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Research Article

SECOND AND THIRD ORDER DERIVATIVE SPECTROPHOTOMETRIC ESTIMATION OF NEBIVOLOL HYDROCHLORIDE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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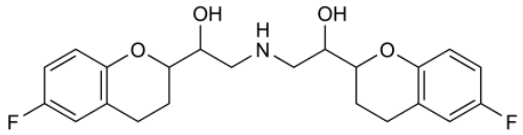
ABSTRACT

Two simple, accurate and reproducible derivative spectrophotometric methods were developed for the determination of Nebivolol hydrochloride in bulk drug and in pharmaceutical dosage forms. The quantitative determination of the drug was carried out using second derivative values measured at 296nm (n=2) and third derivative values measured at 290nm (n=4). Calibration graphs constructed at their wavelengths of determination were linear in the concentration range of Nebivolol using 40-80 µg/ml and 10-60 µg/ml for second and third derivative spectrophotometric methods. The correlation coefficient for both the methods is 0.9997 with the regression equations of Y=0.0003X-0.0002 and Y=0.0003X-0.0003., where 'Y' is the amplitude of peak and 'X' is the concentration of the sample in µg/ml. The proposed methods have been extensively validated as per ICH guidelines. The developed spectrophotometric methods in this study are specific, sensitive, precise and can be routineily utilized for the analysis of pharmaceutical formulations.

Keywords: Nebivolol, Second order derivative spectrophotometry, Third order derivative spectrophotometry.

INTRODUCTION

Nebivolol[1,2] is chemically 1-(6-flourochroman-2-yl)-{[2-(6-fluoro-chroman-2-yl)-2-hydroxy-ethyl] amino}ethanol or 2, 2′-azane-diylbis (1-(6-flourochroman-2-yl) ethanol. Nebivolol is a Long-acting, cardio-selective β_1-receptor antagonist without partial agonist activity[3] and used in treatment of hypertension. Nebivolol is the racemate (dl-nebivolol) of the enantiomers l-nebivolol and d-nebivolol. It is available as Nebivolol Hydrochloride.



NEBIVOLOL

Literature survey reveals that few analytical methods were reported which include liquid-chromatography with tandem mass spectro-metry[4], RP-HPLC and HPTLC methods[5] and first order derivative spectrometric determination[6], liquid chromatography coupled with electro spray ionization tandem mass spectrometry[7], Stability indicating RP-HPLC estimation[8] and Reverse phase HPLC method for the analysis[9] of Nebivolol in bulk and tablets of Nebivolol in bulk and tablets.

In present investigation we have developed simple and rapid second and third order derivative methods which can be applied for quantitative determination of Nebivolol Hydrochloride in bulk and its formulations.

EXPERIMENTAL

All spectral measurements were made on Shimadzu 1700 spectrophotometer with 1cm matched quartz cell was used. All chemicals used were purified. Nebivolol Hydrochloride sample in bulk were obtained from Hetero chemicals ltd. Hyderabad and tablet formulation from Lupin Ltd.., Mumbai. Pharmaceutical preparations are purchased from local market.

Preparation of stock solution

About 100mg of Nebivolol Hydrochloride (pure or formulation) was accurately weighed and dissolved in 50-60ml of Methanol. Allow it to stand for 10mins to ensure complete solubalisation. The solution was filtered by using whatmann filter paper. The residue was washed 3times with 10 ml portions of methanol and the total volume of the filtrate made upto100 ml with methanol. The final concentration was made to 1000µg /ml (1ml=1000µg) stock solution-I. 10ml of stock solution-I was taken in 100ml volumetric flask and the volume made up to the mark with Methanol (100 µg/ml).

Derivative spectrophotometric method

Fresh aliquots of standard stock solution were pipette out and suitably diluted with Methanol to get 40-80 µg/ml and 10-60 µg/ml for second and third order derivative respectively. The solutions were scanned in the spectrum mode from 300nm to 250nm wavelength range on Shimadzu 1700 spectrophotometer. Second order derivative spectra were obtained at n =2 a sharp peak was obtained at 296 nm (Fig-1) and the calibration curve were found to be linear in the concentration range of 40-80µg/ml (Fig-2).Third order derivative spectra were obtained at n =4 a sharp peak was obtained at 290 nm (Fig-3) and the calibration curve were found to be linear in the concentration range of 10-60µg/ml (Fig-4).

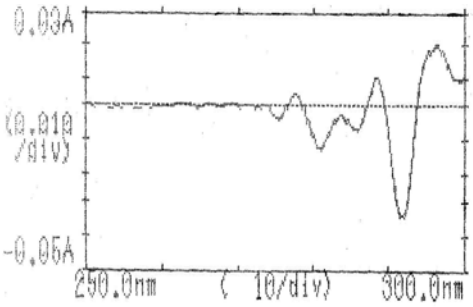


Fig. 1: Second order derivative spectrum of Nebivolol in Methanol (60µg/ml)

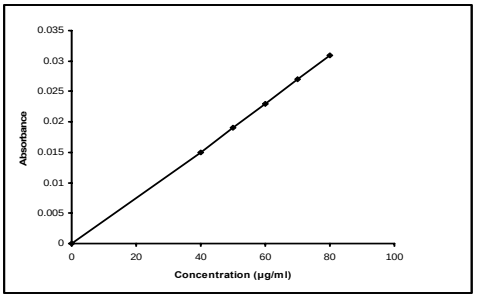


Fig. 2: Calibration curve of Nebivolol in Methanol

RESULTS AND DISCUSSION

Nebivolol being soluble in Methanol, all the solutions were prepared in Methanol. The solutions of different concentrations were prepared and scanned in Second derivative and Third derivative modes. Appropriate wavelengths were selected for subsequent analysis. Analysis was extended to formulation with two selected wavelengths 296 nm and 290 nm in second and third derivative modes respectively. The linearity were found in the concentration range of 40-80 µg/ml in second derivative mode and 10-60 µg/ml for third derivative mode.

The optical characteristics such as absorption maxima, Beer's law limit, were calculated. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation coefficient(r) obtained from different concentrations and the results will be summarized in Table-1.

The percent relative standard deviation and percent range of errors (0.05 and 0.01 level of confidence limits) calculated from the eight measurements are summarized in Table-1. The results showed that the methods have reasonable precision. Results obtained with proposed methods are compared with the results obtained with UV spectrophotometric method developed in our laboratory.

The results obtained with proposed methods confirmed the suitability of these methods for pharmaceutical dosage forms the other ingredients and exicipients present in pharmaceutical dosage forms did not interfere in the estimation when some commercial dosage from (T_1, T_2) were analyzed by this method.

The method was validated for various parameters like accuracy, precision and recovery is presented in Table-2.

CONCLUSION

The methods reported are found to be simple, sensitive, accurate, precise, and economical and can be used in the determination of Nebivolol from pharmaceutical dosage forms in a routine manner.

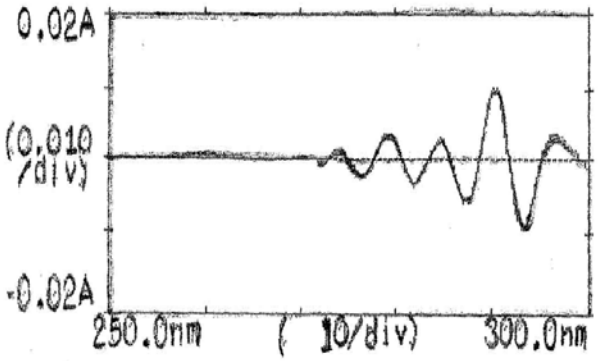


Fig. 3: Third order derivative spectrum of Nebivolol in Methanol (60µg)

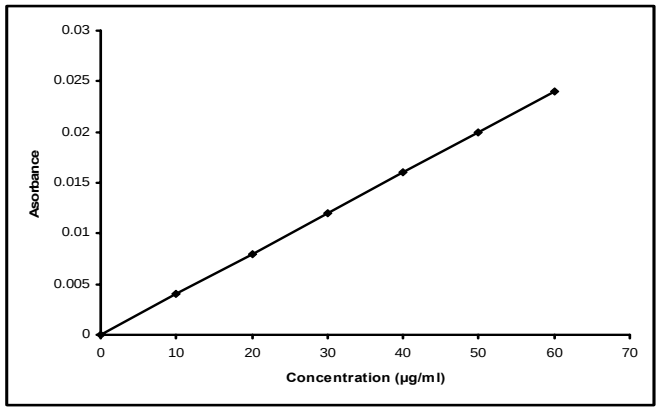


Fig. 4: Calibration curve of Nebivolol in Methanol

Table 1: Optical characteristics and Precision

Parameters	Second order	Third order
λ max (nm)	296	290
Beer's Law limit (µg/ml) (C)	40 – 80	10 - 60
Molar absorptivity (lit. mol $^{-1}$cm^{-1})	0.17123 x 10^3	0.16939 x 10^3
Regression equation(Y*)		
Slope(b)	0.00038	0.00038
Intercept(a)	0.00023	0.00035
Correlation coefficient (r)	0.9997	0.9997
LOD (µg ml^{-1})	13.717	3.428
LOQ (µg ml^{-1})	39.83	10.28
Range of errors**		
Confidence limits with 0.05 level	±0.001513	±0.000724
Confidence limits with 0.01 level	±0.002239	±0.001070

*Y = bC +a, Y is the absorbance unit and C is the concentration in µg/ml.; **Eight measurements

Table 2: Estimation of Nebivolol in pharmaceutical preparations

Sample	Labeled amount (mg)	Amount obtained (mg)			Percentage recovery*	
		Proposed methods		Reference method (UV method)		
		Second order (D_2)	Third order (D_3)		Second order	Third order
T1(Lupin)	5	4.94	4.986	99.98	98.80	99.732
T2(Torrent)	5	4.98	4.989	99.90	99.60	99.786

*Mean and standard deviation of eight determinations.

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REFERENCES

1. O'Neil M.J.(ed.).The Merck Index-an Encyclopedia of Chemicals, Drugs and Biologicals.Merck&Co.,Inc,14th Edition; 2006; 6432.

2. Sweetman S.C.(ed.), Martindale-The complete Drug Reference, Pharmaceutical Press, London(U.K.), 35th edition; 2007; 121.
3. Joel GH, Lee EL,(ed.), Goodman and Gilman's The Pharmacological Basis of Therapeutics. New York, 10th Edition; 2001; 257.
4. Thevis M, Opferman G, Schanzer W, *Biomed chromatogram*, 2001; 15; 393-402.
5. Patel L.J, Suhagia B.N. and Shah P.B. *Indian journal of pharmaceutical sciences,* 2007; 69(4); 594-596.
6. Atul A, Shrikhedkar, Prasad M.Bugdane, Sanjay J.Surana, *Pharma Review*, Feb 2008; 141.
7. Rama Krishna NVS, *J.Of Pharma and Bio.Ana.* 2005; 39(5, 4); 1006-1013.
8. A. Shah, K.K. Bhatt, R.S. Mehta, S.L. Baldania and T.R. Gandhi, *Indian J. pharm Sci.,* 2008; 70(5); 591-595.
9. Sastry B.S, Srinivasulu D, and Ramana H, *JPRHC*, July 2009; 1(1); 25-33.