



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

A Novel Method Development and Validation of Diltiazem Hydrochloride in Pure and Pharmaceutical Dosage Forms by Using UV- Spectrophotometric Method

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ABSTRACT

A Novel, simple, accurate, and precise Area under curve spectroscopic method was developed and validated for the estimation of Diltiazem Hydrochloride in Pure and pharmaceutical dosage forms and has an absorption maximum between 232-242nm in 0.1M Sulphuric acid. The stock solution was made to produce 1000 µg/ml with 0.1M Sulphuric acid. The linearity was found in the concentration range of 1-3.5 µg/ml. The correlation coefficient was found to be 0.9999. The regression equation was found to be $Y=0.1013x+0.002$. The method was validated for linearity, accuracy, precision, limit of detection, limit of quantitation and ruggedness. The limit of detection and limit of quantitation for estimation of Diltiazem Hydrochloride was found to be 0.01066µg/ml and 0.1066µg/ml, respectively. Recovery of Diltiazem Hydrochloride was found to be in the range of 100.02-101.68 %. The %RSD values were less than 2. The method has been validated according to ICH guidelines. The Proposed method was successfully applied for the quantitative determination of Diltiazem Hydrochloride in pharmaceutical dosage forms.

Keywords: Diltiazem Hydrochloride, Area under curve Spectroscopy, 0.1M Sulphuric acid, accuracy.

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Received 10 November 2019, Accepted 29 November 2019

Please cite this article as: Suresha DN *et al.*, A Novel Method Development and Validation of Diltiazem Hydrochloride in Pure and Pharmaceutical Dosage Forms by Using UV- Spectrophotometric Method. American Journal of PharmTech Research 2019.

INTRODUCTION

Diltiazem hydrochloride is a calcium channel antagonist used in the treatment of angina, hypertension and arrhythmias in humans as well as hypertrophic cardiomyopathy in cat.^{1,2} Diltiazem is chemically described as, (2S, 3S)-5- [2- (dimethyl amino) ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepin-3- yl-acetate.³

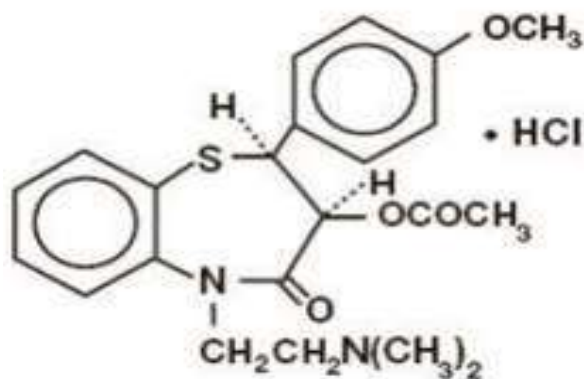


Figure 1: Chemical structure of Diltiazem hydrochloride

It has a molecular formula of $C_{22}H_{26}N_2O_4S$ and molecular weight of 414.519 g/mol. It has the structural formula (Figure 1). Diltiazem hydrochloride is a white crystalline powder which is freely soluble in 0.1M H_2SO_4 .

Literature Survey revealed that the drug has been estimated by Diltiazem hydrochloride is official in IP 2010, BP 2009 and USP 2005^{4,5,6}. Few methods such as HPLC⁷⁻¹¹, HPTLC¹², gas chromatography (GC)¹³, gas chromatography coupled with mass spectrometry (GC-MS)¹⁴, and capillary electrophoresis (CE)¹⁵ methods has been reported so far.

The aim of present work was to develop and validate a novel, simple, accurate and precise Area under curve Spectrophotometric method for estimation of Diltiazem hydrochloride in its Pure and Pharmaceutical dosage form.

MATERIALS AND METHOD:

Instrument:

UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on analytical balance.

Chemicals:

Diltiazem hydrochloride was given as a gift sample by Natco Pharma Limited, Hyderabad. Tablets of Diltiazem hydrochloride were procured from local market.

Solvent:

0.1 M H₂SO₄

Selection of analytical wavelength:

Appropriate dilutions were prepared for drug from the standard stock solution and the solution was scanned in the wavelength range of 200-400 nm. The absorption spectra thus obtained was showing the absorption maxima at 237nm and Area under curve in absorption spectra were measured between the wavelength range of 232-242nm which illustrated in Figure 2.

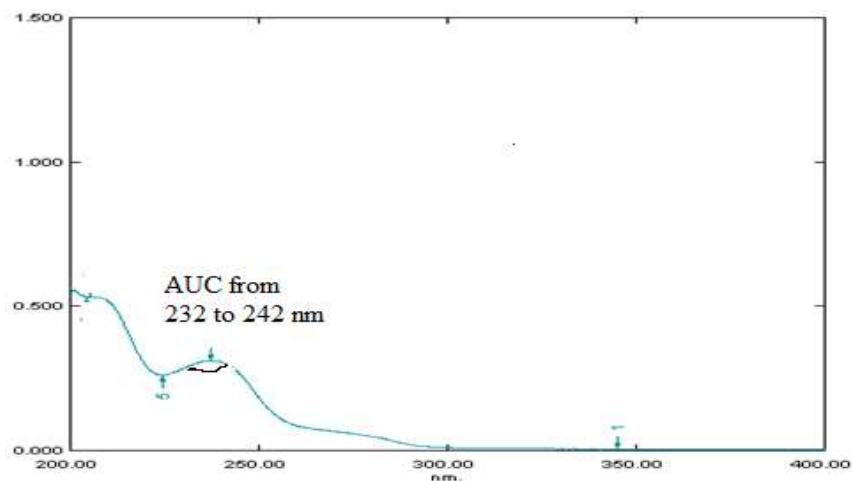


Figure 2: Typical Zero order spectra of Diltiazem hydrochloride showing AUC from 232-242nm

Preparation of Standard stock solution:

Accurately weigh 100mg of Diltiazem hydrochloride was transferred into 100ml volumetric flask and diluted with 0.1 N H₂SO₄ up to the mark. From this pipette out 10ml into 100ml volumetric flask and diluted with 0.1M H₂SO₄ up to the mark, from this solution pipette out 0.1, 0.15, 0.2, 0.25, 0.3, and 0.35 ml into 10ml individual volumetric flask and add 0.1M H₂SO₄ up to the mark, this gives 1, 1.5, 2, 2.5, 3, and 3.5 µg/ml concentrations.

Preparation of Sample solution:

The commercially available CARDIZEM 120 contains 120 mg of Diltiazem hydrochloride. From this twenty tablets were weighed and powdered. The tablets powder equivalent to 100 mg of Diltiazem hydrochloride was transferred into 100 ml volumetric flask then it was diluted with 0.1M H₂SO₄ and made up to the mark and the solution was filtered through whatman filter paper NO. 41. From the above solution 10 ml was pipetted out into 100 ml volumetric flask and the volume was made up to the mark with 0.1M H₂SO₄. The final concentration of Diltiazem hydrochloride was brought to 20µg/ml.

Method validation: The method is validated according to the ICH guidelines^{16, 17,18}

RESULTS AND DISCUSSION:

Method: Area under curve spectroscopy.

Linearity:

The working standard solution were diluted serially with Distilled water to obtain the range of 1-3.5µg/ml. a calibration curve for Diltiazem hydrochloride was obtained by measuring the absorbance between 232nm to 242nm and absorbance values are shown in Table.1 and Calibration graph were presented in Fig.3. Statistical parameters like slope, intercept, coefficient of correlation, and Sandel's sensitivity were determined and presented in Table.2.

Table 1: Results of calibration curve for Diltiazem hydrochloride by Area under curve Spectroscopy.

Sl. No	Concentration in µg/ml.	Absorbance between 232-242nm
1.	1	0.101
2.	1.5	0.146
3.	2	0.203
4.	2.5	0.252
5.	3	0.303
6.	3.5	0.354

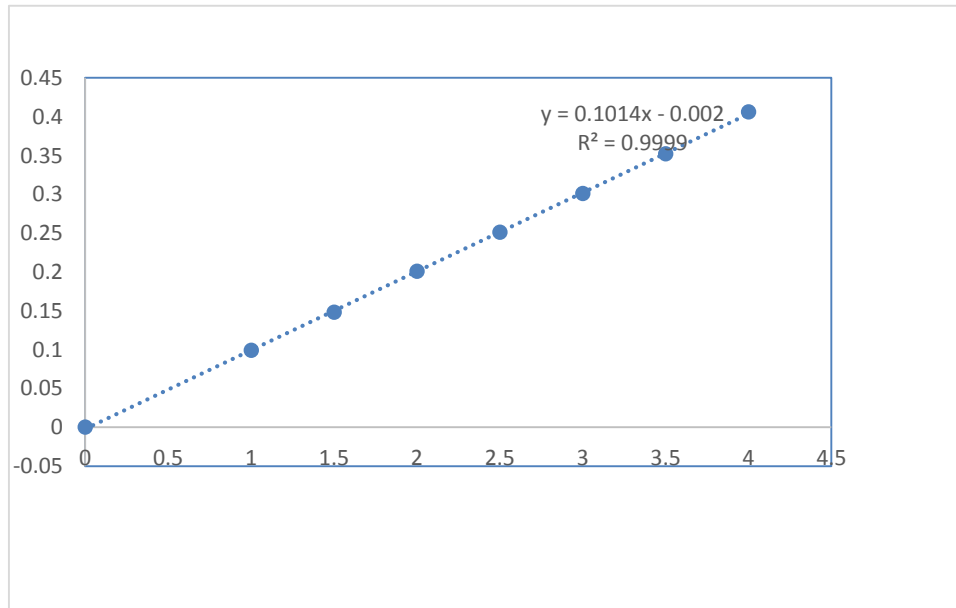


Figure 3: Calibration curve for Diltiazem hydrochloride by AUC Spectroscopy

Table 2: Regression parameters for Diltiazem hydrochloride by AUC spectroscopy

Regression Parameters	Diltiazem hydrochloride
Range	1-4
Max	232-242nm
Regression Equation	$Y=0.1014x+0.002$
Slope (b)	0.1014
Intercept(a)	0.002
Correlation coefficient (r ²)	0.9999
Sandell's Sensitivity	0.0099

Precision:

Precision of the method was studied as intra-day and inter-day precision. Intra-day precision was determined by analyzing the 1, 1.5, 2, 2.5, 3, and 3.5 µg/ml concentration for three times in same day. Inter-day precision was determined by analyzing the same concentration of solution daily for three days. Precision results are shown in Table.3.

Table 3: Determination of precision results for Diltiazem hydrochloride from 232nm to 242nm by AUC spectroscopy

Concentration (µg/ml)	Intraday Absorbance ±SD**	%RSD	Inter day Absorbance ±SD**	%RSD
1	0.101±0.001528	1.54	0.102±0.001	0.98
1.5	0.152±0.001	0.65	0.147±0.001	0.68
2	0.200±0.002082	1.04	0.198±0.00208	1.05
2.5	0.252±0.001732	0.69	0.249±0.00208	0.83
3	0.302±0.000577	0.18	0.299±0.002	0.66
3.5	0.352±0.001528	0.43	0.351±0.0025	0.71

Accuracy:

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i. e, 50%, 100% and 150%. In which the formulation concentration was kept constant and varied pure drug concentration. Accuracy results were shown in Table.4.

Table 4: Determination of accuracy results for Diltiazem hydrochloride by AUC spectroscopy.

Spiked levels	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered	%Recovery ±SD**	%RSD
50	2	1	3.02	100.02±0.0033	0.003
100	2	2	4.06	101.68±0.0037	0.0035
150	2	3	5.06	101.20±0.0020	0.0018

**Average of six determinations

Ruggedness:

Ruggedness was determined between different analysts. The value of %RSD was found to be less than 2 were shown in Table.5.

Table 5: Determination of Ruggedness results for Diltiazem hydrochloride by AUC Spectroscopy

Analysts	Analyst-1	Analyst-2
Mean absorbance	0.202	0.199
Standard deviation	0.002083	0.00207
%RSD	1.03	1.05

Limit of detection and Limit of Quantitation:

The LOD and LOQ of the present method were calculated based on standard deviation of the Response and slope of linearity curve. LOD and LOQ values of Diltiazem hydrochloride were found to be 0.01067 μ g/ml and 0.1067 μ g/ml.

CONCLUSION:

Thus, the developed method was found to novel, simple, accurate and precise UV-spectrophotometric method for the routine estimation of Diltiazem hydrochloride in Pure and pharmaceutical dosage form.

ACKNOWLEDGEMENT:

We like to thanks Management, Principal, teaching and non-teaching staff of Bharathi college of pharmacy for their continues co-operation and support.

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