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Precise and Accurate RP-HPLC Method Development for Quantification of Valsartan in Tablet Dosage Form

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ABSTRACT

A simple, precise, accurate and reproducible RP-HPLC method has been developed for determination of Valsartan in Tablet dosage form. A Perkin Elmer HPLC series 200 with software Perkin Elmer total chrome navigator was used. The C-18 (Kromasil, 250 × 4.6 mm) having particle size of 5µm was used. The gradient mobile phase was selected consisting of solution A ACN, solution B phosphate buffer of pH 3.5 added few drops of Triethylamine in of buffer solution. The run time of 10 min was selected. The mobile phase composition keep on varying up to the 10 min of run time. The flow rate of 1.0 ml/min was used and Perkin Elmer series 200 UV/VIS detector wavelength was set at 250 nm. The retention time of Valsartan was found to be 5.19 min. The percentage recovery was found to be up to 99% to nearly 100% and percentage RSD was found to be less than 2.0%. Proposed method was validated for precision, accuracy, linearity range, robustness and ruggedness. The method was successfully applied for quantitative determination of valsartan in tablet dosage form.

Keywords: Valsartan, RP- HPLC, Validation, C-18 Kromacil.

INTRODUCTION

Valsartan is chemically N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl) [1, 1'-biphenyl]-4-yl] methyl]-L-valine. [1-2] Valsartan is potent Angiotensin II receptor blocker. It is mainly used as anti-hypertensive drug. [3-4] Valsartan is official in USP 1. [5] There were few methods reported for determination of valsartan individually. The valine molecule of the Sertraline has one chiral centre. The (S) enantiomer is essentially used. [6-7] The aim of the present study was to develop accurate, precise and selective reverse phase HPLC assay procedure for the analysis of VAT in bulk drug formulation. The validation of proposed method is done according to the ICH guideline validation was done according to ICH guidelines. [8]

MATERIALS AND METHODS

Acetonitrile HPLC grade, Methanol HPLC grade, Triethylammine HPLC grade, Potassium Dihydrogen orthophosphate GR grade, Millipore water was used during the analysis. Chromatographic separation was performed using piston pump. Precision loop injector Rheodyne was used. Perkin Elmer series 200 total chrome navigator software. C-18 Kromacil Kromasil column having dimension of 250 × 4.6 mm and particle size of 5µm was used for separation.

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Wavelength scan

The solution of Valsartan of strength100µg/ml was prepared in methanol and scanned for dictating the maximum absorbance wavelength. The maximum absorbance of Valsartan was found around 250nm.

Preparation of Mobile Phase and Standard solution

Gradient condition was used for the separation. Mobile phase A of ACN and mobile phase B of Phosphate buffer of pH 3.5 added with Triethylamine measuring 0.001% of Volume of buffer solution. The mobile Phase B was filtered through whatman filter paper no. 42. The stock solution of 1.0 mg/ml in methanol was prepared. The injection volume of 20 µl was kept constant throughout the analysis. The flow rate of 1.0ml/min was selected. The total run time for 10 min was set and the UV detection was carried out at 250 nm.

Preparation of sample solution

Twenty tablets (Valant 80, Lupin Pharmaceuticals Ltd. Aurangabad, India) containing 80 mg of valsartan were taken and average weight was determined. Weight equivalent to 80mg of Valsartan was taken in 100 ml volumetric volumetric flask and 50 ml of Methanol were added in that. The flask was sonicated for 30 min after complete sonication volume was made up to the mark with Methanol and shaken for five minutes. Dilutions were made in order to get the final solution of 80ppm, 100ppm and 120ppm.

Assay Method

The optimised method was found with trial and error and steady base line was recorded. The standard solution was injected and chromatogram was recorded. The retention time of the peak was found to be 5.19 min. the procedure was repeated for the sample solution and peak area of standard and sample solution were recorded. The concentration of drug was found out by comparing with the standard.

Table 1: Mobile Phase composition

Time (min)	ACN %	Buffer %
0.5	40	60
2	55	45
4	85	15
2	40	60
2	40	60

Table 2: Chromatogram of Valsartan Hydrochloride

Peak No.	Name of Peak	Retention Time (Min)	Area µAU sec
1	Valsartan	5.19	703217.24

Table 3: Linearity of Valsartan Hydrochloride

S. No	Concentration (ppm)	Area µAU sec
1.	10	589254.26
2.	20	1143180.74
3.	30	1534952.84
4.	40	2266264.24
5.	50	2791574.02

Table 4: Repeatability of Valsartan Hydrochloride

Conc (ppm)	Area µAU sec
20	1297076.58
20	1283010.66
20	1295764.73
20	1317231.46
20	1321118.81
20	1322187.26
Average	1306064.92
R.S.D.	1.25

Table 5: Interday precision

S. No	Conc (ppm)	Area 1 µAU sec	Area 2 µAU sec	Area 3 µAU sec	Average µAU sec	% R.S.D.
1.	20	1267076.58	1283010.66	1285764.73	1278617.32	0.789
2.	30	1841526.56	1843690.28	1852105.27	1845774.04	0.303
3.	40	2380476.67	2382540.79	2386658.23	2383225.23	0.132

Table 6: Intraday precision

S. No	Conc (ppm)	Area 1 µAU sec	Area 2 µAU sec	Area 3 µAU sec	Average µAU sec	% R.S.D.
1.	20	1317231.46	1283010.66	1322187.26	1320179.177	0.198
2.	30	1841526.56	1843690.28	1843586.87	1842891.793	0.033
3.	40	2380476.67	2382540.79	2571032.65	2567097.857	0.1343

Table 7: Recovery study

S. No	Conc (µg/ml)	Amount Added (µg/ml)	Amount found (µg/ml)	Amount recovered (µg/ml)	% recovery
1.	50	40	89.34	39.34	99.27
2.	50	50	99.92	49.92	99.92
3.	50	60	109.86	59.86	99.87

RESULTS

The method enables the quantification of the Valsartan. The sufficient resolution and precise quantification was obtained by the proposed HPLC method. The results obtained from the analysis were satisfactory. This method can be used for the routine HPLC analysis.

Method Validation

The proposed method was validated as per ICH guideline as follow.

Linearity

The linearity of the method was calculated by the injecting the Standard solution of concentration ranges between 10µg/ml to 100µg/ml. The calibration curve were plotted where concentration of injected solution on X- axis and area under cure the response factor on Y- axis. The slope and intercept value for calibration curve was y= 55373x+3204. The coefficient of correlation was found to be 0.996.

Repeatability

Six injection of 20µg/ml were injected to check the repeatability response of method. The percentage R.S.D. of method was calculated. The R.S.D. was found to be 1.25.

Ruggedness

Interday and intraday studies were carried out to determine the ruggedness of the proposed method. Three replicate of the standard drug were injected to carry out the interday and intraday study. The R.S.D. and S.D. of the each injection were determined. The results of the observation were found to be well under the limit and no marked differences were observed. No significant change in the chromatogram of both interday and intraday study proved that the method was rugged**.**

Recovery

The accuracy of the method was determined by using the recovery method. The recovery method was carried out by at three level 80%, 100% and 120% by standard addition method. The percentage recovery and standard deviation were calculated. From the analysis it was found that standard drug was accurate.

These studies are carried out by adding the particular amount of the sample solution in the stock solution. Three different strengths are prepared.

Robustness

Robustness of the method was determined by changing the flow rate of the system. The proposed flow rate of 1ml/min was changed to 0.8 ml/min and 1.2 ml/min.

Table 8: Robustness study of flow rate 0.8 ml/min

Cons (ppm)	Area µAU sec
50	5408454.87
50	5506228.13
50	5594254.28
Average	5502979.093
RSD	1.688945298

Table 9: Robustness study of flow rate 1.2 ml/min

Conc (ppm)	Area µAU sec
50	3014713.48
50	3096293.33
50	3057557.16
Average	3056187.99
R.S.D.	1.335230548

DISCUSSION

Good separations of the chromatographic peaks were observed and no interfering peaks were found. The calibration curve was linear; the linearity between concentration and area shows its suitability in in-vitro analysis. The precision and accuracy of the method was found to be satisfactory. The recovery study results were found satisfactory and method was robust.

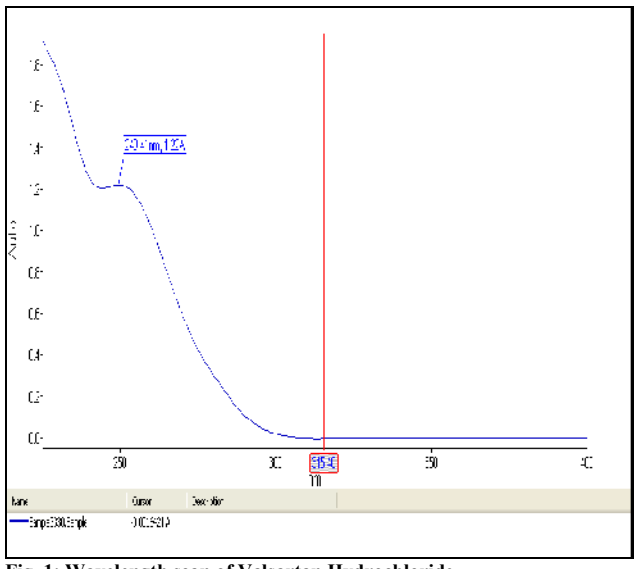

Fig. 1: Wavelength scan of Valsartan Hydrochloride

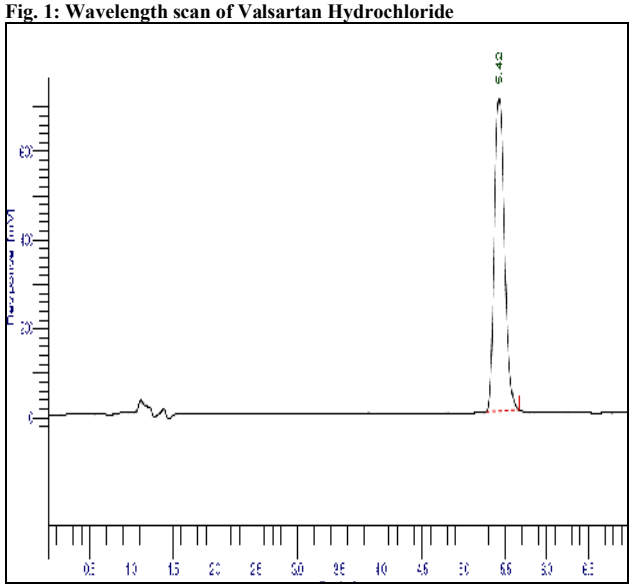

Fig. 2: Chromatogram of Valsartan Hydrochloride

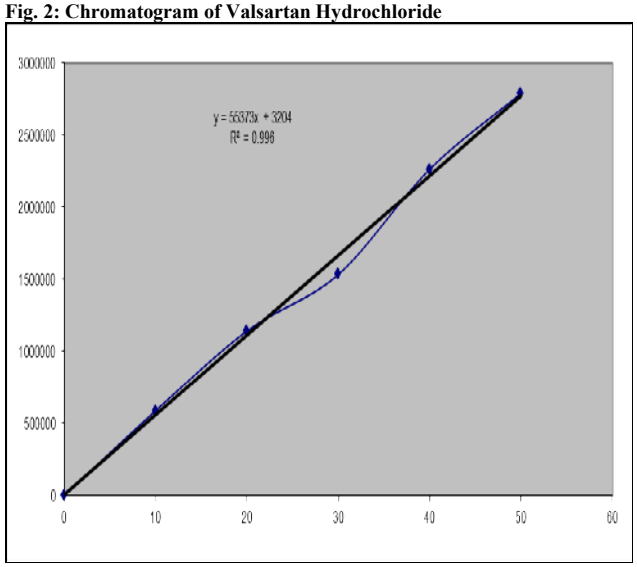

Fig. 3: Concentration response curve of valsartan hydrochloride

The proposed HPLC method is sensitive, simple, precise and reproducible. It can be successfully applied for estimation of Valsartan in tablet dosage form by HPLC method. The statistical analysis results that carried out method are revealing good results.

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