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Development, validation and stability study of UV-VIS spectrophotometric method for determination of olmesartan medoxamil in bulk and pharmaceutical dosage forms

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ABSTRACT

A Simple, fast & reliable spectroscopic method has been developed for development, validation & stability study of OLMESARTAN MEDOXAMIL in the pharmaceutical dosage forms. The quantitatitive determination of the drug was carried out by using the UV spectrophotometric method and detection was carried out at 254nm. This method was validated as per ICH guidelines and can be used for determination of Olmesartan Medoxamil in the pharmaceutical dosage forms.

Key words: Olmesartan Medoxamil, uv-vis spectrophotometer, bulk and pharmaceutical dosage form, validation.

INTRODUCTION

Olmesartan Medoxamil,chemically, 2,3-dihydroxy-2-butenyl4-(1-hydroxy-1-methylethyl)-2-propyl-1-[p-(o-1H-tetrazol-5-ylphenyl)benzyl]imidazole-5-carboxylate, cyclic 2,3-carbonate having Molecular formula:- $C_{29}H_{30}N_6O_6$ is an ACE inhibitor used in treatment of hypertension, by blocking the binding of angiotensin II to the AT_1 receptors in vascular muscle so as it reduces vasoconstriction and secreting of aldosterone which lowers blood pressure by producing vasodilatation. Analytical techniques like uv-vis spectrophotometers have been developed for the assay of in pharmaceutical dosage form. In present study, an attempt has been made to develop a simple and efficient uv-vis spectrophotometric method for determination of olmisartan medoxamil in pharmaceutical dosage form.

MATERIAL AND METHODES

Instruments

1. SHIMADZU-UV-1700 PHARMASPEC UV-VIS Spectrophotomètre.
   spectral band width of
   Wavelength accuracy of
i. Matched quartz cells of 10mm Optical path length.
2. Afcoset ER 200A electronic balance.
3. SIGMA-200/A SUPER balance.
4. Ultra Sonicator (ENERTECH).
5. Borosil glass wares.

Solvents

1. Methanol.
2. Distilled water.

Scanning and determination of maximum wavelength (λ_{max})

In order to ascertain the wavelength of maximum absorbance (λ_{max}) of the pharmacodynamic agents solutions of particular concentrations of drugs 100 mg/ml and 10 mg/ml in methanol were scanned within the wavelength range of 200-400nm against a corresponding reagent blank. The resulting spectra were presented in (fig-1). The absorption curves showed characteristic absorption maxima at 254nm for olmesartan medoxamil.

Preparation of Standard solution

An accurately weighed 100mg of Olmesartan Medoxamil was transferred to 100mL volumetric flask. It was dissolved in 100mL of methanol and then volume was adjusted to 100mL with distilled water to obtain a stock solution of drug of concentration of 1mcg/mL.Working standard solution of Olmesartan Medoxamil were prepared by taking 10ml from stock solution and made the volume unto 100ml with methanol to get 100mg/mL of Olmesartan Medoxamil. The absorbance measured at 254nm for solution against methanol.(Table-1)

Preparation of Sample solution

Twelve tablets of Olmesartan Medoxamil of same batch were weighed and crushed into fine equivalent powder. An accurately amount of 10mg equivalent powder of Olmesartan Medoxamil was transferred 50ml volumetric flask and dissolved in methanol to get 10mcg/mL solution. Sonicater was used for 15min to complete dissolution. Then the solution was filtered and diluted with methanol to get a concentration within the linearity

rang and measured the absorbance at 254nm against methanol. Then 1ml ,1.5ml and 2ml were taken and made up to 10ml.This solution were analyzed and the amount of was determined. The result were estimated by using the standard graph (fig-2)

STABILITY STUDY

Stability testing is a routine procedure performed on drug substances and products. It is involved at various stages of product development. Testing under more gentle conditions (those recommended for long-term shelf storage), and slightly elevated temperatures, can be used to determine a product's shelf life and expiration dates. In these types of studies, the product is analyzed at intervals for various parameters, which may include assay of the active ingredient, measurement of known degradation products, dissolution time, appearance, etc. Additionally, samples from production lots of approved products are retained for stability testing in case of product failure in the field. Retained samples can be tested alongside returned samples to ascertain if the problem was manufacturing or storage related.

Stress degradation studies and results:

Photolytic degradation

Specific amount of bulk drug was weighed accurately & putted into the UV chamber for three days. After three days 10mg drug was weighed and made 1000 ppm solution with specified solvent i.e. methanol. Then an appropriate concentration was prepared & absorbance was measured in UV spectrophotometer as shown in (fig-3)

Thermal degradation

A specific amount of Bulk drug was taken in a Petridis which was previously cleaned & dried then the Petridis along with bulk drug was put it into the oven for 48 hrs then it was taken out & weighed 10mg then prepare 1000ppm solution with Methanol. After this a required concentration was made & absorbance was measured in UV spectrophotometer. (fig-4)

Acid degradation

0.1N HCLwas taken in a 10 ml volumetric Flask then accurately weighed 10mg bulk drug was dissolved in it. To make soluble the drug, few drops of Methanol was added then volume is made by 0.1N Hcl. Then the solution was refluxed for 4 hrs then from this solution 1ml was taken & the volume was made with Methanol.

After this absorbance is measured by scanning the prepared Solution of required concentration in U.V Spectrophotometer.(fig05)

Alkali Degradation

First of all 0.1N NaoH was prepared. Accurately weighed 10mg bulk drug was taken in 10ml volumetric flask. Then the volume was made with 0.1N NaoH. Then this solution was refluxed for 4 hrs then from it 1ml was taken out and volume was made. Then absorbance was measured by scanning the prepared solution of required concentration in a U.V spectrophotometer.(fig06)

Oxidation with H_2O_2

Specific amount of bulk drug was weighed accurately, 2-3 drop of Methanol was added to make the drug soluble then the volume was made up by 3% H2O2 & kept in a dark place for 42 hrs, the sample was taken out & then the required concentration was prepared & then it was scanned in U.V spectrophotometer.(fig07)

VALIDATION OF PROPOSED METHOD

Linearity study

A calibration curve was constructed at optimum experimental conditions using absorbance value versus concentration in the range 10ppm to 90ppm.it has shown linear relationship with the regression equation Y=0.047x-0.057, where 'Y' is the intercept at wavelength 254nm and 'x' is the concentration of the sample in µg/ml high value of correlation coefficient (r=0.999) indicates good linearity and adherence of the method to Beer's law.

Table-1.

Conc. Of drug (µg/ml)	Absorbance (n=6)	C.V
0	0	0
10	0.414	0.57
20	0.89	0.26
30	1.346	0.01
40	1.79	0.19
50	2.30	0.12

60	2.69	0.09
70	3.24	0.10
80	3.635	0.06
90	4.250	0.10

Table.2

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed concentration of the drug with in the beer's range and finding out the absorbance by the proposed method. From this absorbance mean, Standard deviation, %R.S.D was in table.2

CONCENTRATION OF DRUG (mcg/ml)	OBSERVATION CONCENTRATION OF DRUG (mgm/ml)			
	INTER DAY		INTRADAY	
	MEAN (N=6)	COEFFICIENT OF VARIATION	MEAN (N=6)	COEFFICIENT OF VARIATION
Olmesar-20mg(30)	1.330	0.25	1.299	0.002
Olmat-20mg(30)	1.320	0.26	1.310	0.26

Accuracy / Recovery Study

To determine the accuracy of the proposed method recovery studies were carried out adding different amounts (80%, 100%, and 120%) of the bulk sample of *Olmesartan Medoxamil* to the previously analyzed solution of formulation of concentration 20 mg/ml. The results were shown in table no 3.

Table-3

AMOUNT OF DRUG ADDED (MGM) TO SOLUTION OF FORMULATION.	RECOVERY FORM TABLET FORMULATION	
	MEAN (+SD) AMOUNT (mgm) FOUND	MEAN(±SD)% RECOVERY (N = 6).
16	16 ± .016	96.16 ±.016
20	20 ±.020	97.75 ±.020
24	24 ±.024	98.1 ±.024

Limit of detection and Limit of Quantification

Limit of detection (LOD) and Limit of quantification (LOQ) of Olmisartan Medoxamil was calculated by using equation given in the ICH guidelines. The result of the same is shown in the table no.4

TABLE 4.

Sl.no	Parameters	SD*	**b	Formula	Calculation
	LOD	0.043021	026	$3.3(S.D/b)$	5.4603
	LOQ	0.043021	026	$10(S.D/b)$	16.5465

S.D*=Standard Deviation, b**= slop (from calibration curve)

RESULTS AND DISCUSSION

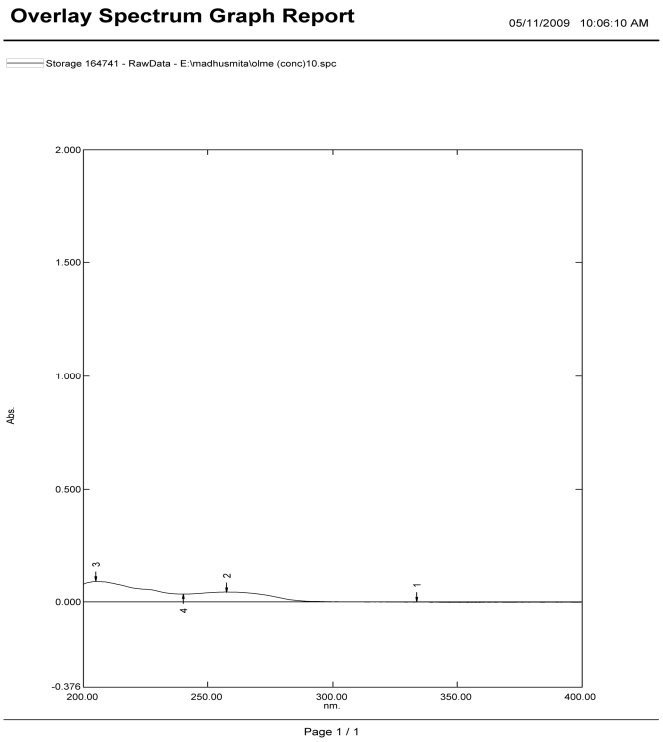

Fig-1 Determination of max.wavelength of *Olmesartan Medoxamil* by using methanol as solvent

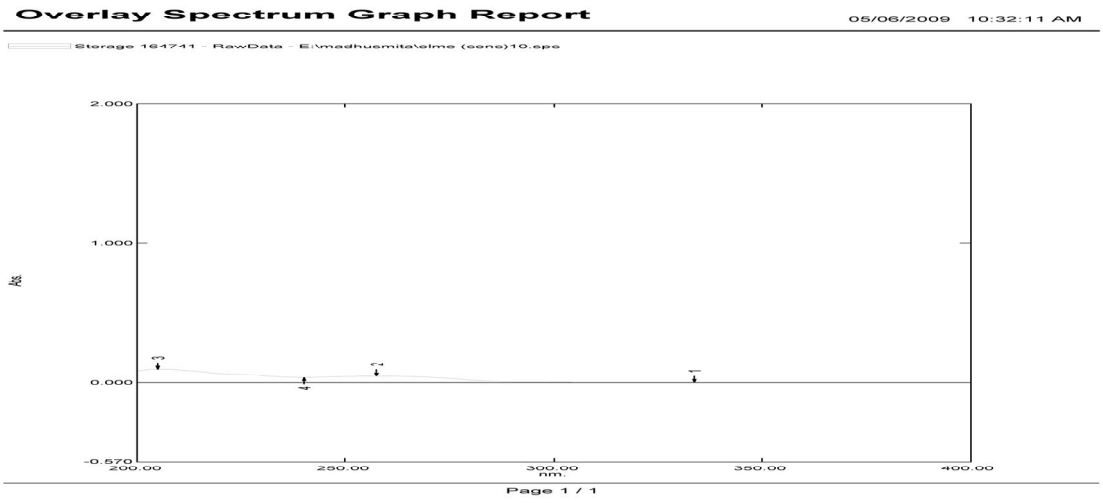

Fig-3: - Model spectra for Olmesartan Medoxamil in UV chamber at 254nm

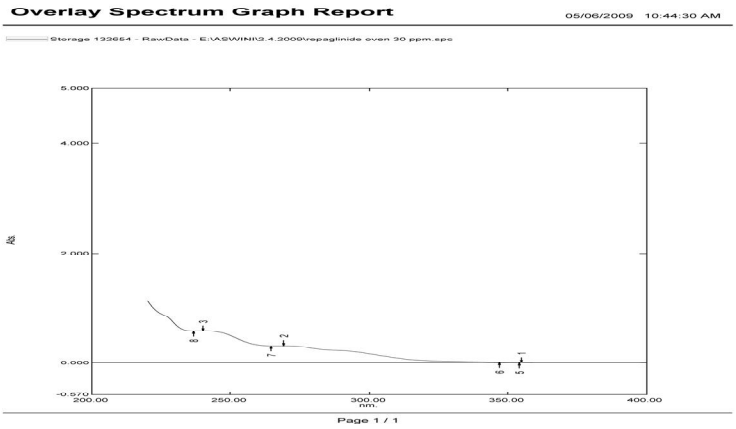

Fig-4: -Model spectra for Olmesartan Medoxamil in hot air oven at 60^0C

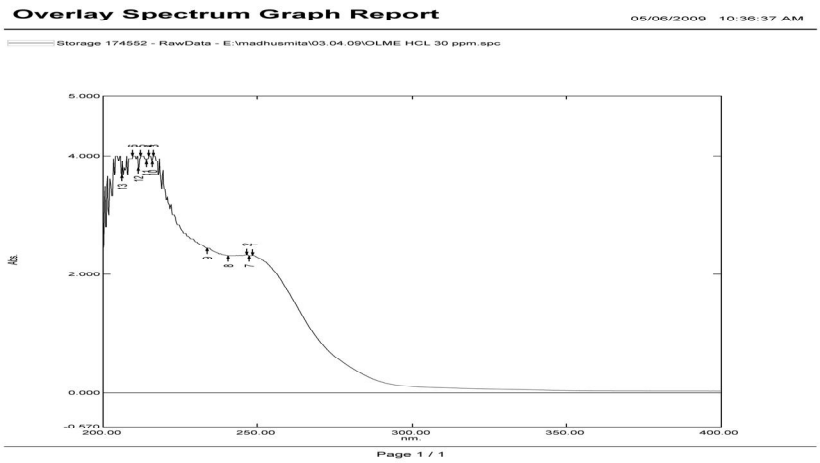

Fig-5: - Model spectra for Olmesartan Medoxamil in 0.1 N HCl

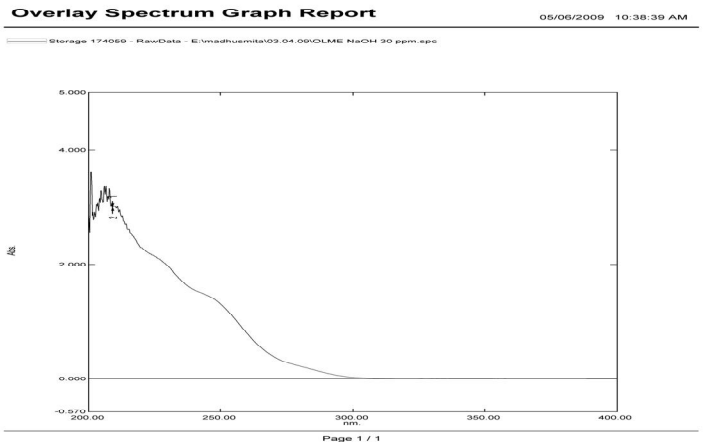

Fig-6: - Model spectra for Olmesartan Medoxamil in 0.1 NaOH

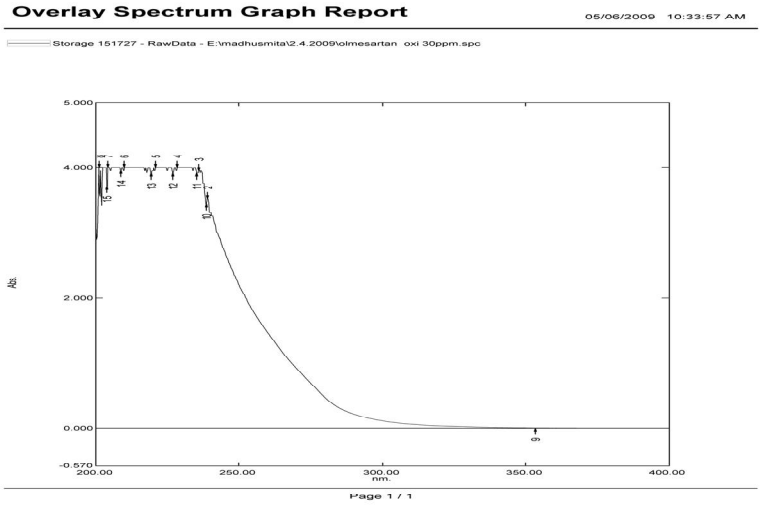

Fig-7: - Model spectra for Olmesartan Medoxamil in 3% H_2O_2

From the optical characteristics of the proposed method it was found that OLMISARTAN MEDOXAMIL obeys linearity within the concentration range of 10 – 100 mcg/ml. From the results shown in tables it was found that the % R.S.D. is less than 2% which indicates that the method has good reproducibility. From the result shown in accuracy tablet was found that the percentage recovery values of pure drug from the pre analyzed solution of the formulation were in between 96 – 98% which indicates that the method is accurate and also reveals that the commonly used excipients and additives in the pharmaceuticals formulations were not interfering in the proposed method. The study conducted shows that there is degradations of the drug under the stress condition like, Photolytic degradation, thermal degradation, acid degradation, alkali degradation and oxidation with 3% $H_2 O_2$.

Summary of Stress Degradations Results

Stress Condition	Time	% Assay Of Active Substance	% Assay of Degraded product	Mass balance
Alkali Hydrolysis (0.1N NaOH)	4 Hour	90.38	9.61%	99.99
Acid Hydrolysis (0.1N HCL)	4 Hour	137.5	37.58%	175.1
Oxidation (3% H_2O_2)	42 Hour	113.1	13.17%	126.3
Dry heat (60^0C)	42 Hour	86.9	13.01%	99.91
Photolytic degradation (254nm)	42 Hour	85.9	14.1%	100

CONCLUSION

The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulation without interference of excipients and the other additives. Hence, this method can be used for routine determination of *OLMISARTAN* in bulk samples and

pharmaceutical formulations. The proposed the method for stability study shows that there is appreciable degradation found in stress conditions of *olmisartan*

The proposed UV-Spectrophotometric method has been evaluated over the linearity, accuracy, precision, specificity, LOD and LOQ and proved to be convenient and effective for the quality control and stability studies of *olmisartan*. A new simple analytical method has been developed to be applied for the evaluation of the stability of *olmisartann* and quantify *olmisartan* and its degradation products in a solid premix dosage forms.

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