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Research Article

QUANTITATIVE ESTIMATION OF VALSARTAN IN PURE AND CAPSULE DOSAGE FORMS BY RP-HPLC

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ABSTRACT

A rapid and precise reverse phase high performance liquid chromatographic method has been developed for the estimation of Valsartan in its pure form as well as in Capsule dosage forms. Chromatography was carried out on a Inertsil, C-18, 250 x 4.6mm. 5µusing a mixture of Ammonium dihydrogenortho phosphate and Methanol (50:50v/v) as the mobile phase at a flow rate of 1.0 mL/min the detection was done by UV at 210nm. The retention time of the drug was 3.80 ±.25 min. The method produced linear responses in the concentration range of 10-100µg/ml of Valsartan. The method was found to be reproducible for analysis of the drug in Capsule dosage forms.

Keywords: Valsartan, RP-HPLC, Method validation.

INTRODUCTION

Diovan (valsartan) is a nonpeptide, orally active, and specific angiotensin II receptor blockeracting on the AT_1receptor subtype.Valsartan is chemically described as N-(1-oxopentyl)-N-[[2 '-(1H-tetrazol-5-yl) [1,1 '-biphenyl]-4-yl]methyl]-L-valine.is a powerful chemical that attaches to angiotensin receptors found in many tissues but primarily on smooth muscle cells of blood vessels[1,2]. Angiotensin's attachment to the receptors causes the blood vessels to narrow (Vasoconstrict) which leads to an increase in blood pressure (hypertension). Valsartan blocks the angiotensin receptor. By blocking the action of angiotensin, valsartan dilates blood vessels and reduces blood pressure.A literature survey revealed that only a few HPLC[3- 5] methods are available for the estimation of Valsartan. The authors now propose a new validated, sensitive and reproducible HPLC method for the determination of Valsartan and the capsule dosage forms was also observed.

EXPERIMENTAL

Chromatographic conditions

A prominence isocratic HPLC system (Younglin HPLC YL9000 series) with YL 9110 Pump and with “autochro 3000” software and UV-Vis detector YL9120,Inertsil C_{18} ODS column (250x4.6mm, 5µ). A 20µL Hamitton injection syringe was used for sample injection. HPLC grade, a freshly prepared Ammonium dihydrogenortho phosphate and Methanol (50:50v/v) was used as the mobile phase. The solvents was filtered through a 0.45µ membrane filter and sonicated before use. The flow rate of the mobile phase was maintained at 1.0mL/min. the column temperature was maintained at room temperature, the detection of the drug was carried out at 210nm.

Selection of mobile phase
The solution of Valsartan was injected into the HPLC system and run in different solvent systems. Different mobile phases containing methanol, water, acetonitrile and phosphate buffer in different proportions were tried and finally phosphate buffer and methanol (50:50 v/v) was selected as an appropriate mobile phase which gave good resolution and acceptable peak parameters for Valsartan.

Preparation of Mobile Phase
Mobile phase comprised of 10 mM Ammonium dihydrogenortho phosphate (Adjusted to P^H 3.5±0.05 with Ortho phosphoric acid), and Methanol (50:50 v/v). Mobile phase was filtered through a 0.45-µ m membrane filter, degassed with a helium spurge for 20 min and pumped from the respective solvent reservoir to the column (flow rate, 1.0 ml/min), which yield a column back pressure of 653-750 psi .Run time was set as 5 min, column was equilibrated for 60 min with mobile phase flowing through the system. Eluents were monitored at 210 nm and data were acquired, stored and analyzed with the software"Autochro-3000" (Young Lin).

Selection of analytical wavelength
From the standard stock solution, further dilutions were prepared using mobile phase and scanned over the range of 200 – 400 nm and the spectrum was overlain. It was observed that 210 nm is the λ_{max} for Valsartan and the wavelength suitable for Valsartan was preferred.

Checking the resolution of drug and material standard
The column was saturated with the mobile phase (indicated by constant back pressure at desired flow rate). Standard solution of Valsartan was injected to get the chromatogram. The retention time for Valsartan was found to be 3.80 ±.25 min.

Preparation of Standard Solutions
A stock solution of Valsartan was prepared by dissolving Valsartan (100 mg) in a volumetric flask (100 ml) containing 25 ml of diluent, sonicated for 20 min and then made up to the volume with diluent. Working standard solution of Valsartan (300µg/ml) was prepared by suitable dilution of stock solution with diluent. Linearity solutions were prepared in diluents containing RS (10-100µg/ml). Each of these drug solutions (20µl) was injected into the column and the peak area and retention times were recorded.

Estimation of Valsartan in Capsules
Two commercial samples of the Capsules containing the drug were chosen for testing the suitability of the proposed method to estimate Valsartanin Capsules. For this, Weigh accurately quantity of the powdered contents of capsule equivalent to about 100mg of Valsartan in to 100mL volumetric flask, add about 60mL of diluents, Sonicate for about 30min and dilute to 20 ml with water and methanol. Filter through 0.45 micron filter. The contents of the flasks were made up to the volume with the mobile phase and mixed well. From the above stock 50 µg/mL sample solution was prepared with mobile phase. Twenty micro liters of each of these solutions was then injected five times in to the column. The mean peak area ratios of the drug to the five such determinations were calculated and the drug content in the tablets was quantified using the regression equation obtained for the pure sample.

RESULTS AND DISCUSSION

The present study was carried out to develop a sensitive, precise and accurate RP-HPLC method for the analysis of Valsartan in bulk drug and pharmaceutical dosage forms. The retention time for Valsartan was 3.4 minutes for a run period of 5 minutes (Fig.1 and Table1). Each sample was injected five times and the similar retention times were observed in all cases. The peak areas of different concentrations set up as above were calculated and average value for 5 such determinations are shown in Table-2 The peak area for drug solution was reproducible as indicated by low coefficient of variation(Fig.2).
A good linear relationship (r = 0.999) was observed between the concentration of Valsartan and the respective peak areas. The calibration graph was found to be linear in the range of 10-100 µg/mL, when the Valsartan solution was analyzed by the proposed RP-HPLC method. In intra and inter day variation studies, Inter day and intraday precision was determined by analyzing the drug sample at three different concentration levels.
The results are presented in the form of %RSD which is below 1.00 (Tables 3,4 and 5) which shows that the proposed HPLC method was highly precise. The method was robust as

observed from insignificant variation in the results of analysis by changes in flow rate, Mobile phase composition and temperature separately.

The drug content in the Capsules was quantified using the proposed analytical method. The capsules were found to be contain an average 100.02% of the labeled amount of drug. The proposed reversed phase HPLC method was found to be simple, precise, highly accurate, specific and less time consuming.

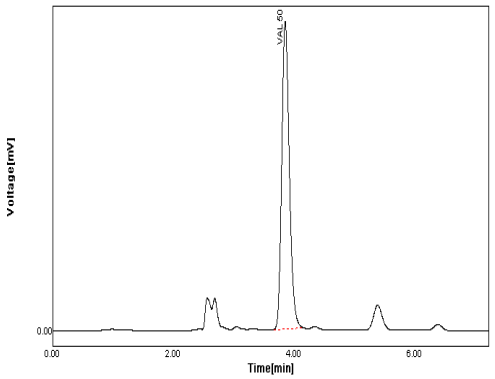

Fig. 1: A typical chromatogram for Valsartan standard solution (50µg/ml)

Table 1: A parameters for typical chromatogram for Valsartan standard solution

S. No.	Drug	RT (min)	Peak Area	Height	Plates	HETP	LOD	LOQ
1.	Valsartan	3.80±.25 min	3883448	43314	5632	0.0435	0.056µg/ml	0.156µg/ml

Table 2: Calibration of the proposed method

S. No.	Concentration (µg/ml)	Retention time (min)	Peak area
1	10	3.825	824576
2	25	3.832	2356214
3	50	3.852	3896572
4	75	3.815	5742139
5	100	3.829	7842369

Table 3: Intra-day Precision for Valsartan

Concentration (µg/ml)	Peak Area	Mean(n=5)	S.D	% RSD
50	3873448	3683425.5	47054.3	0.32
50	3862621			
50	3883425			
50	3793748			
50	3923218			

Table 4: Inter day Precision for Valsartan

Concentration (µg/ml)	Peak Area	Mean (n=5)	S.D	% RSD
50	3965423	3833523	75500.5	0.35
50	3874569			
50	3754685			
50	3845123			
50	3845698			

Table 5: Recovery data of Valsartan

Amount taken µg	Amount found (µg/ml)	% recovery	Mean Recovery	% RSD
20+25= 45	45.01	100.03	100.01	0.01
20+25= 45	44.96	99.96		
20+25= 45	45.06	100.04		
25+25=50	49.99	99.99	100.04	0.12
25+25=50	50.06	100.04		
25+25=50	50.09	100.09		
25+30=55	55.09	100.06	100.03	0.25
25+30=55	55.03	100.05		
25+30=55	54.8	99.99		

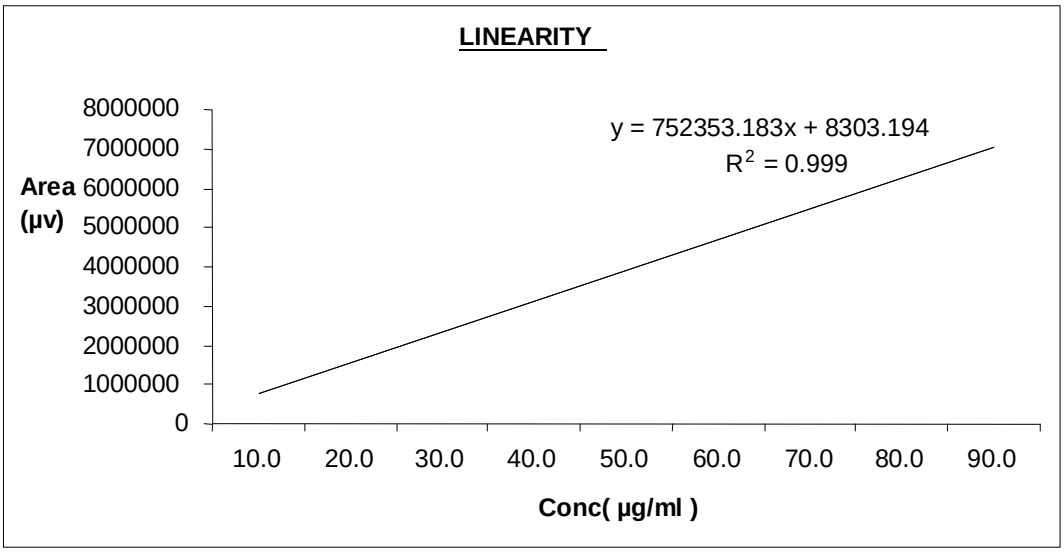

Fig. 2: Linearity curve of Valsartan

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