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Rapid and selective UV Spectrophotometric method for the analysis of Olmesartan medoxomil in bulk and dosage form.

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Abstract

A new UV spectrophotometric method was developed for quantitative evalution of Olmesartan medoxomil preparations. The UV detector was set at 256nm. Beers law is obeyed in the concentration range of 2.0 -14.0 µg/ml. The method was found to be selective, linear, accurate and precise in the specified ranges. Intra and interday variability for the method were < 2% relative standard deviation common excipients used as additives in pharmaceutical preparations do not interfere with the proposed method. This method was successfully used for quantification of Olmesartan medoxomil in pure form and in pharmaceutical preparations.

Keywords: Olmesartan medoxomil, UV-Spectrophotometry, Recovery, Validation.

Introduction

Olmesartan medoxomil (OLM) is a prodrug. It is hydrolyzed to Olmesartan during absorption from the gastrointestinal tract [1–3]. Olmesartan is a selectiveAT1 subtype angiotensin II receptor antagonist. OLM is described chemically as 2, 3-dihydroxy-2-butenyl4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1Htetrazol-5ylphenyl) benzyl] imidazole -5-carboxylate, cyclic 2,3-carbonate [4]. There is no reference for determination of this drug in both bulk and dosage forms in official compendia. A literature survey reveals that several methods were reported for the estimation of OLM in plasma, serum and tablets by liquid chromatography.[5-7].The use of LC hyphenated techniques for identification of degradation products in stressed tablets of OLM was published in.[8] OLM has been determined in biological fluids using LC coupled to fluorescence and tandem mass spectrometry[9-11]. There are also reports on capillary electrophoresis for the quantitative determination of this drug in coated tablets.[12] However, only one UV spectrophotometric method is reported for the analysis of OLM in pharmaceutical dosage forms [13]. Therefore, it is a necessity to develop a new and simple method. Therefore, in the proposed work, a successful attempt has been made to develop analytical method with due consideration of accuracy, sensitivity, rapidity, economy.

Experimental

Instrumentation

A JASCO UV- Vis spectrophotometer 630 with matched quartz cells of 1cm optical path length was used for spectrophotometric measurements were performed at 20±0.1 ^{0}C.

Materials and Reagents

All chemicals used were of analytical grade. OLM reference substances (99.9%) were kindly provided by Cipla Pharmaceutical Ltd, Mumbai, India and the commercially available tablets were purchased from local market.

Determination of λmax

Weighed amount of OLM was dissolved in methanol: water (10:90) to obtain a 100 µg/ml stock solution. Absorption maxima was studied by diluting the above solution to 20 µg/ml and scaned from 200- 400 nm

Standard stock solutions of OLM (reference substance)

Prepared by dissolving 10mg OLM reference substance in methanol 10mg and volume was made up with distilled water in a 100ml volumetric flask (100 µg/ml).

Linearity and calibration

The aliquots standard stock solution was diluted serially with water to obtain the concentration range of 2.0-14.0 µg/ml. A calibration curve for OLM was obtained by measuring the absorbance at the λmax 257nm. Statistical parameters like the slope, intercept, co-efficient of correlation, Beer's law, Molar Absorptivity, Sandell's sensitivity were determined.

Assay

Twenty tablets of OLM were weighed; average weight was determined and powdered in glass mortar. Amount equivalent to 10 mg of OLM was transferred to 100ml volumetric flask, dissolved in 10ml of methanol, sonicated and made up the volume with distilled water to obtain a concentration of 100 µg/ml. This solution was then filtered through whatmann filter paper no.41. From this filtrate, 2ml was withdrawn and transferred to 10ml volumetric flask, volume was adjusted to the mark and absorbance was recorded against distilled water as a blank at 257 nm (Table -2)

Accuracy

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i.e. 80%, 100%and 120%.To the preanalysed sample solution a known amount of standard drug solution was added at three different levels, absorbance was recorded. The % recovery was then calculated as % Recovery = [(A-B)/C] 100, where A is total amount of drug estimated; B is amount of drug found on preanalysed basis; C is amount of pure drug added to formulation(Table-3)

Precision

Precision of the method is studied as repeatability, intra-day and inter-day precision. Repeatability was determined by analyzing OLM (8µg/ml) for six times (Table 4).Intra- day precision was determined by analyzing the 6,8 and10 µg/ml of OLM for three times in the same day. Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days (Table 5). In intermediate precision study, % RSD values were not more than 2% in all the cases.

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogeneous slot by two analyst using same operational and environmental conditions (Table 6)

Limit of detection and Limit of quantitation

Limit of detection (LOD) and Limit of quantitation (LOQ) were determined by using the formula based on standard deviation of the response and the slope. Limit of detection (LOD) and limit of quantitation (LOQ) were calculated by using the equations LOD = 3 /S and LOQ= 10 /S, where is standard deviation of intercept, S is slope of the line. (Table 1)

Results and discussion

The absorption spectrum of the final solution exhibits an absorption peak at 256nm (figure2).linearity of the method was observed in the expected concentration the range of 2.0-14.0 µg/ml. Stastical analysis of the calibration curve was done and the results are summarized in (Fig 3). The correlation co-efficient (r^2 = 0.9998) shows the validity of beers law. The proposed method was applied to pharmaceutical formulation and percent amount of drug estimated was found in good agreement with the label claim. The excipients used in the pharmaceutical preparation do not interfere in this analysis. The recovery experiment was carried out at three different levels i.e., 80%, 100% and 120%. The percentage recovery was found to be in the range 99.9-100.1; the low values of % RSD are indicative of accuracy and reproducibility of the method .The precision of the method was studied as an intra-day and inter-day and repeatability. Ruggedness of the proposed method was studied with the help of two analyst. Repeatability f the samples also carried out which show low values of % RSD. The limits of Detection and Quantification for OLM with a lower concentration were 0.193 and 0.640µg/ml respectively, values which are under the lowest expected concentrations in the samples.

Conclusion

The present study was undertaken with an objective of developing simple, sensitive and reliable analytical method like UV-Spectophotometry for estimation of OLM in tablet dosage form. The method has sufficiently good accuracy, precision and permitted as a cost effective as other methods. The analytical method is simple, sensitive, rapid and specific. Further it can be conveniently employed for the routine analysis and the quality control of OLM in tablet formulation.

Acknowledgements

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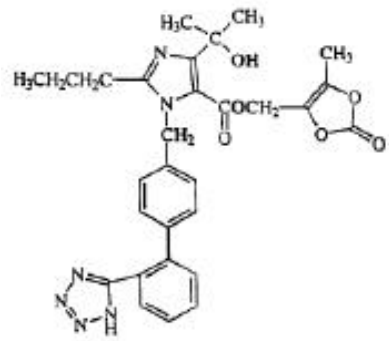

Fig.1 Chemical structure of Olmesartan Medoxomil

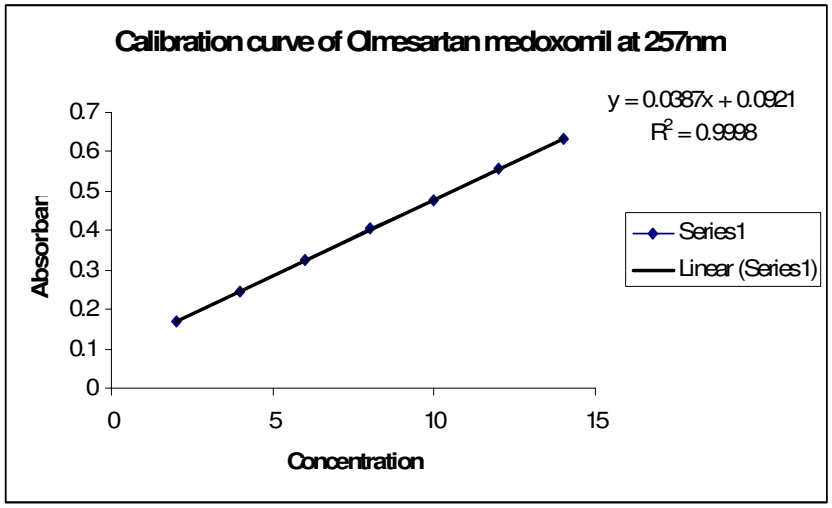

Fig 2 Calibration curve of Olmesartan medoxomil at 257nm

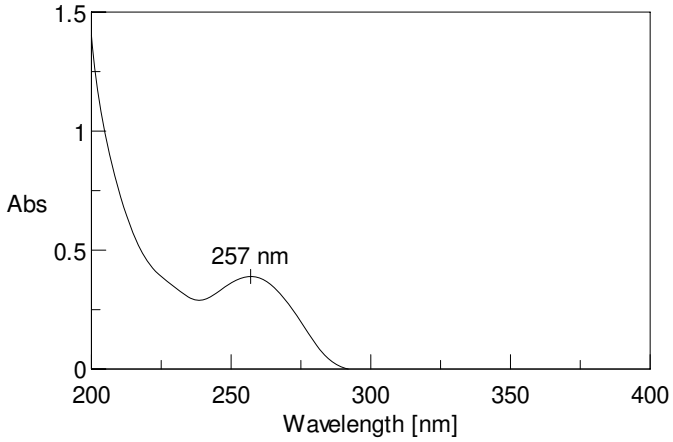

Fig 3 Scan of Olmesartan medoxomil in distilled water

Table 1 Optical characteristics and regression equation for OLM

Parameter	value
Λ max (nm)	257
Beer's range (µg/ml)	2-14
Regression equation	Y= 0.0387x + 0.0921
Intercept (a)	0.0921
Slope(b)	0.0387
Correlation co-efficient (r2)	0.9998
Molar Absorptivity (lit/mole/cm)	2.8002×10^{4}
Sandells sensitivity (µg/sq.cm/0.001	0.01995
LOD(µg/ml)	0.1938
LOQ(µg/ml)	0.6459

Table 2 Assay of OLM tablet 20mg

Formulation	Label claim(mg)	% Claim found	% RSD
F-I	20	99.8	0.112
F-II	20	100.1	0.29

* Mean of five observations

Table 3 Results of Recovery study for Olmesartan medoxomil tablets 20mg

Labeled amount (mg)	Amount of drug added%	Amount of drug recovered(mg)	Percentage recovery	%RSD
20	80	36.01	100.05	0.06
20	100	39.99	99.96	0.18
20	120	44.02	100.1	0.20

*Mean of three observations

Table 4 Results of repeatability studies

Label Claim(mg)	Amount taken (µg/ml)	Amount found %	% RSD
20	8	99.9±0.42	0.42

* Mean of six observations

Table -5 Intra –day and Inter-day precision

Concentration(µg/ml)	Intra-day	%RSD	Interday	%RSD
6	5.97± 0.02	0.31	5.87±0.03	0.41
8	8.02± 0.07	0.62	8.01±0.09	0.80
10	10.08±0.23	1.45	10.81±0.21	1.35

* Mean of three observations

Table -6 Results of Ruggedness study

Label claim	Analyst I Amount found %	% RSD	Analyst II Amount found %	% RSD
20mg	99.48±0.62	0.65	99.46±0.73	0.73