Research Article

DEVELOPMENT OF FIRST ORDER AND SECOND ORDER DERIVATIVE FLUOROMETRIC METHODS FOR CARVEDILOL IN BULK AND FORMULATIONS

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ABSTRACT

Objective: A simple, accurate, precise, easily accessible fluorometric estimation method has been developed for Carvedilol in 0.1 M Methanolic sodium hydroxide. **Method:** Fluorescent properties of Carvedilol have been studied in 0.1 M Methanolic sodium hydroxide showed linearity in the range of 1 to 10µg/ml. First derivative and second derivative method of applied and found to be sensitive to small changes in concentration. **Results:** Zero order readings are used for statistical calculation of validation parameters. Thus obtained readings were used calculate First and second order graphs to study the sensitivity of the drug with change concentration of the drug. On validation of the method shows correlation coefficient of 0.996556, Standard deviation of 32.97, Intercept 8.5333, slope was 9.0121, and Relative standard deviation was 0.03512. **Conclusion:** The fluorometric properties of Carvedilol were studied in various solvents and fluorometric property in methanolic sodium hydroxide was used to develop fluorometric method for estimation. Analytical method was validated for parameters like accuracy, precision, specificity, ruggedness, robustness and percentage recovery and all parameters were found within the specified range.

Keywords: Fluorometry, Carvedilol, Methanolic sodium hydroxide, Derivative spectroscopy.

INTRODUCTION

Carvedilol is β-blocker used to treat high blood pressure and cardiac failure. Chemically Carvedilol is 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxy phenoxy) ethyl amino]-, (±)-; (±)-1-(Carbazol-4-yloxy)-3-[[2-(o-methoxy phenoxy) ethyl] amino]-2-propanol. There are various methods of estimation Carvedilol have been described such as UV-Visible spectrophotometry [1-8], RP–HPLC[9-10] and HPLC methods[11-13]. Fluorescent properties of Carvedilol and fluorometric estimation methods[14-16]. Under the present study we have studied fluorometric properties of Carvedilol in Methanolic sodium hydroxide. Literature survey revealed that Fluorometric property of Carvedilol in Methanolic sodium hydroxide has not been reported and it was observed that the fluorescent property of Carvedilol increases in methanolic sodium hydroxide.

MATERIALS AND METHODS

All reagents and solvents used in the experimental work are analytical grade. Elico Fluorometer model CL-53 was used. The fluorescence intensity of test and reference solutions was recorded in 3 ml borosilicate cells. The Relative Intensity or % Transmission was measured with filters of excitation wavelength of 366 nm and emission wavelength of 475 nm.

Preparation of 0.1 M Methanolic NaOH: 4.2 gm NaOH dissolved in 5 mL distilled water. Sufficient aldehyde free methanol added to produce 1000 ml. The solution is allowed to stand in tightly stopper bottle.

Procedure for estimation: Stock solution of Carvedilol was prepared with 100 mg of Carvedilol dissolved in 100 ml of 0.1 M Methanolic sodium hydroxide solution and various concentrations in the range of 1µg/ml to 10µg/ml were prepared for recording. Highest concentration was used set 100% intensity of Fluorometer. The 0.1 M Methanolic sodium hydroxide solution was as blank. Sample readings were recorded using commercial brands of Carvedilol. Standard dilutions in the range of 1-10µg/ml prepared for linearity measurement

Estimation of commercial tablets: 20 tablets were weighed and ground to fine powder. The tablet powder equivalent to 100 mg of

carvedilol was weighed and transferred to 100 ml volumetric flask; 50 ml of 0.1 M Methanolic sodium hydroxide was added, filtered and final volume was adjusted to 100ml. Dilution containing highest concentration of 10µg/ml was used to set 100% intensity and readings were recorded against 0.1 M methanolic sodium hydroxide as blank.

RESULTS AND DISCUSSION

Fluorometric method is sensitive which can measure the sample in low concentration. Carvedilol is fluorescent substance and this property of fluorescence is increased in 0.1M Methanolic sodium hydroxide solution. The influence of other solvents on fluorescence prpeprty of carvedilol was also studied (Fig 2). Pure drug and marketed formulations were used to get the results. Linearity range of carvedilol in 0.1M Methanolic sodium hydroxide solution was 1µg/ml to 10µg/ml. The validation parameters such as precision, accuracy, coefficeint correlation, standard deviation and relative standard deviation were also calculated. All results obtained were within the range of standard values (table 1). The results of zero order were used for first and second order calculations, graphs were plotted accordingly. First and second order graphical representation showed that the percentage of Transmission is optimum at different concentrations. In the graph of a zero-order derivative change in %Transmission and concentration produces a straight line. The expected shapes of the curves for change in %Transmission and concentration with concentration for a first-order derivative. A plot of squares of change in %Transmisssion and concentration with concentration then the reaction is second order (Fig 1, 3 and 4).

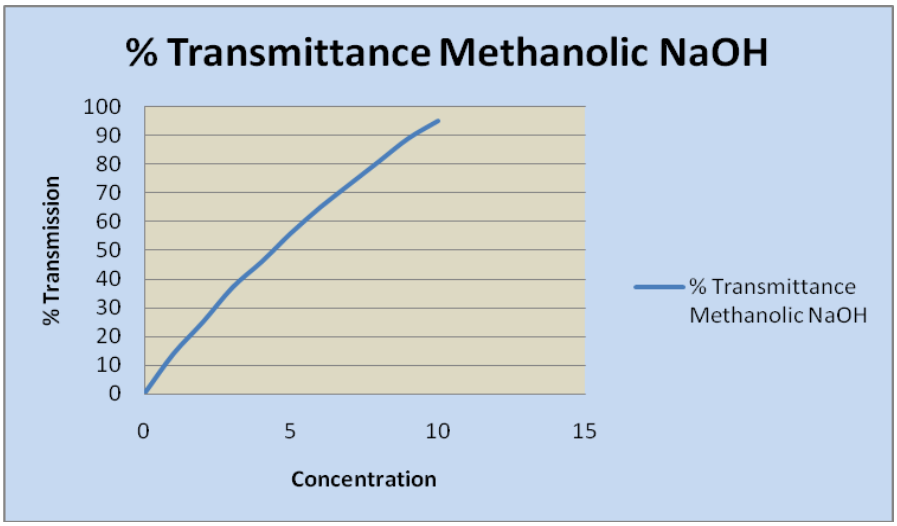

Fig. 1: Linear relationship between % relative intensities and Concentration

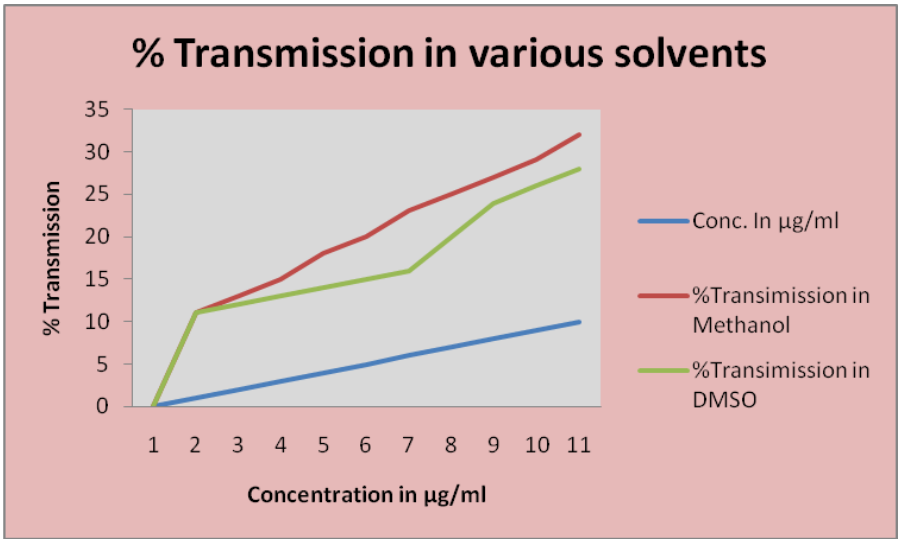

Fig. 2: % Transmission with carvedilol in different solvents

Table 1: Stastical calculations of validated parameters

Validation Parameter	Calculated Value
Range and Linearity	1 µg/ml to 10 µg/ml
Relative Standard Deviation	0.03512015
Coefficient Correlation	0.996556
Accuracy	91% to 95%
Slope	9.012121
Intercept	8.533333

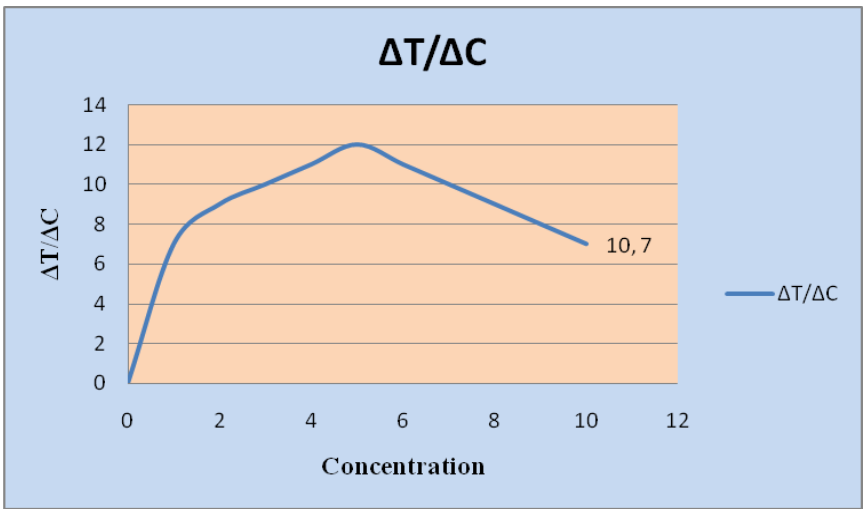

Fig. 3: Graphical representation of First Order derivative

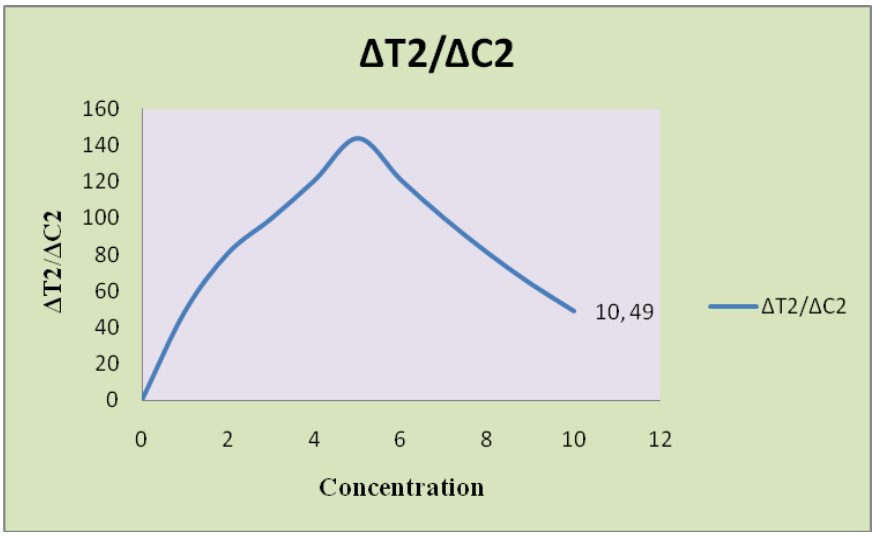

Fig. 4: Graphical representation of Second Order derivative

CONCLUSION

The developed method is easily accessible, precise, and accurate and showed linearity in range of 1µg/ml to 10µg/ml. Thus developed can be successfully applied for estimation of Carvedilol in pure and bulk formulations.

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REFERENCES

1. AD Mali. Simultaneous Determination of Carvedilol and Hydrochlorothiazide in Pharmaceutical Dosage Form by First Order Derivative UV Spectrophotometry. Int J Pharm PharmSsci, 2015; 7( )9: 371-74.
2. A Mali, V Kekan, R Dongare, S Gholve, R Bathe. Simultaneous UV Spectrophotometric Methods for

Estimation of Carvedilol and Hydrochlorothiazide in Bulk and Tablet Dosage Form. Asian J. Pharm. Tech. 2016;6(1):15-20.
3. Desai DC, Karkhanis VV. Simple Spectrophotometric Estimation of Carvedilol phosphate in Bulk and in Tablet Dosage Forms. Int Res J Pharm 2012;3(2):114-16.
4. C. Theivarasu, S Ghosh, T. Indumathi. UV Spectrophotometric Determination of Carvedilol in Pharmaceutical Formulations. Asian J Pharm Clin Res 2010;3(4): 64-68.
5. NS Abdelwahab. Spectrophotometric methods for simultaneous determination of Carvedilol and Hydrochlorothiazide in combined dosage form. Arabian J Chem 2016; 9:S355–S360.
6. RV Rele, PP Tiwatane. UV Spectrophotometric Estimation of Carvedilol hydrochloride by First Order Derivative and Area Under Curve Methods in Bulk and Pharmaceutical Dosage Form. Der Pharmacia Sinica 2014;5(6):29-35.
7. Shinkar DM, Dhake AS, Setty CM. Development of UV Spectrophotometric Method for Estimation of Carvedilol in Bulk and Pharmaceutical Formulations. Asian J. Research Chem.2013; 6 (10): 956-959.
8. DN Shetty, B. Narayana. Simple Methods for the Spectrophotometric Determination of Carvedilol. ISRN Spectroscopy 2012; Article ID 373215, 6 pages.
9. Basaveswara RMV, Nagendrakumar AVD, Yedukondalu M, Raman BV. New Validated RP–HPLC Method for the Estimation of Carvedilol in Pharmaceutical Formulation. Int J Pharm Pharm Sci 2012; 4(2):253-58.
10. KB Naidu, MR Mohan Reddy, NV Naidu. Development and validation of RP-HPLC method for determination of carvedilol in bulk and pharmaceutical dosage forms. Der Pharmacia Lettre, 2014; 6 (6):198-206.
11. Pattana Sripalakit, Somsak Kaewnok, Sakawrat Tubtonglang. Development of carvedilol assay in tablet dosage form using HPLC with fluorescence detection. Maejo Int. J. Sci. Technol. 2010;4(01):8-19.
12. Ettireddy S, Chandupatla V, Ciddi V. HPLC Method Development and Validation of S(-)-Carvedilol from API and Formulations. American J Ana Chem 2015;6, 437-445.
13. V Bechara, EVS Subrahmanyam, R Shabaraya. . New Analytical Methods and Their Validation for the Estimation of Carvedilol in Bulk and Marketed Formulation. Inter J Pharma Sci Res 2015;6(2): 421-24.
14. LX Xu, N Hui, LY Ma, HY Wang. Study on Fluorescence Property of Carvedilol and Determination of Carvedilol by Fluorimetry. Spectrochimica Acta Part A 2005; 61: 855–859.
15. Wang HU, Xiao Y, Han J. Simultaneous determination of Carvedilol and Ampicillin Sodium by first derivative fluorometry in the presence of Human Serum Albumin. Ana Sci 2005;21:537-540.
16. Inna L, Darya A, Alla Y. Determination of Ccarvedilol by its Quenching Effect on the Luminescence of Terbium Complex in Dosage Form. Acta Poloniae Pharmaceutica n drug research, 2011;68(3):325-330.