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Zero and first order derivative Ultraviolet spectrophotometric approach for determining Azilsartan medoxomil

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Abstract: *: Azilsartan medoxomil (AZIL), which is used to treat hypertension, reliably lowers blood pressure and is tolerable. By inhibiting the activity of the hormone angiotensin II at the AT1 receptor, which constricts blood vessels and limits water excretion through the kidneys, it decreases blood pressure. For the purpose of quantifying Azilsartan in bulk and pharmaceutical dose form, various approaches have been developed to date. Ultravoilet Spectrophotometry is one of the analytical techniques used in pharmaceuticals. This study has developed and validated a rapid, ultraviolet spectrophotometry: a highly precise and sensitive method for measuring Azilsartan medoxomil. λmax for the working standards were determined by using 0.1N Sodium hydroxide and distilled water in a ratio of 3:7 as a diluent and the λmax was found to be 245 nm for Azilsartan Medoxomil (AZIL) for zero order, 219 nm for First order derivative methods, parameters were found to be satisfactory. Analysis outcomes were examined for accuracy, precision, LOD, LOQ. The developed method can be used for day-to-day analysis.*

Keywords: *Azilsartan medoxomil (AZIL), , Derivative spectroscopy, Zero order and First order.*

Introduction

Azilsartan medoxomil (AZIL) are Angiotensin II Receptor antagonists. The chemical name for Azilsartan medoxomil is (5-methyl-2-oxo-1, 3-dioxol-4-yl) methyl 2-ethoxy-1-([2'-(5-oxo-4,5-oldihydro-1,2,4-oxadiazol- 3-yl) biphenyl-4-yl] methyl)-1H-benzimidazole-7-carboxylate, and its molecular weight 456.6g.

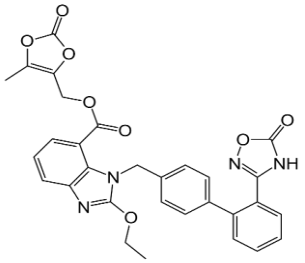

Figure 1: Structure of Azilsartan medoxomil

It is used either on its own or in conjunction with other drugs to treat excessive blood pressure. It lowers blood pressure, which reduces, chance of cardiovascular deaths, nonfatal heart attacks events, notably strokes and myocardial infarctions. These drugs lowers blood pressure by inhibiting Angiotensin-II at AT1 receptor, a hormone that contracts blood vessels and reduces water excretion through the kidneys. Adverse effects include Nausea, Hypotension/orthostatic hypotension, Asthenia, Fatigue, Muscle spasm, Dizziness and Cough.

The scope of present investigation were to develop[1] and validate[2] derivative (Zero & first order) [3] spectroscopy method for qualitative and qualification of

Azilsartan medoxomil and in pharmaceutical dosage form. Literature survey reveals, Azilsartan medoxomil can be estimated by, RP-HPLC[9-12], LC-MS[13] and few Spectroscopic[4-8] methods. However, to the best of our knowledge, no derivative UV-spectrophotometric methods were reported for estimation of Azilsartan medoxomil.

MATERIAL AND METHODS

Materials

The reference standard of Azilsartan Medoxomil API was procured from MSN Laboratories. Sodium hydroxide and water are used as reagents were of analytical grade. 0.1N Sodium hydroxide and distilled water in a ratio of 3:7 as a diluent.

Instruments

Shimadzu UV-1800 double beam spectrophotometer connected to a computer loaded with Shimadzu UV Probe 2.34 software was used for all the spectrophotometric measurements. In 1cm quartz cells, absorbance spectra of reference and test solutions, measured over the 200–400 nm range.

Preparation of stock solution

Standard stock solution AZIL (1000µg/ml) were prepared by dissolving 25 mg of drug in 3ml of 0.1N NaOH and make up to 25 ml with distilled water individually. Working standard solution: 100µg/ml was prepared by transferring 2.5 ml from stock solution to a 25 ml volumetric flask and dilute up to 25 ml with distilled water individually. Appropriate and Stock solution aliquots with precise volumes were transferred to 10-milliliter calibrated flasks and filled to capacity with distilled water.

Preparation of sample solution

Weigh20 tablets, AZIL with label claim of 40 mg and 50 mg and powdered each drug individually. Then transfer the analyte equivalent to 25 mg into 25 ml volumetric flask and add 3 ml of 0.1 N sodium hydroxide add 7 ml of distilled water and sonicate for 5 minutes. Filter through 0.45µ Whatmann filter paper and make up to 25 ml with distilled water. Secondary stock solution was prepared by taking 2.5 ml solution from primary stock solution in to the 25 ml volumetric flask and made up to the mark with water to produce 100 µg/ml. From this 12 µg/ml and 5 µg/ml were prepared by transferring 1.2 ml and 0.5 ml from secondary stock solution to a 10 ml volumetric flask and dilute up to 10 ml with distilled water respectively.

Zero order UV derivative spectroscopic method[3]

Prepare a series of dilutions in the concentration range of 4-20 and 1-9 µg/ml were scanned in the wavelength range of 200-400 nm using distilled water as blank. The UV spectrum of AZIL showed their λmax at 245.

Preparation of calibration curve

Absorbance at 245 nm were plotted against the respective concentration. The method shows good linearity range of 4-20 µg/ml for AZIL.

First-order UV derivative spectroscopic method[3]

It involves the conversion of the normal spectrum into first derivative spectrum. Spectra were derivatized using first order, delta lambda 16000 and scaling factor 10. The first order derivative spectrum of AZIL showed a sharp peak at 219 nm respectively. The absorbance difference at n = 1 ($dA/d\lambda$) was calculated. The amplitudes were measured for all the solutions and plotted against concentration to get calibration curve. Laboratory prepared mixtures and pharmaceutical formulations were successfully analyzed using the developed method.

Preparation of calibration curve

The amplitudes at 219 nm were plotted against the respective concentration of AZIL. The method shows good linearity range of 4-20 µg/ml for AZIL.

RESULTS

Linearity and Range

AZIL showed linearity within the range of concentration for 4-20 µg/ml with correlation co-efficient, slope and intercept 0.9998, 0.0323 and 0.0151 for Zero order, 0.0358, 0.0161 and 0.9997, for first order derivative method.

Precision

Inter-day and intra-day precision for Zero and First-order Derivative Spectroscopic Method were calculated in terms of % RSD. Three times a day, the experiment was conducted again. for intra-day and on 3 different days for inter-day precision.

Accuracy

Accuracy of the method was confirmed by recovery study form marketed formulation at three levels of concentration i.e. 50%, 100%, and 150% of label claim by standard addition technique. Recovery greater than 90% with low SD justified the accuracy of the method.

LOD and LOQ

Calibration study was repeated for 5 times and standard deviation (SD) of the intercepts was calculated.

LOD =3.3*SD/slope of calibration curve

LOQ= 10*SD/ slope of calibration curve

SD= standard deviation of intercepts.

Analysis of marketed formulation

Applicability of the suggested technique was examined by analyzing the commercially available samples.

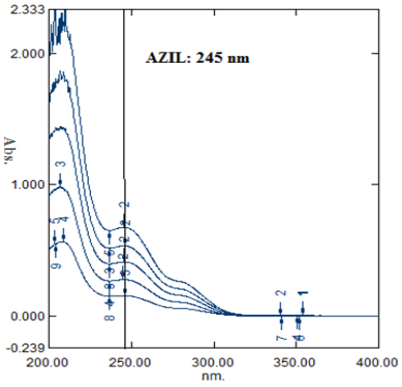

Figure 2: Zero order absorption spectra of Azilsartan

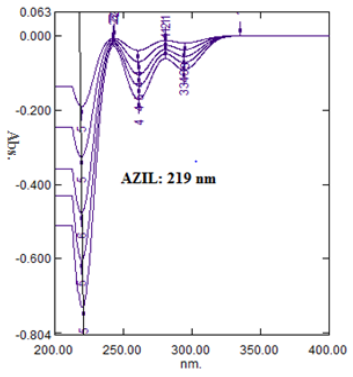

Figure 3: First order absorption spectra of Azilsartan

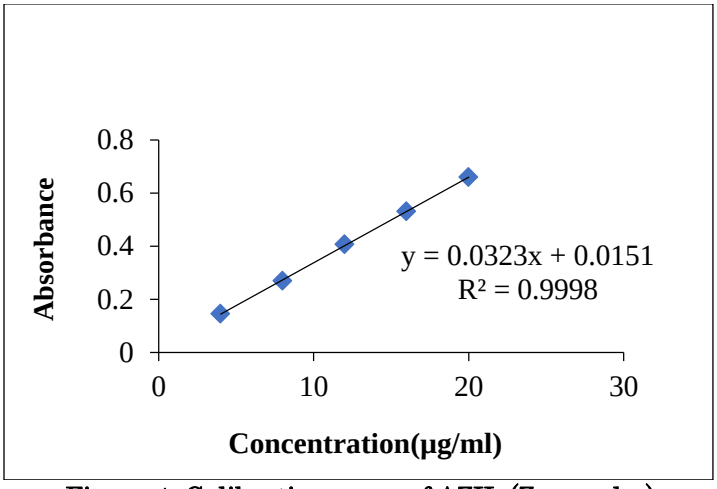

Figure 4: Calibration curve of AZIL (Zero order)

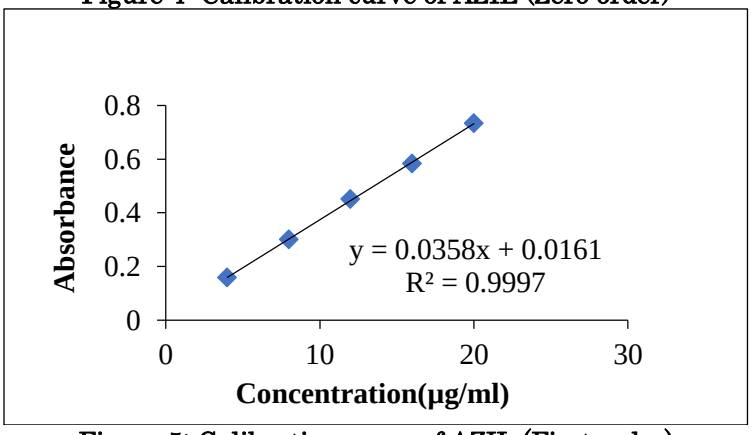

Figure 5: Calibration curve of AZIL (First order)

Table 1: Zero and First order derivative spectroscopic methods Validation parameters

Parameters assessed	Zero order	First order
	AZIL	
Beer's law range (µg /ml)	4-20	4-20
Wavelength (nm)	245	219
Correlation Coefficient (r^2)	0.9998	0.0358
Slope	0.0323	0.0161
Intercept	0.0151	0.9997
LOD	0.14	0.68
LOQ	5.04	1.47
Intra-day precision(%RSD)	0.85	1.65
Inter-day precision(%RSD)	0.53	1.54

Table 2: Recovery studies

Derivative spectroscopic method	% addition of label claimed	Amount of standard added (µg/ml)	Obtained amount (µg/ml)	Recovery%±SD
Zero order AZIL	50	2	14.58	104.21±0.20
	100	4	16.47	102.95±0.15
	150	6	18.74	104.12±0.28
First order AZIL	50	2	14.248	101.77±0.32
	100	4	16.148	100.92±0.26
	150	6	18.466	102.59±0.15

*Amount of AZIL in the pre-analyzed sample is 12 µg/mL.

Table 3: Results of Assay of formulation by Zero and First derivative spectroscopic methods

Method	Drug	Labeled claim	Amount obtained	% Found*±SD
Zero order	AZIL	40 mg	41.46	103.65±0.35
First order	AZIL	40 mg	41.46	103.65±0.35

*Average of three experiment

Conclusion

Derivative Spectrophotometric (Zero & First order) methods were developed and validated to analyze Azilsartan medoxomil (AZIL) in its individual dosage form. The developed Spectrophotometric methods for the quantitative estimation of Azilsartan medoxomil (AZIL) was found to be accurate, precise and economical and were validated as per the ICH guidelines and can be used for regular analysis of Azilsartan Medoxomil in Quality Control Laboratories. The results of this study highlight the effect of different solvents on the spectral characteristics of organic molecules of pharmaceutical importance. Statistical analysis proves that this method was repeatable and selective for the analysis. The present study has employed common solvents for the validation of a UV spectrometric method for the determination. The results indicated that the methods are accurate, precise, robust, economical, and rapid for the assay of Azilsartan medoxomil (AZIL) .

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