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Simultaneous estimation of nebivolol and valsartan by RP-HPLC method in tablet dosage form

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ABSTRACT

A simple, specific, accurate, and precise RP-HPLC method has been developed and validated for the estimation of Nebivolol and Valsartan in bulk drug and pharmaceutical dosage forms. A Xterra Symmetry C18 column having 150 mm x 4.6 mm, 5 µm in isocratic mode, with mobile phase containing Phosphate buffer (pH 2.8 with Ortho phosphoric acid) : Acetonitrile[35 : 65, v / v] is used. The flow rate is 0.9 ml / min and effluents are monitored at 282 nm. chromatogram showed peak at a retention time of 3.096 ± 0.008 min for Nebivolol and 4.110 ± 0.008 min for Valsartan. The method is validated for system suitability, linearity, precision, accuracy specificity, ruggedness, robustness, LOD and LOQ. Recovery of Nebivolol and Valsartan is found to be in the range of 99.22 - 100.11 % and showing linearity in the range of 10-50 µg / ml. The LOD and LOQ for estimation of Nebivolol and Valsartan are found to be 0.2 µg / ml, 0.76µg / ml, and 0.16µg / ml , 0.56 µg / ml respectively. Proposed method can be successfully applied for the quantitative determination of Nebivolol and Valsartan in bulk drug and Pharmaceutical dosage form.

Keywords: *Nebivolol, Valsartan, RP-HPLC, Xterra Symmetry C18 column..*

1. INTRODUCTION

Nebivolol is a third generation β_1 adreno receptor blocker with nitricoxide-potentiating vasodilatory effect used in treatment of hypertension, also for left ventricular failure. It is highly cardioselective under certain circumstances and has additional nitric oxide-mediated vasodilating and antioxidant properties, along with a favourable metabolic profile. Nebivolol has also been paired with another blood pressure lowering medication, the angiotensin receptor blocker valsartan [1].

Valsartan is mainly used for treatment of high blood pressure, congestive heart failure, and after a heart attack. It is an angiotensin II receptor antagonist (commonly called an ARB, or angiotensin receptor blocker), that is selective for the type I (AT_1) angiotensin receptor. Valsartan blocks the actions of angiotensin II, which include constricting blood vessels and activating aldosterone, to reduce blood pressure. The drug binds to angiotensin type I receptors (AT1), working as an antagonist [2].

Review of literature for Nebivolol and Valsartan gave information regarding its physical and chemical properties, various analytical methods that were conducted alone and in combination with other drugs. Literature survey reveals that certain spectrophotometric methods were reported for simultaneous estimation of Nebivolol and Valsartan and single method is available for such estimation by RP-HPLC method. In view of the need for a suitable RP-HPLC method for routine analysis of Nebivolol and Valsartan in formulations, attempts were made to develop simple, precise and accurate analytical method for simultaneous estimation of Nebivolol and Valsartan and extend it for their determination in formulation [3-8].

2. MATERIALS AND METHODS

Pure samples of Nebivolol and Valsartan were obtained from Hetero drugs Pvt.Ltd. for the simultaneous estimation of Nebivolol and Valsartan in commercial formulations. HPLC grade Orthrophosphric acid, Acetonitrile and Methanol were procured from Merck. High pure water prepared by using Millipore Milli Q. Necessary PPE (personal protective equipment) was used during the analysis. Destruction of solid samples and disposition of solvents was done.

2.1. Selection of wavelength

A solution of 100 µg/ml of Nebivolol and Valsartan were prepared in milliQ water. The resulting solutions were scanned individually on HPLC PDA detector from 190to 400 nm and also in UV-Visible spectrophotometer. The optimal response for both of them was obtained at 282 nm. Hence the complete method was processed at the wavelength of 282 nm.

2.2. Preparation of standard solution

10 mg of Nebivolol and 10 mg of Valsartan were accurately weighed and transferred into a 10 ml clean dry volumetric flask,about 7 ml of diluent was added, sonicated to dissolve it completely and the volume was made up to the mark with the same solvent to give a concentration of 1000 µg/ml (Stock solution) Further 0.05 ml of Nebivolol& 0.8 ml Valsartan were pipetted outfrom the above stock solution into a 10 ml volumetric flask and diluted up to the mark with diluent to give a concentration of 5 µg/ml and 80µg/ml respectively.

2.3. Preparation of sample solution

20 Tablets of contents were weighed and triturated in glass mortar. The quantity ofpowder equivalent to 10 mg of active ingredient present in 20 tablets (1734.5mg) wastransferred into a 10 ml clean dry volumetric flask, 7 ml of diluent was added to it andwas shaken by mechanical stirrer and sonicated for about 30 minutes by shaking atintervals of five minutes each and was diluted up to the mark with diluent to give aconcentration of 1000 µg/ml and allowed to stand until the residue settles beforetaking an aliquot for further dilution (stock solution). 0.8 ml of upper clear solutionwas transferred to a 10 ml volumetric flask and diluted with diluent up to the mark t ogive the respective concentrations.

3. RESULTS AND DISCUSSION

3.1. Validation of the developed method:

From the system suitability studies it was observed that % RSD of retention time was found to be 0.019 and 0.75 for Nebivolol and Valsartan respectively, % RSD of peak area was found to be 1.4 and 1.9 for Nebivolol and Valsartan respectively. A graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) was plotted and the correlation coefficient was calculated. From the Linearity data it was observed that the method was showing linearity in the concentration range of 60-100 µg/ml for Nebivolol and 96-160 µg/ml for Valsartan.The standard solution was injected for five times and the area for all five injections was measured in HPLC. The % RSD for the area of five replicate injections was found to be within the specified limits. The % RSD of Nebivolol for repeatability and intermediate precision was found to be1.3 and 0.46, for Valsartan it was found to be 1.3 and 0.45. It passes repeatability and intermediate precision. Assay was performed in triplicate for various concentrations of Nebivolol and Valsartan equivalent to 80, 100, and 120 % of the standard amount was injected into the HPLC system The recoveries of pure drug from the analyzed solution of formulation were 99.22 % to 100.11 %, which shows that the method was accurate. The Chromatograms of Standard and Sample are identical with nearly same Retention time. No interference due to Placebo and Sample at the retention time of analyte which shows that the method was specific. As the % RSD of retention time and asymmetry were within limits for variation in flow rate (± 0.1 ml). Hence the allowable flow rate should be within 0.8 ml to 1.0 ml/min.

Table - 1: Optimized chromatographic conditions

Parameter	optimized condition
HPLC system	WATERS 2690 (Empower software)
Column	Symmetry C18 (4.6x150mm, 5µm, Make:XTerra)
Detector wavelength	282 nm
Flow rate	0.9 ml per min
Run time	8 min

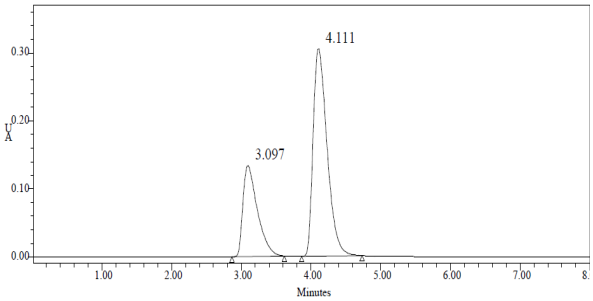

Figure – 1: Standard Chromatogram for Optimised Method.

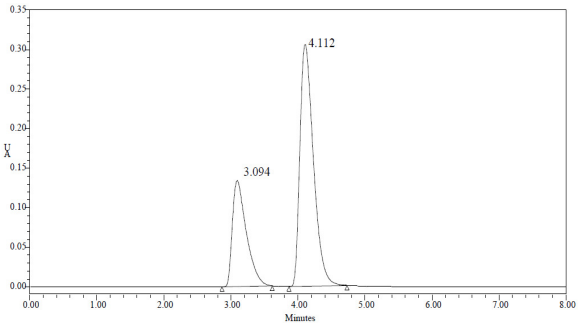

Figure – 2: Sample Chromatogram for Optimized Method.

Method was optimized and the retention time was reported as 3.097 and 4.111 minutes for Nebivolol and Valsartan respectively. The Chromatograms were recorded as Fig no: 1, 2 for standard, sample respectively.

Table - 2: System suitability parameters

Parameter	Nebivolol	Valsartan
Tailing factor	1.5	1.7
Theoretical plates	2196	2645
resolution		2.1

Table - 3: Validation parameters

Parameter	Nebivolol	Valsartan
Linearity	R^2= 0.999	R^2=0.998
Precision	% RSD= 1.30	% RSD= 1.30
Intermediate precision	% RSD= 0.46	% RSD= 0.46
Accuracy	% recovery=99.69 %	% recovery=99.71 %
Robustness (flow rate)	% RSD= 0.141	% RSD= 0.109
LOD (µg/ml)	0.2	0.16
LOQ (µg/ml)	0.76	0.56

4. CONCLUSION

Good agreement was seen in the assay results of Pharmaceutical formulation by developed and validated method. The method was validated for parameters such as system suitability, linearity, precision, accuracy, specificity, ruggedness robustness, LOD and LOQ. The system suitability parameters were within limit, hence it was concluded that the system was suitable to perform the assay. Hence it can be concluded that the proposed method was a good approach for obtaining reliable results and found to be suitable for the routine analysis of Nebivolol and Valsartan in Bulk drug and Pharmaceutical formulation.

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