrophotomerty. The concentration in the range of 5-30 µg/ml of working standard and sampling wavelength of 257.8 (λmax of olmesartan medoxomil) gave optimum accuracy, precision, economy, safety, and sensitivity for this method. The proposed method was successfully applied to the determination of olmesartan medoxomil in the commercially available (tablet) and laboratory prepared formulations and the results are shown in table 2.

Table 6: Results from validation and system suitability study

Parameter	Value
LOD	2.0733
LOQ	6.28286
Interday precision (n=3)	0.5043 ± 0.873 - 1.4374 ± 0.432
Intraday precision (n=3)	0.05228 ± 0.274- 1.5869 ± 0.401
Linearity	5-30 µg/Ml
Standard deviation	0.347

These methods were validated as per ICH guidelines. A standard calibration curve of the drug was constructed by plotting absorbance versus concentration. Linear absorbance versus concentration gave equation Y= 0.360x + 0.054 with a correlation coefficient of 0.9990. Beer's law obeyed over the concentration range 5-38 µg/ml. The limit of detection (LOD) and limit of quantification (LOQ) were calculated to be 2.0733 and 6.28286 µg/ml. The linear regression equation with correlation coefficient of 0.9990 indicates a good linearity between absorbance and concentration in the range of 5-30 µg/ml. The value of percentage relative standard deviation less than 2% and low percentage range of error confirm the high degree of precision and accuracy of the proposed method. To examine the absence of either positive or negative inference of the excipients used in the formulations recovery studies were carried out by addition of known quantities of standard drug solution to preanalyzed sample at different concentration levels and the determination was repeated.

Result of formulation analysis and precision study are summarized in table. 6 indicated that method is precise. % Recovery (%RSD) was found within the range that is less than 2% for a method to be precise.

CONCLUSION

Being simple, rapid, sensitive, safe, accurate and economical, the method can be recommended for the routine determination of olmesartan medoxomil formulations. This is also first report of UV-visible spectrophotometric determination of olmesartan medoxomil using ethanol (class 3 solvent) in pharmaceutical formulations.

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