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Spectrophotometric Estimation of Olmesartan Medoxomil in Tablet Dosage Form with Stability Studies

Prabhakar K. Verma[1*], Vipan K. Kamboj[1], Sudhir Ranjan[2]

[1]DEPARTMENT OF PHARMACEUTICAL SCIENCES, M.D. UNIVERSITY, ROHTAK, HARYANA-124001, INDIA
[2]DEPARTMENT OF BOTANY, S.D.A.N. COLLEGE, JEHANABAD, BIHAR-804401, INDIA

**Corres. Author: vermapk422@rediffmail.com, vk.kamboj123@gmail.com*
Mob. No. +919992581437, Fax: 01262272535

ABSTARCT : A simple accurate and precise spectroscopic method was developed for determination of Olmesartan medoxomil in tablets. The dA/dλ was measured at 257nm for Olmesartan and calibration curves were plotted as dA/dλ versus concentration respectively. The method was found to be linear from 2-20µg/mL for Olmesartan ($r^2 \geq 0.9979$) at 257nm. The within day and between day variation showed coefficient of variation (CV%) valued less than 1.6% for drug. The limit of detection was 0.13 µg/mL for Olmesartan. Results of analysis for method were validated statistically and by recovery studies. The proposed method are economical and sensitive for the estimation of Olmesartan in bulk drug and its tablet dosage form.
Keywords: Olmesartan medoxomil, Methanol, Tablet dosage form.

INTRODUCTION

(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl5-(2-hydroxypropan-2-yl)-2-propyl-3-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methyl]imidazole-4-carboxylate Olmesartan medoxomil (OM) (5-methyl-2-oxo-1,3-dioxolen-4-yl) methoxy-4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)-phenyl]phenyl} methylimidazol-5-carboxylate, is a potent and selective angiotensin AT1 receptor blocker[1](fig. 1). It has been approved for the treatment of hypertension in the United States, Japan and European countries. The drug contains a medoxomil ester moiety and is cleaved rapidly by an endogenous esterase to release the active metabolite Olmesartan[2].

The literature survey revealed that few analytical methods are reported for estimation of Olmesartan medoxomil in biological fluids and in combination with other drugs in tablet dosage form. There is no analytical method reported for estimation of Olmesartan medoxomil in bulk and tablet dosage form[3-13]. The aim of present study is the development of a simple, accurate and sensitive spectroscopic method for the determination of Olmesartan in bulk and tablet dosage form. The proposed method was validated as per International Conference on Harmonization guidelines (ICH guidelines).

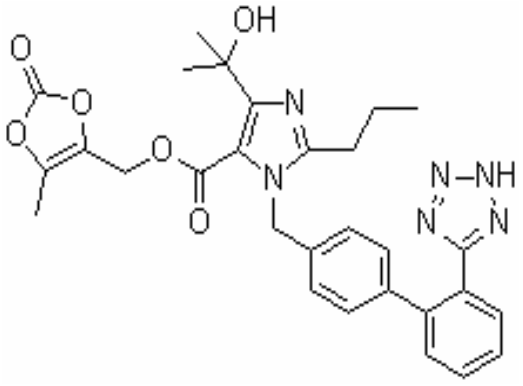

FIGURE I: Structure of Olmesartan medoxomil

MATERIAL AND METHODS

CHEMICAL AND REAGENTS:

OM were a kind gift from Blessing Pharmaceuticals India, Nagpur, Maharashtra, India. All the chemicals and solvent used in the present study were procured from E-merck, Qualigens, Rankem (Mumbai, India). Commercial pharmaceuticals preparation (OLMEZEST® AM tablets, Sun Pharma India, Batch no GK-61246) was purchased from the local pharmacy. The declared content of tablets were Olmesartan medoxomil 20mg per tablet.

INSTRUMENTATION:

Spectroscopic analysis was carried out on a UV 2401 PC (Shimadzus) double beam UV/Visible spectrophotometer. The absorption spectra were recorded over the wavelength range of 200 to 400 nm, against solvent blank in quartz cuvets with 1 cm diameter. The wavelength selected was 257 nm.

STANDARD AND CALIBRATIONS:

Standard stock solutions of a concentration of 1.0 µg/mL of Olmesartan were prepared using methanol. Appropriate volume of stock solution was diluted with methanol to obtain concentration of 100 µg/mL of Olmesartan. Further dilutions made from these solutions in same solvent to get linearity concentration 2-20 µg/mL of Olmesartan.

LINEARITY AND RANGE:

Calibration curves were constructed by analysis of working standard solution of Olmesartan with at least 5 different concentration ranges 2 to 20 µg/mL. Each concentration was analyzed in triplicate. The absorption value of Olmesartan was measured at 257nm. A calibration curve was plotted absorbance on Y-axis and concentration on X-axis. The relation between drug concentration (X) and its corresponding absorbance (Y) is expressed by the equation:

$Y = mx+b$

Where m is slope and b is intercept.

ACCURACY AND PRECISION:

To establish the reliability of proposed method 10 µg/mL of Olmesartan and 10, 20, 30 µg/mL of Olmesartan plus in each 10 µg/mL were prepared respectively and analysed as discussed above. Precision of analytical method was calculated by within day and between day. Accuracy of the proposed method was ascertained on the basis of recovery studies performed by standard addition method.

ANALYSIS OF TABLETS:

A total twenty tablets (OLMEZEST® AM) were accurately weighed and finely powered. An accurately weighed tablet powder equivalent to 5mg of OLM was transferred in 50 mL volumetric flask and 25 mL methanol was added. The flask content was sonicated for 15 min and volume was adjusted to 50 mL with methanol solution obtained was filtered through whatman no 42 filter paper and diluted with methanol to obtain the final concentration of 10 µg/mL of OLM. The concentration of Olmesartan in tablets were calculated using the following methods:

Method 1: Using absorpitivity A (1% 1cm)

% Estimation = At × DT × Avg Wt / A (1%cm) × LC × Wt taken

Where,
At= Absorbance of sample,
DF= Dilution Factor,
LC= Labeled claim A (1%; 1cm) –absorptivity

Method 2: Direct comparison method

% Estimation = At × Conc Std × Avg Wt × 100 / Astd × LC × Wt Taken

Where
At= Absorbance of sample,
Astd= Absorbance of standard,
LC-=Labelled claim

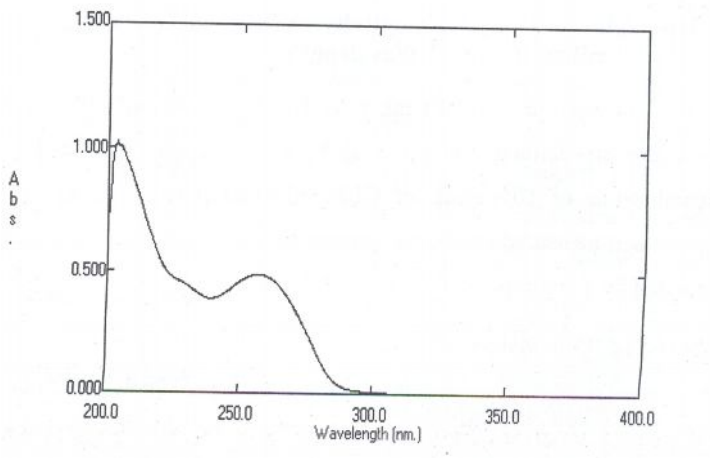

FIGURE II: Absorption spectra for Olmesartan (10 µg/mL) in methanol

RESULTS AND DISCUSSION

The UV spectra of Olmesartan were shown in fig 2.
The wavelength selected was 257nm (**TABLE I)**.

VALIDATION:

ACCURACY AND PRECISION:

Accuracy of the proposed method was determined by using standard addition method. The mean recoveries and SD are illustrated in **TABLE II and III**. Data of these tables showed a good accuracy and precision over the entire concentration range. The within day and between day variation showed coefficient of variation (CV%) values less than 1.5% for all selected concentration rule. The data indicate that the proposed UV spectroscopic method is highly precise during one analysis and between different run and it can be adopted for routine analysis of Olmesartan medoxomil in tablet dosage form. The result obtained from the recoveries of drugs showed excellence accuracy as shown in **TABLE II-V**. No interference were observed from the excipent in the amounts, which are commonly present in tablet dosage form. Study of stability of Olmesartan in solution during analysis showed that analytes were stable at least for 3 days in solution.
The tablet sample of OLM were analyzed by adopting proposed method by two different spectrometer to instrument variation and results are shown in **TABLE IV**.
The tablet sample of OLM was analyzed using proposed method on three different days **(TABLE V)**.

SPECIFICITY:

Accurately weighed six quantities of finely powdered tablet equivalent to about of 5 mg OLM were transferred to six different 50 mL volumetric flasks. All these solution were stored for 24 h under following different condition (**TABLE VI)**.

STABILITY STUDIES:

Stability study was performed using standard stock solution of bulk drug and tablet powder. The solution were stored for one month at 40 □ c and secondly at room temperature prevented from light in methanol and acetonitrile. During this time period UV absorbance of these solution noted periodically and compared with freshly prepared solution and it was found from the spectra of drug and marketed formulation, stable for at-least one month.

CONCLUSION

A rapid simple and specific UV spectroscopic method has been developed for the estimation of Olmesartan medoxomil in tablet and bulk dosage form. This can be useful for the routine drug analysis in quality control laboratories.

Table I: RESULTS OF ESTIMATION OF OLMESARTAN MEDOXOMIL IN TABLETS OLMEZEST TABLET (Avg Wt 154.01 mg for 20 mg of OLM)

Sr No	Sample Weight (mg)	Std Conc (µg/mL)	Abs at 257nm % drug estimation			
			Std	Sample	Method 1*	Method 2*
1	39.25	10	0.4898	0.4888	100.27	100.12
2	38.82	10	0.4898	0.4892	101.16	101.23
3	38.41	10	0.4898	0.4885	100.25	100.13
4	39.01	10	0.4898	0.4876	100.17	100.12
5	38.16	10	0.4898	0.4902	101.29	101.06
				Mean	100.19	100.13
				±SD	1.3412	0.9406
				% RSD	1.3409	0.9389
OLMESAR TABLET (Avg Wt 327.10 mg for 20 mg of OLM)						
1	80.98	10	0.4898	0.4887	99.95	99.45
2	80.99	10	0.4898	0.4890	98.78	98.68
3	80.76	10	0.4898	0.4883	101.02	101.03
4	81.12	10	0.4898	0.4889	99.83	99.63
5	81.16	10	0.4898	0.4901	100.01	100.02
				Mean	99.67	99.87
				±SD	1.1705	0.9568
				% RSD	1.1786	0.9567

*Each value is mean of five observations

Table II: RESULTS OF RECOVERY STUDY
OLMEZEST TABLET (Avg Wt 154.01 mg for 20 mg of OLM

Sr no	Sample wt +Pure drug added (mg	Std conc (µg/mL)	Abs at 257 nm		% Recovery	
			Standard	Sample	Method 1*	Method 2*
1	19.67±1.50	10	0.4898	0.4888	99.45	99.67
2	19.03±2.50	10	0.4898	0.4891	100.02	100.13
3	19.95±3.50	10	0.4898	0.4876	100.06	100.78
				Mean	100.07	100.18
				±SD	0.1589	0.8998
				% RSD	0.9201	0.8988
OLMESAR TABLET (Avg Wt 327.10 mg for 20 mg of OLM)						
1	40.96±1.50	10	0.4898	0.4878	99.18	99.23
2	41.13±2.50	10	0.4898	0.4876	101.13	100.79
3	40.89±3.50	10	0.4898	0.4887	101.24	100.33
				Mean	100.48	100.06
				±SD	1.1701	0.9897
				% RSD	1.1499	0.9979

*Each value is mean of five observations

Table III: RESULTS OF PRECISION STUDIES BY DIFFERENT ANALYST

Different analyst	% Drug Estimation			
	Olmesar		Olmezest	
	Method 1*	Method 2*	Method 1*	Method 2*
I	101.16	100.25	100.23	10139
II	99.75	99.89	99.13	100.32
III	99.08	99.78	99.09	99.29
Mean	100.76	100.79	100.13	100.19
±SD	0.8235	0.8946	0.8347	1.0872
% RSD	0.8313	0.8856	0.8342	1.0912

*Each value is mean of five observation

Table IV: RESULTS OF PRECISION STUDIES BY DIFFERENT UV SPECTROPHOTOMETER

Sr no	UV Spectrophotometer	Observation	% drug Estimation			
			Olmesar		Olmezest	
			Method 1*	Method 2*	Method 1*	Method 2*
1	UV1601 Shimdazu	1	100.72	100.28	101.23	101.49
		2	100.23	100.16	101.10	100.12
2	UV2401 Shimdazu	1	99.98	98.85	99.62	99.82
		2	99.89	102.31	99.65	98.79
		Mean	100.13	100.98	99.98	0.8827
		±SD	0.3412	0.852	0.7567	0.8912
		% RSD	0.3401	0.8469	0.7212	0.8893

*Each value is mean of five observations

Table V: RESULTS OF PRECISION STUDIES ON INTERDAY AND INTRADAY

Sr no	Observation	% Drug Estimation			
		Interday		Intraday	
		Olmesar Method 1*	Olmezest Method 2*	Olmesar Method 1*	Olmezest Method 2*
1	I	101.26	101.29	100.32	100.26
2	II	100.16	101.84	100.29	101.52
3	III	100.45	99.89	100.01	101.23
	Mean	100.29	101.03	100.45	101.29
	±SD	0.6021	1.4023	0.8412	0.7342
	% RSD	0.6012	1.4121	0.8536	0.7353

*Each value is mean of five observations

Table VI: RESULTS OF SPECIFICITY STUDIES

Sr no	Treatment	Weight of Tab (mg)	Conc (µg/mL)	% Drug Estimation	
				Method 1*	Method 2*
1	Normal	A_1 37.99 A_2 80.98	10 10	101.30 100.42	100.29 100.43
2	0.1N NaOH	A_1 39.01 A_2 81.02	10 10	95.29 94.78	94.29 95.64
3	0.1N Acid	A_1 38.04 A_2 80.72	10 10	94.29 94.73	93.25 94.16
4	3% H_2O_2	A_1 40.02 A_2 40.04	10 10	102.22 103.11	102.12 102.36
5	60 □ c Heat	A_1 38.29 A_2 81.02	10 10	100.15 102.26	102.56 101.38
6	UV	A_1 37.99 A_2 81.72	10 10	106.29 107.82	107.32 107.24

*Each value is mean of five observations
A_1 Olmezest Tab, A_2 Olmesar Tab

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