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UV-SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF AZILSARTAN MEDOXOMIL IN PHARMACEUTICAL DOSAGE FORM.

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ABSTRACT

In the present research work simple, accurate, precise Area under curve method have been developed and Validate for Azilsartan Medoxomil in Active Pharmaceutical Dosage form Azilsartan is an angiotensin II receptor antagonist used in the treatment of hypertension. U.S. Food and Drug Administration (FDA) approved Azilsartan Medoxomil for the treatment of high blood pressure in adults. This method involves calculation of integrated value absorbance with respect to wave lengths of 239nm and 259 nm respectivelyan absorption maximum was found to be at 249 nm with the solvent system methanol. The drug follows Beer law in the range of 4-14 µg/ml with correlation coefficient of 0.989. The percentage recovery of Azilsartan Medoxomil ranged from 99.9 to 100.3 % in pharmaceutical dosage form.The developed methods are validated according to ICH guidelines. Hence these methods can be used for the routine analysis of Azilsartan Medoxomil in bulk and tablet dosage form.

KEY WORDS: Azilsartan Medoxomil(AZM),Area under the Curve (AUC) Method, Validation.

INTRODUCTION

Chemically Azilsartan Medoxomil is (5-methyl-2-oxo-4-yl)methyl2-ethoxyl-1([2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-ylbiphenyl-4-yl]methyl)-1-Hbenzimidazole-7- arboxylate,with chemical formula C25H20N4O5. Azilsartan Medoxomil is a white to nearly white powder with molecular mass: 456.48g/mol.It is practically insoluble in water and freely soluble in methanol. AzilsartanMedoxomil acts by antagonizing the angiotensin II type 1 receptor. Where angiotensin II is potent vasoconstrictor; which also causes synthesis and release of

aldosterone. By blocking AT1 receptor it blocks the aldosterone and vasoconstrictor effects of angiotensin II. Azilsartan' Medoxomil has an ability to remain tightly bound to AT1 receptor for very long period of time.Azilsartan Medoxomil is used for treatment of essential hypertension.AzilsartanMedoxomil was found to be superior to olmesartan and valsartan. The literature survey revealed very few analytical methods have been reported in combination of Azilsartan Medoxomil and Chlortalidone to best of our knowledge AUC methods are not available. The objective of the present research work deals with simple, accurate, precise UV spectroscopic method using AUC method for estimation of Azilsartan Medoxomil in bulk and validated as per ICH guidelines.

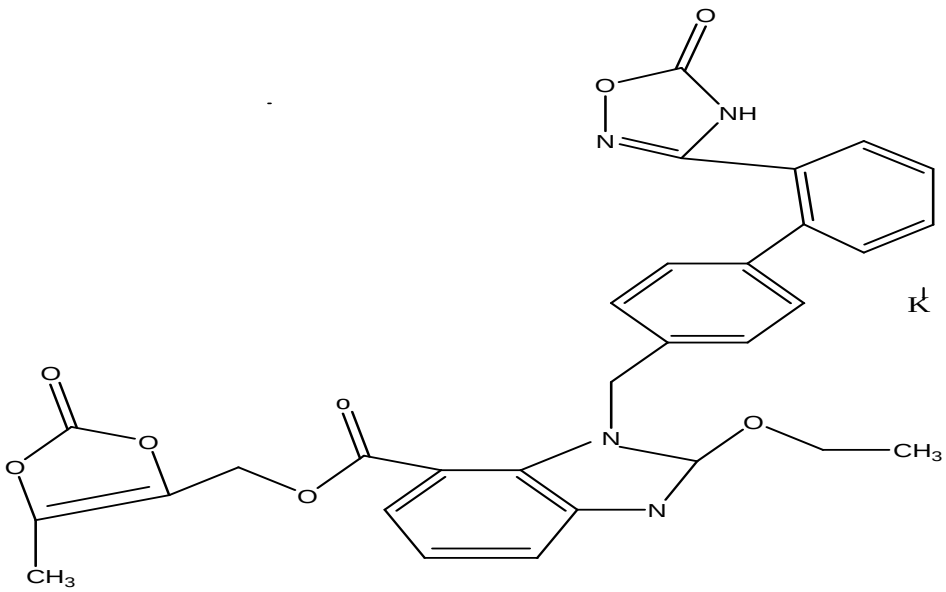

Figure 1: Chemical structure of Azilsartan Medoxomil.

MATERIALS AND METHODS

Instrumentation

A double beam UV spectrophotometer Jasco (630) with UV probe software (2.31) and 10mm matched quartz cells. Weighing balance schimadzu (220h) was used.

Chemicals and Materials

Azilsartan Medoxomil (99.76%) working Standard drug was obtained from Hetero labs ltd Hyderabad, India. Methanol of AR grade was purchased from Merck fine chemicals (Mumbai, India).

METHOD DEVELOPMENT

Calibration of proposed method

Preparation of standard stock solution

The standard stock solution of Azilsartan Medoxomil was prepared by dissolving accurately weighed 10mg in 10ml volumetric flask containing 5ml of methanol shaken for 5min then remaining volume made up with methanol. The final concentration obtained was 1000µg/mlmethanol. From the above solution working standard solution of concentration 100µg/ml was prepared. From this aliquots were prepared to get a concentration range of 4-14µg/ml.

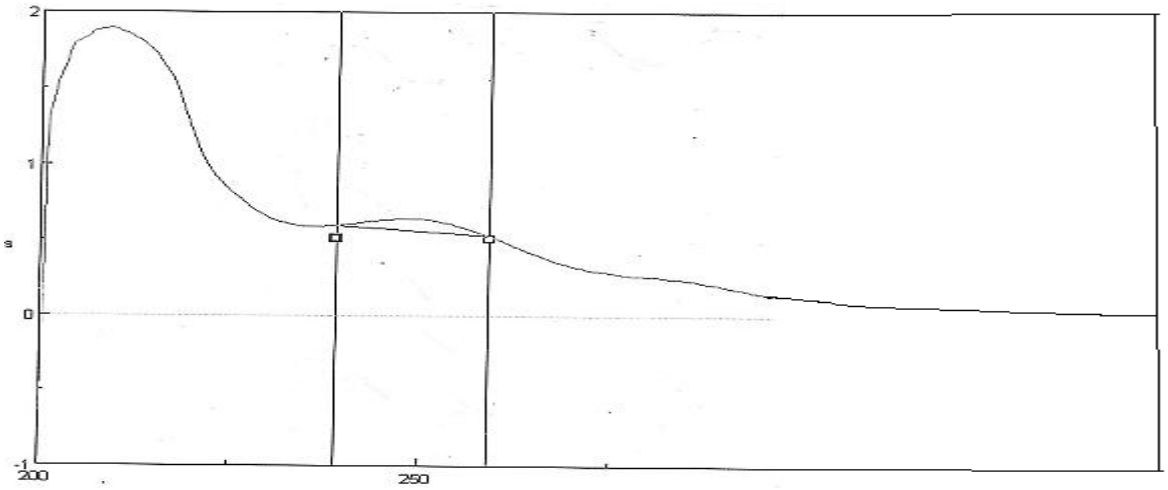

Fig. 1: Area under curve spectrum of Azilsartan Medoxomil

Calibration curve for Azilsartan Medoxomil

From the standard stock solution appropriate dilutions were made to obtain concentration in range of 4, 6, 8, 10 , 12 and 14 µg/ml. For the determination of Azilsartan Medoxomil using the area under curve (AUC) method, suitable dilutions of the working stock solutions (100 µg/ml) of Azilsartan Medoxomil were prepared methanol and scanned in the range of 200 - 400 nm. For Area under curve method, the sampling wavelength ranges from 239-259 nm. (Figure No. 1) were selected for estimation of Azilsartan Medoxomil and area were integrated between these selected wavelength range, which showed linear response with increasing concentration.

Method Validation

The methods were validated according to ICH guidelines to study linearity, precision and accuracy.

Linearity

The linearity of the proposed UV spectroscopic methods were evaluated by analyzing different concentrations of standard solutions of Azilsartan Medoxomil and by plotting Area under curve of analyte against concentrations of the analyte. Beer's law was obeyed for the methods in the concentration range of 4-14µg/ml. A good linear relationship (R2=0.9989) was observed between the concentrations of Azilsartan Medoxomil and the corresponding Area under curve. The regression analysis was made for slope, intercept and correlation coefficient values. The slope, intercept and the correlation coefficient of the drug were shown in below.Table.1

Table 1:Optical characteristics

Method Parameter	Value
Beer's limit (µg/ml)	4-14
Molar extinction coefficient (L/Mol.cm)	0.026
Correlation coefficient (r2)	0.9989
Slope (a)	0.0847
Intercept (b)	0.0941

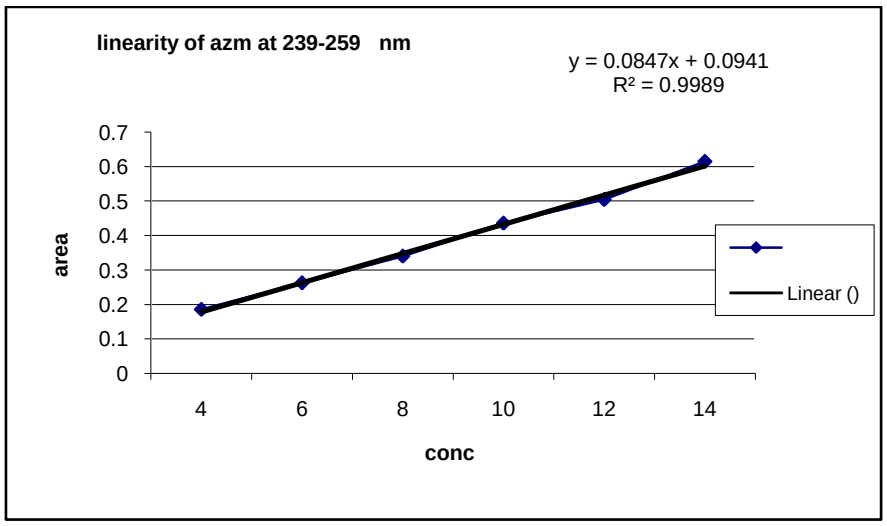

Fig. 2: Calibration curve of Azilsartan Medoxomil

Accuracy

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. The accuracy of the method was determined by performing recovery studies at three different levels of standard additions. Accuracy was checked by adding 80, 100 and 120 % amount of Azilsartan Medoxomil to pre-analyzed sample. Result are shown in Table .2

Table 2: Accuracy data of the drug

Recovery	Conc of Sample	Recovery in µg/ml	% Recovery
80%	8	7.89	98.62
100%	10	10.12	101.20
120%	12	11.99	99.91

(*=mean of three readings)

Precision

Precision is the measure of closeness of values between each concentration under same analytical conditions. It is determined by performing inter-day and intra-day studies. In intra-day studies three standard replicate injections of three different concentrations were injected on same day and same standard different concentrations were injected on three successive days in inter-day precision studies. Where, the %RSD was found to be within limits (<2). Table 3.

Table:3 Summary of validation Parameters

Parameter	Azilsartan Medoxomil
Linearity range(µg/ml)	4-20
Coefficient Correlation	0.9989
Precision(RSD)	
Inter day(n=3)	0.164-0.565
Intra day(n=3)	0.102-0.618
Accuracy (%)	98.62-99.91
Repeatability(RSD, n=3)	0.029-0.1

RESULTS AND DISCUSSION

The proposed methods for estimation of Azilsartan were found to be simple, precise, accurate and economical,From the optical characteristics of the proposed method, Azilsartan was shown its λ max at 239-259 nm in the solvent methanol with a good correlation coefficient 0.998. it was found that Azilsartan Medoxomil obeys beer's law in the range of 4-14 µg/ml. The accuracy data of the drug was shown good percentage recovery and %RSD with the range of 99.96-100.25 and 0.1-0.4 respectively.The inter-day and intra-day precision values were found to be 0.15 and 0.6 respectively,which indicates that the proposed method has good precision

CONCLUSION

A simple, precise, accurate, economic, sensitive, reliable and reproducible UV Spectrophotometric method for estimation of Azilsartan Medoxomil in Active

pharmaceutical dosage form has been developed and validated. Hence, these methods can be easily and conveniently used for routine analysis of Azilsartan Medoxomil in pure form.

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