International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 03 Issue 03 March 2023

Page No: 102-106

DOI: https://doi.org/10.47191/ijpbms/v3-i3-03, Impact Factor: 6.858

Development and Validation of Novel Analytical Method for Estimation of Diltiazem HCL

Pooja M[1], Chaithra CN[2], Rajasekaran S.[3]

[1,2,3] Department of Pharmaceutical Analysis, Ikon Pharmacy College, Bidadi, Ramanagara Taluk and District, Karnataka, India – 562 109

ABSTRACT

A novel, simple, accurate and precise Zero order derivative spectroscopic method was developed and validated for the estimation of Diltiazem HCl in bulk and Pharmaceutical dosage forms and has an absorption maximum at 193 nm in 0.05N Sulphuric acid. The Linearity was found to be in the concentration range of 3-18 µg/ml and the correlation coefficient was found to be 0.998 and it has showed good linearity, reproducibility, precision in this concentration range. The regression equation was found to be Y = 0.0971x + 0.0268 .The % recovery values were found to be within 99.3 -102.06 % showed that the method was accurate. The LOD and LOQ were found to be 0.222 and 0.675µg/ml, respectively. The % RSD values were less than 2. The method has been validated according to ICH guidelines for linearity, accuracy, precision, ruggedness, Limit of detection and limit of quantitation. Proposed method was successfully applied for the quantitative estimation of Diltiazem HCl in bulk and pharmaceutical dosage form.

KEYWORDS: Diltiazem HCl, Zero order derivative Spectroscopy, 0.05 N Sulphuric acid, Linearity, Precision, Reproducibility, and Accuracy.

ARTICLE DETAILS

Published On:
04 March 2023

Available on:
https://ijpbms.com/

INTRODUCTION

Diltiazem is a cardiovascular drug, a calcium channel blocker (CCB), a non-dihydropyridine derivative, which is widely used in the treatment of cardiac ischemia (angina), arrhythmia, and hypertension. CCB works by competitively blocking calcium channels with their agonists, thereby reducing the amount of extracellular calcium that enters the cell. [1]

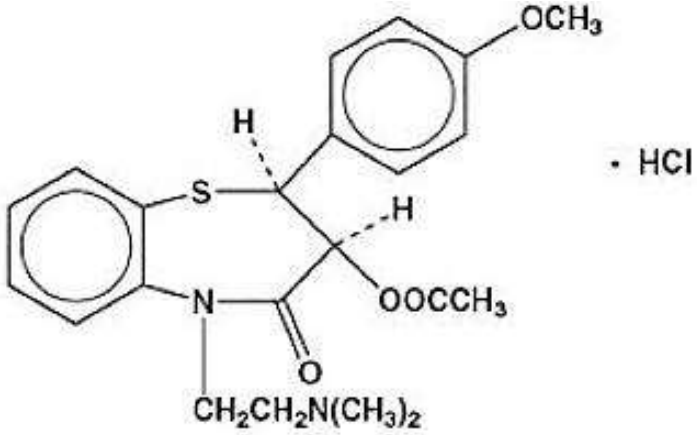

Figure.1: Chemical structure of Diltiazem hydrochloride.[2]

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]with the chemical formula $C_{22}H_{26}N_2O_4S.HCl$ (Figure 1) and a molecular weight of

450.98. It is in the form of crystal powder or small crystal, white, odourless, and fused at 210 °C with decomposition. It has solubility that is easily soluble in chloroform, methanol, formic acid, and water, rather difficult to dissolve in absolute ethanol and insoluble in ether. The partition coefficient value in octanol / water is 2.79[4].

Literature survey revealed that the drug has been estimated by UV-Spectrophotometric and RP- HPLC method.

The aim of present work was to develop and validate a novel, rapid, simple, precise, and specific Zero order derivative UV-Spectrophotometric method for estimation of Diltiazem HCl in its bulk and pharmaceutical dosage form.

MATERIALS AND METHOD

Instrument

UV-Visible spectrophotometer, SHIMADZU (model UV-1900i) with Lab solution software. All weights were taken on analytical balance.

Chemicals

Diltiazem HCl pure form was obtained as a gift sample Micro labs private Ltd. and its pharmaceutical dosage form DILZEM-30 (Torrent pharmaceutical Ltd) 15 Tablets labelled claim 30 mg were purchased from a community pharmacy.

Solvent

0.05N Sulphuric acid (prepared by dissolving 1.375ml and making the volume to 1000ml with distilled water).

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 190-400 nm. The absorption spectra obtained were derivatised from Zero order method. It shows maximum absorbance at 193 nm shown in Fig.1 and Zero order overlain spectra of Diltiazem HCl at 193 nm were shown in Fig.2.

Preparation of Standard stock solution

Accurately weighed 100 mg of Diltiazem HCl was transferred into 100 ml volumetric flask and diluted with 0.05N Sulphuric acid up to the mark. Pipetted out 10 ml of the stock solution into 100 ml volumetric flask and diluted with 0.05 N Sulphuric acid up to the mark, from this solution transferred 0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 ml into 10 ml individual volumetric flask and add 0.05 N Sulphuric acid up to the mark, to obtain 3, 6, 9, 12, 15 and 18 µg/ml concentrations.

Preparation of Sample solution

Twenty tablets were weighed and powdered, the tablet powder equivalent to 100 mg of Diltiazem HCl was transferred into100 ml volumetric flask and diluted with 0.05 N Sulphuric acid, the solution was filtered through Whatmans filter paper no.41. To a 100 ml volumetric flask 10 ml of the stock solution was transferred and diluted to the volume using 0.05N Sulphuric acid. Transferred 0.6 ml into 10 ml volumetric flask and diluted to the volume 0.05N Sulphuric acid, to obtain 6 µg/ml concentrations.

Method validation

The method is validated according to the ICH guidelines.

RESULTS AND DISCUSSION

Method: Zero order derivative spectroscopy.

Linearity

The working standard solution were diluted serially with 0.05 N Sulphuric acid to obtain the range of 3-18 µg/ml. a calibration curve for Diltiazem HCl was obtained by measuring the absorbance at the λ max of 193 nm 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 Sandell's sensitivity were determined and presented in Table.2.

Precision

Precision of the method was studied as intra-day and inter-day precision. Intra-day precision was determined by analyzing the 3, 6, 9, 12, 15 and 18 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.

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.

Ruggedness

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

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 HCl were found to be 0.222 µg/ml and 0.675 µg/ml.

CONCLUSION

From the above it can be concluded that all validation parameters such as precision, accuracy, linearity, LOD, LOQ and Ruggedness met the predetermined acceptance criteria as mentioned in ICH guidelines. The developed spectrophotometric method is simple, rapid, accurate, and precise and can be applied for routine analysis of Diltiazem HCl in bulk and its dosage forms.

TABLES

Table 1: Results of calibration curve at 193 nm by zero order Spectroscopy.

SL. NO	Concentration in µg/ml.	Absorbance± Standard deviation
1	3	0.350± 0.019107
2	6	0.598± 0.125822
3	9	0.940± 0.006802
4	12	1.158± 0.020798
5	15	1.489± 0.005391
6	18	1.773± 0.005785

Table 2: Regression parameters for Diltiazem HCl by zero order spectroscopy

Regression Parameters	Diltiazem HCl
Range	3-18 µg/ml
λMax	193 nm
Regression Equation	Y=0.0971x+0.0268
Slope (a)	0.0971
Intercept(b)	0.0268
Correlation coefficient (r2)	0.998
Sandell's Sensitivity	0.010

Table 3: Determination of precision results for Diltiazem HCl at 193 nm by zero order derivative spectroscopy.

Concentration (µg/ml)	Intra-day Absorbance ±SD**	%RSD	Inter-day Absorbance ±SD**	%RSD
3	0.356±0.003606	1.012	0.393±0.007506	1.900
6	0.647±0.002517	0.389	0.652±0.006658	1.021
9	0.939±0.005508	0.586	0.937±0.005508	0.587
12	1.167±0.012124	1.037	1.226±0.006658	0.543
15	1.487±0.004359	0.293	1.488±0.005686	0.382
18	1.772±0.003215	0.181	1.773±0.00755	0.425

Table.4: Determination of accuracy results for Diltiazem HCl at 193 nm by Zero order derivative spectroscopy.

Spiked levels	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered	%Recovery ±SD**	%RSD
50	06	03	8.94	99.3±1.501	1.51
100	06	06	12.12	101±1.414	1.40
150	06	09	15.31	102.06±0.1.423	1.39

**Average of six determinations

Table.5: Ruggedness results of Diltiazem HCl at 193 nm by Zero order Spectroscopy

Analysts	Analyst-1	Analyst-2
Mean absorbance	1.143	1.174
Standard deviation	0.016093	0.008386
%RSD	1.407	0.713

FIGURES

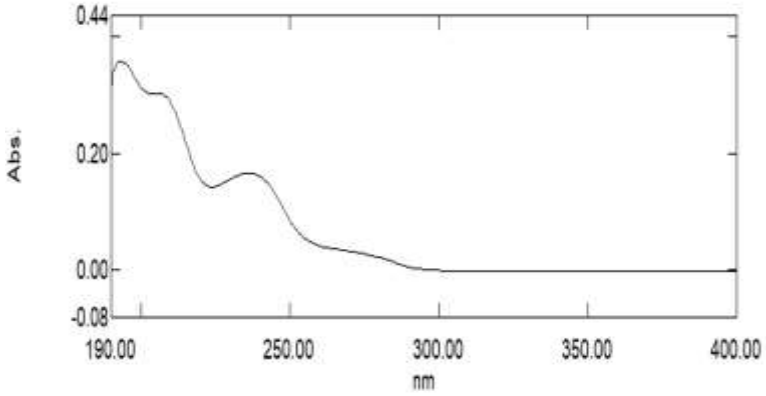

Fig.1: Zero order spectra of Diltiazem Hcl showing the absorbance at 193 nm.

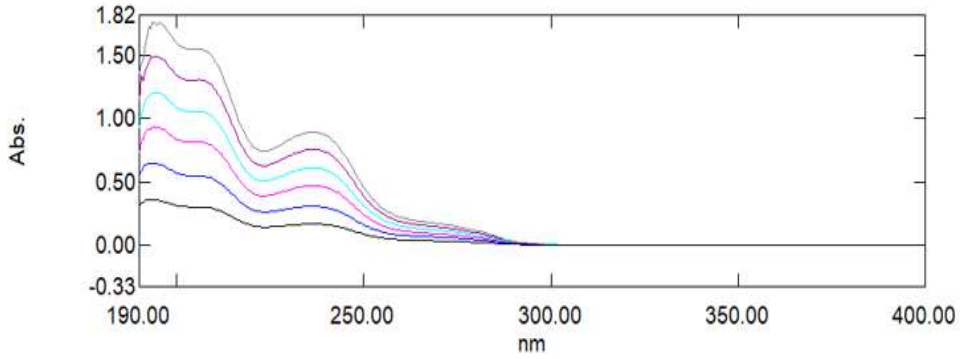

Fig.2: Zero order overlain spectra of Diltiazem Hcl showing absorbance at 193 nm

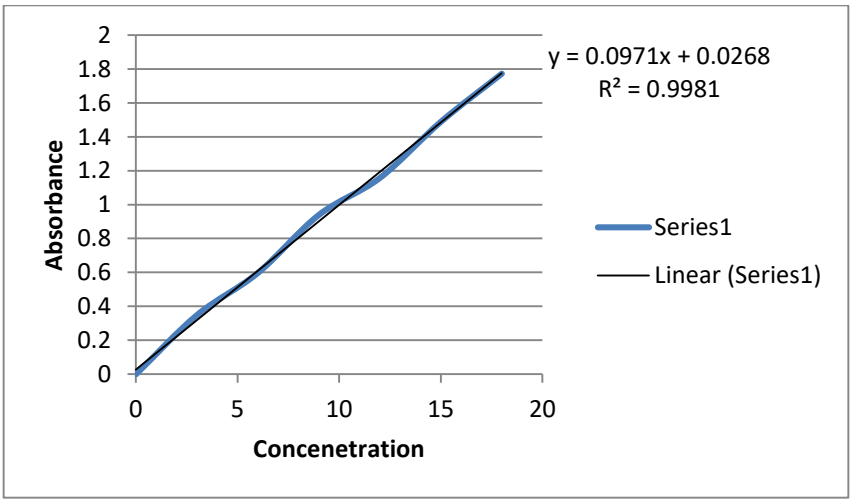

Fig.3. Linearity curves for Diltiazem Hcl at 193 nm by zero order Spectroscopy

REFERENCES

I. Sukandar EY, Andrajati R, Sigit JI, Adnyana IK, Setiadi AAP, Kusnandar. Iso Farmakoterapi. Jakarta: PT ISFI Penerbitan, 2008.

II. Kemenkes RI. Farmakope Indonesia edisi V. Jakarta: Direktorat Jendral Bina Kefarmasian dan Alat Kesehatan Republik Indonesia, 2014.

III. The Merck Index. An encyclopedia of chemicals, drugs and biological. Division of Merckand Co., Inc., 14 th ed., Whitehouse Station, NJ, 2006.

IV. Moffat AC, Osselton MD, Widdop B. Clarke's Analysis of Drugs and Poisons 4th Ed. London: Pharmaceutical Press, 2011.

V. Vivekanand A, Chatpalliwar, Pawan K, Porwala, Neeraj Upmanyu. Validated gradient stability indicating HPLC method for determining Diltiazem Hydrochloride and related substances in bulk drug and novel tablet formulation. Journal of Pharmaceutical Analysis. 2012;2(3):226-37.

VI. Najma Sultana, M. Saeed Arayne, Nighat Shafi, Farhan Ahmed Siddiqui and Azhar Hussain.

Development and Validation of New Assay Method for the Simultaneous Analysis of Diltiazem, Metformin, Pioglitazone and Rosiglitazone by RP-HPLC and its Applications in Pharmaceuticals and Human Serum. Journal of Chromatographic science.2011;49:774-78.

VII. Mateus Araújo Castro e Souza, Carlos Eduardo de Oliveira Pereira, Fernando Henrique Andrade Nogueira, Gerson Antônio Pianetti**.** Development and validation of a stability indicating HPLC method to determine diltiazem hydrochloride in tablets and compounded capsules.Brazillian Journal of Pharmaceutical Sciences.2017;53(3):e00041

VIII. Bhagyashree R. Patil, Bhusnure O.G, Paul B. N, Ghodke A. Y, Suraj S. Mulaje.Analytical Method Development And Validation for the Estimation of Diltiazem Hydrochloride in Bulk and Pharmaceutical Dosage Form By RP- HPLC. International Journal of drug Regulatory Affairs. 2014;2(2):78-84.

IX. Nitin Mahajan, Suparna Deshmukhand Mazahar Farooqui. A novel stability-indicating method for known and unknown impurities profiling for diltiazem hydrochloride pharmaceutical dosage form. Future Journal of Pharmaceutical Sciences.2021;7:204.

X. Suresha DN, Rashmi T, SenthilKumar GP**.** A Novel Method Development and Validation of Deltiazem Hydrochloride in Pure and Pharmaceutical Dosage Forms by Using UV- Spectrophotometric Method. American Journal of Pharmtech Research.2019;9(06):226-32.

XI. Nafisur Rahman, Syed Najmul Hejaz Azmi. Spectrophotometric determination of diltiazem hydrochloride with sodium metavanadate. Microchemical Journal 65.2000; 39-43.

XII. Shabana Shahs, Najma Sultana, Saeed Arayne. Development and Validation for the Simultaneous Quantification of Prazosin, Amlodipine, Diltiazem and Verapamil.Med Chem.2014;4(12):770-77.

XIII. Rudy Bonfilio **,**Taciane Ferreira Mendonça, Eliézer Giannini de Barros, Gislaine Ribeiro Pereira e Magali Benjamim de Araújo. Development and Validation of a Dissolution Test for Diltiazem Hydrochloride in Immediate Release Capsule. International year of chemistry.2011;34(3):520-26.

XIV. Engelhart DA, Iavins ES, Seligman SS, Sutheimer CA, (1997), J Anal Toxicol, 21, 576.

XV. Chankvetadze B, Kartozia I, Blaschke G, (2002), J Pharm Biomed Anal, 27, 161.

XVI. ICH, Q2A Text on Validation of Analytical Procedures; 1994.

XVII. ICH, Q2B Validation of Analytical Methodology; 1996.

XVIII. ICH, Q2 (R1) Validation of Analytical Procedures: text and methodology; 2005.