



SPECTROPHOTOMETRIC DETERMINATION OF METOPROLOL IN TABLET DOSAGE FORM

N. Okechukwu and J. A. Kolawole*

*Department of Pharmaceutical Chemistry,
Faculty of Pharmaceutical Sciences,
University of Jos, Jos, Nigeria.*

Abstract

Metoprolol, a beta-1 selective adrenergic receptor blocker antihypertensive agent is fairly new in Nigeria. In view of the endemic faking and adulterating of drugs in Nigeria, a simple, quick, and accurate method was developed for its assay. Metoprolol was coupled with 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl) in borate buffer (pH 9) and at a temperature of 100°C. An orange coloured metoprolol-NBD-Cl complex was formed within 10 minutes and the complex was stable for another 20 minutes. The reaction product had a λ_{max} of 460 nm. The absorbance-concentration plot was rectilinear (0.998) over the concentration range of 5–40 μ g/ml and with a detection limit of 2 μ g/ml. Recovery was 96.3% with RSD of 6.5%. © 2006: NAPA. All rights reserved.

Keywords: *Spectrophotometry; metoprolol; dosage form*

INTRODUCTION

Metoprolol [1-isopropyl-amino 3 p-(2-methoxyethyl) phenoxypropan-2-ol] is a beta-1 selective adrenergic receptor blocking antihypertensive agent (British National Formulary 2002). Absorption after oral administration of metoprolol is rapid and complete. It is metabolized in the liver (British National Formulary, 2002). Metoprolol tablet has been reported to be analysed by colorimetric method by coupling with chloranil in the presence of silver oxide, (Shinghal and Sardesai, 1987), GLC-MS (Kim *et al.*, 2002), RP - HPLC methods (Mistry *et al.*, 1998). NBD-Cl has been reported in the colorimetric determination of beta blockers including atenolol (Amin *et al.*, 2002; Sheika *et al.*, 2002). With the problem of fake and adulterated drugs on the increase in Nigeria there is the need for easy and inexpensive methods for the assay of

metoprolol. This paper therefore reports the spectrophotometric analysis of metoprolol in solid dosage form using NBD-Cl as coupling agent.

MATERIALS AND METHOD

The materials used in this study include metoprolol tablet 100 mg (Lopresor) by Padro. SA (Lot No B4011, mfg 2005, Exp. 2009), 4-Chloro-7-nitrobenzo-2-oxa-1,3-diazole chloride (NBD-Cl) Merck (Darmstadt, Germany), methanol, ethanol, isopropyl alcohol, potassium chloride (all BDH, Chemical Ltd, Poole, England) and spectrophotometer (Jenway, UK)

Quality control assessment

Initial quality control test was carried out on the metoprolol tablets adopting the assay method described in British Pharmacopoeia 1993, for the pure metoprolol.

Twenty (20) tablets metoprolol 100 mg, were individually weighed and powdered. Ethanol

* Corresponding author. E-mail:kolaja@unijos.edu.ng; Tel: +234-(0)-805-732-5658
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(150 ml) was added to a quantity of the powdered tablets containing 75 mg of metoprolol tartrate. The mixture was placed in the ultrasonicator for 15 minutes, after which sufficient ethanol was added to make up to the 200 ml mark and the mixture was then filtered. Ethanol (30 ml) was added to 20 ml of the filtrate and the absorbance of the resulting solution was taken at 270 nm. The content of $(C_{15}H_{25}NO_3)_2C_4H_6O_6$ was calculated. The reference sample 0.15% w/v solution of metoprolol tartrate.

Proposed assay method

An aliquot portion (0.5 ml each) of the different concentrations of metoprolol solution were transferred into series of 10 ml volumetric plastic flask and labeled A to F. Then 0.5 ml borate buffer (pH 9) and 0.5 ml NBD-Cl solutions were added to each flask. Each flask was immediately immersed in boiling water bath for 10 minutes. After that the solution was cooled and diluted to volume (10 ml) with methanol. The absorbance of the solution was measured at 460 nm against the reagent blank (flask A) that was prepared simultaneously.

The various parameters (pH, temperature, NBD-Cl concentration, time) affecting the assay were individually evaluated, while other parameters were kept constants. This procedure was repeated four more times at different times and the average absorbance readings were used to plot the calibration curve.

Validation procedure (recovery, precision and accuracy)

Different concentrations were prepared from the stock solution in increasing order of 5.0, 15.0, 25.0, and 35.0 mg/ml for the validation parameters. The concentrations were on each occasion prepared and analyzed. For recovery and accuracy the assay was repeated four times on the same day and for precision the assay was repeated on five different days. From the absorbances the corresponding concentration were obtained from the calibration curve. The

percentage relative standard deviations were calculated. Also graphs of absorbance against concentration were plotted and correlation coefficients determined.

RESULT AND DISCUSSION

The result showed that the Metoprolol tablets used in this study complied with official standard (BP 1993). Metoprolol was found to react with NBD-Cl in pH 9 Borate buffer to produce orange colour with wavelength of maximum absorbance of 460 nm. A plot of absorbance against concentration of metoprolol gave a straight line through the origin Beer-Lambert's law was obeyed over concentration range of 5-40 g/ml with a correlation coefficient of 0.998 and a limit of detection of 2.0 g/ml. The validation procedure carried out gave a measure of the degree of precision and accuracy of the method used in plotting the calibration curve and analyzing the sample. The percentage recovery the concentrations ranged between 91.67 and 104.35 with an average of 96.30% and an RSD of 6.5% (Table 1).

A proposed pathway of the complexation reaction between metoprolol and NBD-Cl is as follows (Figure 2). Changing each variable in turn, while keeping the others constant optimized the conditions for the formation of the complex and its stability.

Effect of NBD-Cl concentration.

The effect of NBD-Cl concentration was studied over the range of 100-1000 g/ml. The maximum absorbance was obtained at a concentration of 500 g/ml. Higher concentrations of NBD-Cl resulted in diminished absorbance (Figure 3)

Effect of pH/Buffer

The reaction between metoprolol and NBD-Cl took place only in an alkaline medium. The effect of pH on absorbance reading was studied using borate, carbonate and phosphate buffers in the pH ranges of 5-10. At pH values below pH 7, there was no absorbance. However

as the pH values increased, absorbance increased correspondingly to a maximum at pH 9, with the borate buffer (Figure 4). While carbonate buffer and phosphate buffer at the same pH values had lower absorbance. Comparison of the results showed the borate buffer to be best medium for stability of complex.

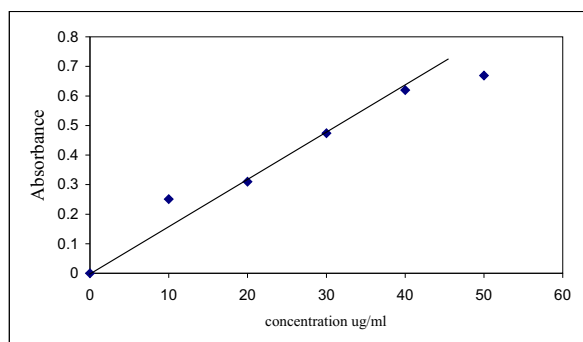


Figure 1: Plot of Absorbance against concentration of Metoprolol.

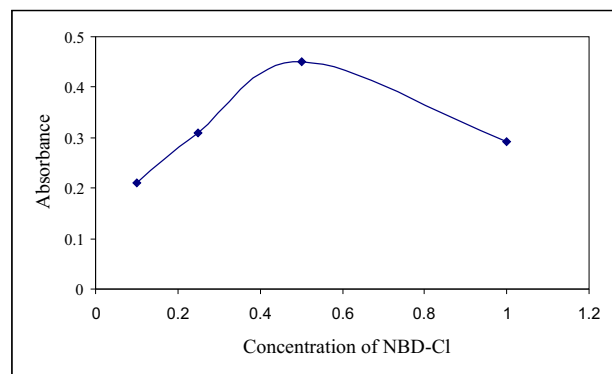


Figure 3 : The effect of NBD-Cl concentration ($\mu\text{g/ml}$) on the absorbance of reaction product complex.

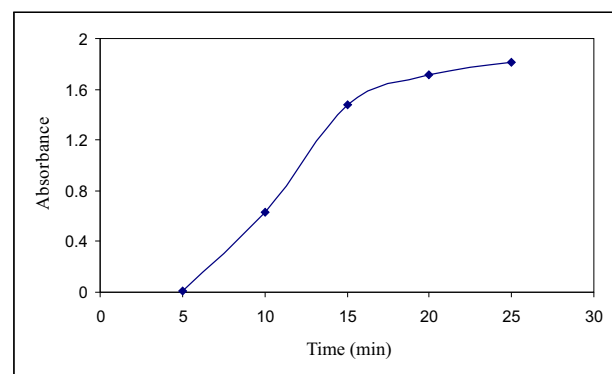


Figure 5: The effect of time of reaction product formation on product colour intensity and stability.

Effect of Temperature and Time

The effect of temperature, showed that the reaction/complexing process took place at 100°C . While the optimum reaction time for the complex formation was 10 minutes and stable for about 20 minutes (Figure 5 and 6).

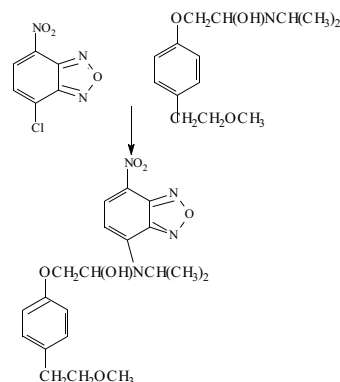


Figure 2: Proposed reaction pathway for the complex formed between metoprolol and NBD-Cl

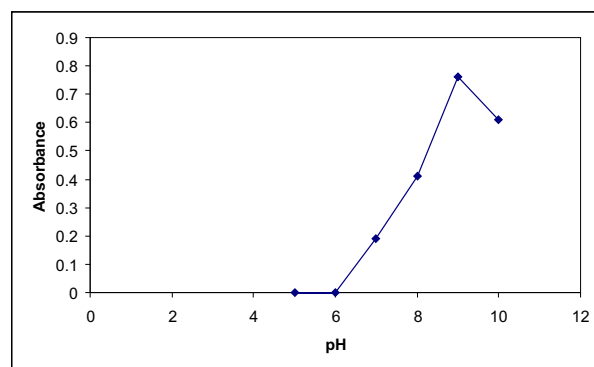


Figure 4: The effect of pH on the reactant/reaction product of metoprolol with NBD-Cl.

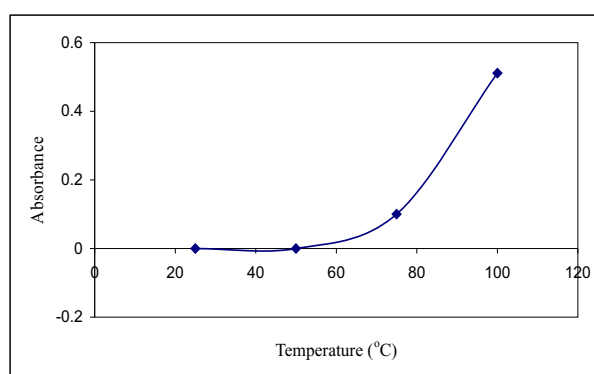


Figure 6: The effect of temperature on the formation of NBD-Cl metoprolol complex.

Table 1: Result validation table

	Concentration ug/ml Spiked	Concentration Obtained ug/ml	% recovery	Mean %RSD
1	5.0	4.64	91.67	7.22
2	15.0	15.66	104.35	7.08
3	25.0	23.82	94.02	8.72
4	35.0	33.32	95.15	2.77
Average	-	-	96.30	6.50

Conclusion

Metoprolol in tablet dosage form can efficiently be assayed using spectrophotometric method with NBD-Cl as the coupling agent.

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