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RP-HPLC Method for Estimation of Nebivolol in Pharmaceutical Dosage Form

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Abstract: Simple, selective, rapid, precise and economical reverse phase high-pressure liquid chromatography method has been developed for estimation of nebivolol in pharmaceutical dosage form. The method was carried out on a Hypersil BDS C_{18} column (5µ particles size) (250 mm X 4.6 mm) consisting of acetonitrile: 0.3M potassium dihydrogen phospate in ratio 50:50 (pH 3.2 adjusted with orthophosphoric acid) as mobile phase at a flow rate of 1.2ml/min. Detection was carried out at 278nm. The retention time of nebivolol was 4.34 min. The results of analysis showed that the amounts of drugs were in good agreement with the labeled claim of the formulations. The method validation parameters were checked as per the ICH guidelines. This method is specific and sensitive.
Key words: Nebivolol, RP-HPLC Hypersil, Potassium dihydrogen phospate

Introduction

Nebivolol is chemically 1-(6-fluorochroman-2-yl)-(2-(6-fluorochroman-2-yl)-2-hydroxy-ethyl)amino) ethanol[1,2]. It is used in the treatment of Hypertension. It blocks the β- receptor of the heart and reduces the force of the contraction and the cardiac output[3,4]. Literature review revealed that some spectrophotometric and HPLC methods have been reported for the estimation of nebivolol in tablet formulation [5,6].

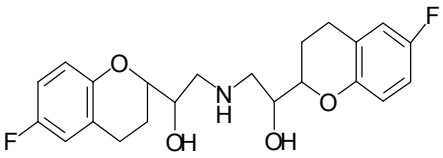

Fig. 1 – Structure of nebivolol

Present work describes the development of simple, selective, rapid, accurate, precise and economical RP-HPLC methods for the determination of Nebivolol in pharmaceutical dosage forms.

Expermental[7-11]

Apparatus and chromatographic condition:
Chromatographic separation was performed on a SPD 10 A UP Shimadzu HPLC system. Hypersil BDS C_{18}, column (5µ particles size) (250 mm X 4.6 mm), was used for separation. Analysis was performed at ambient temperature[7].

Materials
All the chemicals and reagents used were of analytical grade. Standard gift sample of nebivolol was provided by Torrent Pharmaceutical ,Ahemdabad. Tablet formulations of Nebicard and nebilong (5mg each) were procured from a local pharmacy.

Method and Result
Optimization of mobile phase was performed based on various parameters such as retention time, theoretical plates and resolution. The mobile phase consisted of acetonitrile: 0.03M potassium dihydrogen phospate in ratio of 50:50 (pH 3.2 adjusted with orthophosphoric acid) at a flow rate of

1.2ml/min. Mobile phase were premixed and filtered through a 0.2µ membrane filtered and degassed[8].

Study of retention time: A standard dilution of pure drug containing 12 µg/ml of Nebivolol was prepared in mobile phase, filtered through 0.2 µg membrane filter and loaded in injection port of instrument fitted with 20 µL fixed volume loop. The solution was injected and chromatogram was recorded. The mean retention time for Nebivolol was found to be 4.34 min. The representative chromatogram of nebivolol is reported in fig. 2.

Procedure for calibration curve:
Standard stock drug solutions of Nebivolol with concentration of 100 µg/ml prepared in mobile phase. For preparation of calibration curve of drug 4,5,6,7,8 ml standard stock solution of Nebivolol was transferred to series of 50 ml volumetric flasks and volume was made up to the mark with the mobile phase. Each solution was injected after filtration through 0.2 µ membrane filter and chromatogram was recorded. The calibration curve was plotted between concentration of drug and AUC of a peak of Nebivolol is reported in fig. 3. Linearity was found to be in concentration range of 8-16 µg/ml for Nebivolol[9,10].

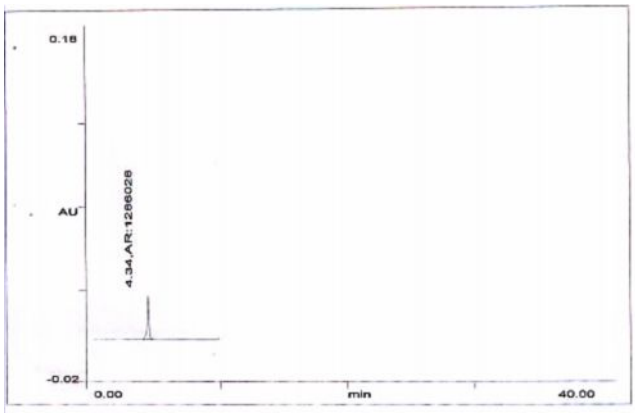

Fig. 2: Chromatogram of nebivolol

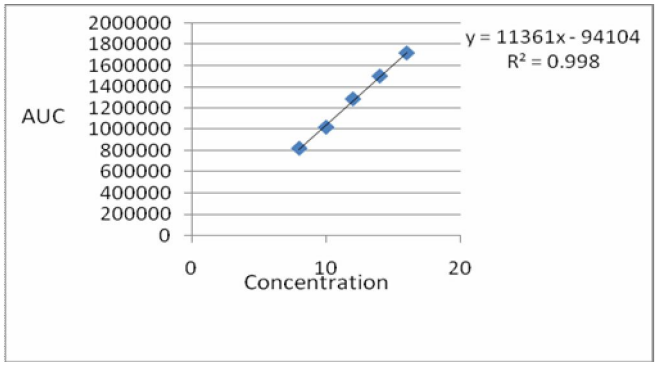

Fig. 3: Calibration curve of nebivolol

Tab. 1 – System suitability parameters for method

Parameters	Values
Detection wavelength	280nm
Linerity range	8-16 µg/ml
Slope	11361
Intercept	94104
Correlation coefficient	0.998
Retention time	4.34min

Assay procedure: Twenty tablets (each tablet containing 5mg Nebivolol) of Nebivolol were weighed accurately. The tablets were finely powdered and powder equivalent to 10.00 mg of Nebivolol was taken in a 100 ml volumetric flask containing 75 ml of mobile phase. The powder mixture was dissolved in the mobile phase with aid of ultrasonication for 10 min. The resultant was filtered through Whatman filter paper no. 41 into another 100 ml volumetric flask. The filter paper was washed several times with mobile phase. The washings were added to the filtrate and final volume was made up to the mark with mobile phase. From this filtrate 6 ml was further diluted to 50 ml with mobile phase. After setting the chromatographic conditions and stabilizing the instrument to obtain a steady base line, the final dilution of tablet sample was loaded in sample loop of the injection port of the instrument. The solution was injected and chromatogram was recorded. The procedure of analysis for tablet formulation was repeated five times with two different tablet formulation and results are reported in table 2.

Recovery study:

Recovery studies were carried out for the developed method by addition of known amount of standard drug solution of Nebivolol to pre-analyzed tablet sample solution at three different concentration levels. The resulting solutions were analyzed by proposed method. The results of recovery study were found to be satisfactory [11].

Tab. 2: Results of analysis of commercial formulations

Brand name	Labeled Claim (mg/tablet)	% Labeled Claim Estimated*	± Standard Deviation	Relative Standard Deviation
Nebicard	5	99.66	0.19621	0.001968
Nebilong	5	99.56	0.33689	0.003383

*Each value is an average of five determinations.

Tab.3: Results of Recovery studies

Brand name	Amount added test (µg/ml)	Amount added (µg/ml)	Amount recovered	% Recovery
Nebicard	6	4	10.16	101.06
	6	6	11.95	99.58
	6	8	14.04	100.28
Nebilong	6	4	10.09	100.9
	6	6	11.92	99.33
	6	8	13.86	99

Discussion

Method - The proposed method was found to be simple and linear in the concentration range 8-16µg/ml for Nebivolol. This method was found to be accurate and precise as indicated by the recovery studies and relative standard deviation. Thus this method is specific and sensitive.

Conclusion

The proposed RP-HPLC methods for estimation of nebivolol from pharmaceutical dosage forms were found to be sensitive, accurate, precise, simple and rapid. Hence the present RP-HPLC method may be used for routine analysis of the pharmaceutical dosage forms.

Acknowledgement

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