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Simultaneous Estimation of Nebivolol Hydrochloride and Valsartan in Bulk and Capsule Dosage Form by Simultaneous Equation Method

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Abstract : Nebivolol Hydrochloride and Valsartan in combination are available as capsule dosage forms in the ratio of 1: 16. A simple, sensitive, accurate, and reproducible methods have been developed for simultaneous estimation of both. The proposed method are based on the simultaneous equation method, using methanol as solvent. Nebivolol Hydrochloride has absorbance maxima at 281 nm and Valsartan at 251 nm and shows linearity in the concentration range of 5-80 µg / ml and 5-50 µg / ml respectively. The limit of detection and limit of quantitation for Nebivolol Hydrochloride was found to be 1.21 µg / ml and 3.63 µg / ml and The limit of detection and limit of quantitation for Valsartan was found to be 1.33 µg / ml and 3.99 µg / ml. The method was validated statistically. Recovery study was performed to confirm the accuracy of the method.
Key words: Nebivolol Hydrochloride, Valsartan, Simultaneous estimation, Validation.

1. Introduction

Nebivolol Hydrochloride, 1-(6-fluorochroman-2-yl)-{[2-(6-fluorochroman-2-yl)-2-hydroxyethyl] amino}ethanol, is a selective β_1 blocker[1-7]. Literature assessment showed that high performance liquid chromatography (HPLC), high performance thin layer chromatography (HPTLC) [8] , and liquid chromatography-mass spectroscopy (LC-MS) [9-11] methods are reported for estimation of in dosage formulations and in biological fluids. Valsartan,3-methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5-phenyl]methyl]amino]butanoic acid, is an angiotensin II receptor antagonist [12] . Both these drugs are used for the treatment of high blood pressure and other cardiovascular pathophysiologic conditions. A LC-MS [13] and HPLC method [14] are reported for estimation of Valsartan in human plasma. The present research work describes rapid, accurate, sensitive and reproducible spectroscopic method for simultaneous estimation of Nebivolol Hydrochloride and Valsartan from the capsule formulation.

2. Experimental

2.1 Instruments and reagents

A Shimadzu UV-1800 UV/VIS spectrophotometer was used with 1 cm matched quartzcell.

All the chemicals used were of analytical grade. Methanol A.R. grade was procured from Loba Chem. Ltd., Mumbai. An analytically pure sample of Nebivolol Hydrochloride and Valsartan were procured as gift sample from Torrent Pharmaceuticals Ltd. (Ahmedabad, India). Capsule formulation [NEBICARD-V ,Torrent Pharmaceuticals Ltd, Ahmedabad] was procured from a local pharmacy with labeled amount 5 mg Nebivolol Hydrochloride and 80 mg Valsartan per capsule.

2.1 Preparation of standard stock solution

Stock solutions (100 µg / ml) of Nebivolol Hydrochloride and Valsartan were prepared by dissolving separately 10 mg of drug in methanol and making up the volume with methanol. The stock solution were suitably diluted to produce solution of

concentration 20 µg / ml, these working solutions were scanned in the entire UV range(200-400 nm) to determine the λ max. Absorption maxima of Nebivolol Hydrochloride and Valsartan were detected at 281 nm (λ_2) and 251 nm (λ_1), respectively and overlain spectra was recorded. A series of standard dilutions of each drug were prepared having concentration range of 5-100 µg / ml. Nebivolol hydrochloride and Valsartan showed linearity with absorbance in the range 5-80 µg / ml and 5-50 µg / ml respectively. The absorbances were measured at 251 and 281 nm an calibration curves were plotted at these wavelengths.

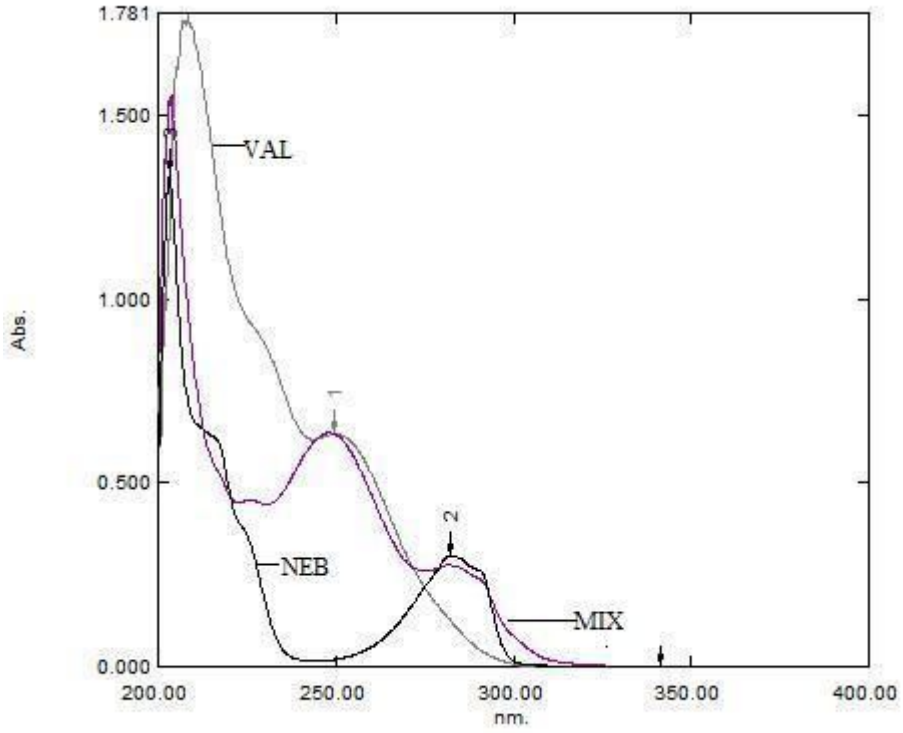
2.3 Analysis of marketed formulations

Twenty capsules of formulation were accurately weighed and average weight calculated. The capsule shell was then opened to collect granules and triturated. An amount of powder equivalent to 5 mg Nebivolol Hydrochloride and 80 mg Valsartan was weighed and transfer into 100 ml volumetric flask than dissolved with methanol and further diluted with methanol. It was kept for ultrasonication for 30 min; this was filtered through Whatman filter paper No. 41 and then final dilution was made with methanol to get the final concentration.

2.4 Simultaneous equations method

Method is based on simultaneous equations method of Vierodt. Absorption maxima of Nebivolol Hydrochloride and Valsartan were 281 nm (λ_2) and 251 nm (λ_1), respectively. Calibration curve for Nebivolol Hydrochloride and Valsartan was prepared in the concentration range 5-80 µg / ml and 5-50 µg / ml respectively. The absorptivity coefficients of the two drugs were determined by using Beer's law: A = E (1%, 1cm) CL and their average value taken. The overlain spectra of Nebivolol Hydrochloride and Valsartan are represented in [Figure - 1]. A set of two simultaneous equations was developed using these absorptivity coefficients. These are: A_1 =0.03374 Cx + 0.0015Cy…(1); and A_2 =0.0075 Cx + 0.0154 Cy…(2), where A_1 and A_2 are absorbances at 251 and 281 nm respectively, and Cx and Cy are concentrations of for Valsartan and Nebivolol Hydrochloride respectively.

Figure-1:



3. Result and Discussion

The method was validated according to International Conference on Harmonization guidelines for validation of analytical procedures [15-17]. Linear regression equations (intercepts and slopes) for mixtures of Nebivolol Hydrochloride and Valsartan were established. The high values of the correlation coefficients and the values of *Y*-intercepts close to zero indicate the good linearity of the calibrations. The values of slope, intercept and correlation coefficient values and given in Table 1. Limit of detection(LOD) and limit of quantitation(LOQ) were determined by using the formula based on the standard deviation of response and the slope. The limit ofdetection and limit of quantification were calculated by using the equation LOD = 3.3 x σ / S and LOQ = 10 x σ / S, where σ is the standard deviation of intercept, S is the slope and it is mentioned in Table 1.

To study the accuracy of the proposed methods, and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition method. This study was performed by addition of know amounts of Nebivolol Hydrochloride and Valsartan to preanalyzed solutions of commercial capsule. The results of analysis of marketed formulation are shown in Table 4. The values obtained are within the limit.

4. Conclusion

The developed method was found to be simple, sensitive, accurate and reproducible and can be used for routine analysis of Nebivolol Hydrochloride and Valsartan in bulk and in pharmaceutical formulations.

Table No. 1 : Calibration parameters

Sr. No.	Parameter	Nebivolol Hydrochloride	Valsartan
1	Absorption Maxima (nm)	281	251
2	Beer's Law limits(mg / ml)	5-80	5-50
3	Regression equation (y)* Slope (b) Intercept (a)	 0.0057 0.0155	 0.0041 0.0102
4	Correlation coefficient	0.9985	0.9987
5	Limit of detection (µg / ml)	1.21	1.33
6	Limit of quantification (µg / ml)	3.63	3.99

*y = a+ bx; when x is the concentration in mg / ml and y is absorbance.

Table No 2: Accuracy and Precision data for determination of Valsartan in the presence of Nebivolol Hydrochloride.

Added amount Valsartan (µg / ml)	Within day* (Amount found ± SD)	Between day* (Amount found ± SD)
10	10.03 ± 0.05	10.06 ± 0.07
20	20.08 ± 0.06	20.18 ± 0.14
30	30.23 ± 0.29	30.23 ± 0.16

* is average of 6 readings.

Table No 3: Accuracy and Precision data for determination of Nebivolol Hydrochloride in the presence of Valsartan.

Added amount Nebivolol Hydrochloride (µg /ml)	Within day* (Amount found ± SD)	Between day* (Amount found ± SD)
2	2.08 ± 0.04	2.04 ± 0.14
4	4.01 ± 0.12	4.08 ± 0.06
6	6.03 ± 0.10	6.17 ± 0.07

* is average of 6 readings.

Table No 4: Assay results of Valsartan and Nebivolol Hydrochloride in capsule.

Drugs	Amount (mg / Capsule)		% Lable claim (%Found ± SD)*
	Labeled (mg)	Found (Mean ± SD)	
Nebivolol Hydrochloride	5 mg	4.97 ± 0.04	99.4 ± 0.95
Valsartan	80 mg	79.94 ± 0.22	99.9 ± 1.13

* is average of 6 readings.

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