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METHOD DEVELOPMENT AND STATISTICAL VALIDATION OF VALSARTAN IN BULK AND TABLET DOSAGE FORM BY UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

A simple, accurate, specific and precise UV Spectrophotometric method has been developed for estimation of Valsartan in bulk and pharmaceutical formulation. The λ max of Valsartan in ethanol was found to be 249 nm. The drug exhibited the linearity in the concentration range of 10-60µg/mL with correlation coefficient of 0.999. the % recovery of the drug for the proposed was found to be between 99.82 to 100.48%. The % RSD values found to be less than 2. No interference was observed in the presence of common pharmaceutical excipients. The method was validated as per ICH guidelines. The developed method was successfully employed for the estimation of Valsartan in pharmaceutical dosage form. The developed method was cost effective with less consumption of solvents and can be used for routine analysis.

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INTRODUCTION

Valsartan,[(S)-3-methyl-2-(N-{[2´-(2H-1, 2,3, 4-Tetrazol-5-yl) biphenyl-4-yl]methyl} Pentanamido) butanoic acid (Figure 1)is a potent Angiotensin receptor blocker which selectively acts on AT_1, the subtype receptor that mediates the cardiovascular actions of angiotensin II, the main vasoactive hormone of the renin-angiotensin-system[1-3].Valsartan is not yet official in any Pharmacopoeia, where, only few analytical methods have been reported for its determination in pharmaceutical formulations and biological fluids. Such methods include HPLC,colorimetry,electrochemistry, and solvent meting method.

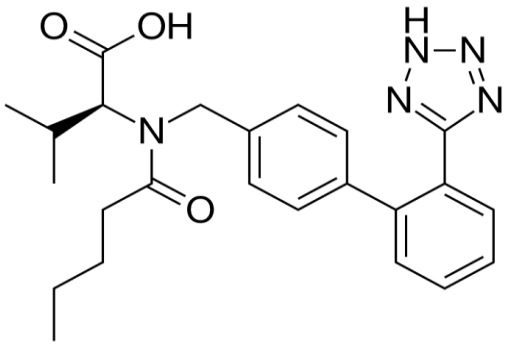

Figure 1: Structure of Valsartan.

Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of their simplicity, specificity, and low cost. This study presents a new spectrophotometric method for the determination of Valsartan in bulk and pharmaceutical formulations. Accordingly, the objective of this study was to develop and validate the UV-spectrophotometric method for the estimation of Valsartan in bulk and pharmaceutical formulations as per ICH guidelines [4-6].

MATERIALS AND METHODS

Materials:

Valsartan was a gift sample from Sun Pharma,Puducherry. All chemicals and reagents used were of analytical grade and purchased from S.D. Fine Chem Limited, Chennai, India.

Spectroscopic analysis was carried out using Double beam Shimadzu recording UV-Visible Spectrophotometer model 1800

METHOD DEVELOPMENT

Solvent Selection:

Solubility was checked with different solvents like water, methanol, and ethanol and found that it was freely soluble in methanol and ethanol. In the present investigation, ethanol was used for all the dilutions since it economical and easily available than other organic solvents.

Selection of wavelength for analysis ofValsartan:

The absorbance of the solutions containing Valsartan at 20µg/mL was determined in the UVrange 190 nm – 400 nm using an appropriate blank. The absorption maxima were found to be 249 nm (Figure 2)

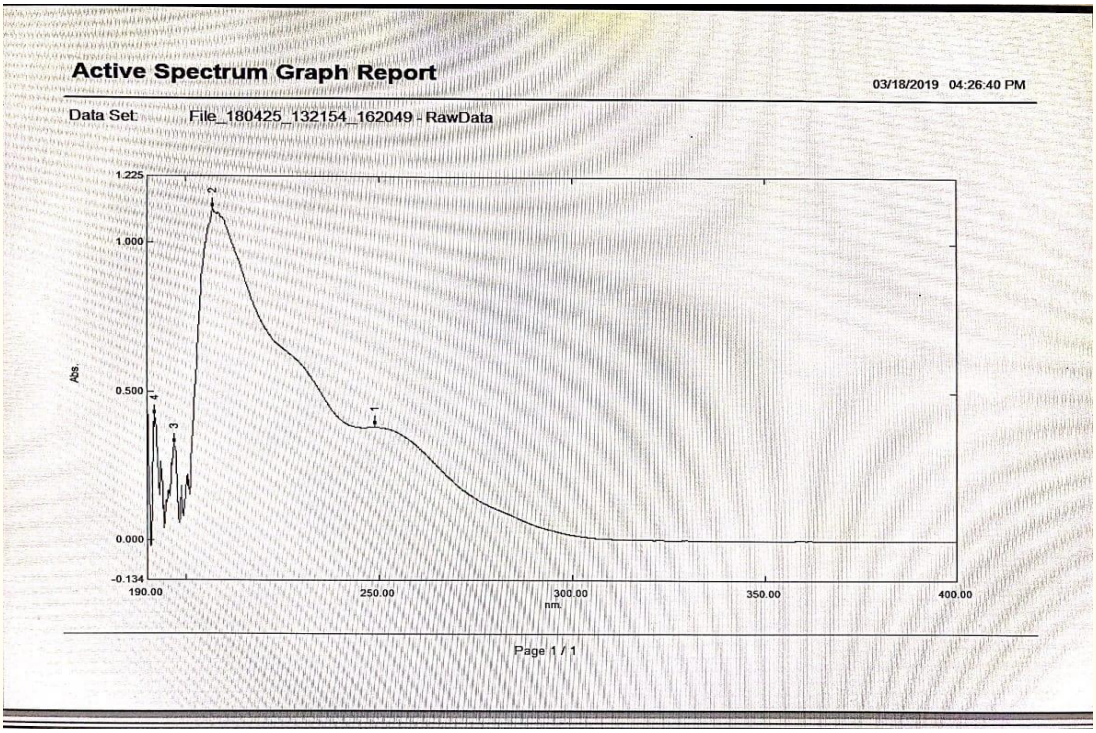

Figure 2: Absorption spectrum of Valsartan.

METHOD VALIDATION

The method was validated in terms of linearity, accuracy, precision and ruggedness.

Preparation of stock solution 1

100mg of Valsartan API was accurately weighed, transferred, dissolved by adding sufficient quantity of ethanol and made up to 50mL using ethanol. The concentration of the standard drug stock solution was 2000µg/mL (2mg/mL).

Preparation of stock solution 2

0.5mL of stock solution was pipette out into a 50mL standard flask and the volume was made up to the mark with ethanol. The concentration of the resulting solution was 20µg/mL. This was used for measuring absorption maxima.

Preparation of standard solution:

30mg of Valsartan API was accurately weighed and transferred to 50mL volumetric flask, shaken with ethanol and diluted up to the mark with ethanol to get stock solution of 500µg/mL. The contents were filtered through Whatman filter paper No: 1. Aliquot portions were further diluted with ethanol to get concentration of 30µg/mL of Valsartan. The absorbance of the final solution was read at selected wavelength as triplicate.

Preparation of test solution:

An accurately weighed quantity of tablet powder equivalent to about 30mg Valsartan was transferred to 50mL volumetric flask, shaken with ethanol and diluted upto the mark with ethanol to get stock solution of 500µg/mL. The contents were filtered through Whatman filter paper No: 1. Aliquot portions were further diluted with ethanol to get concentration of 30µg/mL of Valsartan. The absorbance of the final solution was read at selected wavelength in triplicate.

Linearity

From stock solution 1 (2000µg/mL), 2.5mL was pipette out into 25mL standard flask and the volume was made up to the mark with ethanol (200µg/mL). From this solution 0.5mL, 1mL, 1,5mL, 2mL, 2.5mL and 3mL, of solutions were pipette out and made to 10mL using ethanol subsequently the concentrations were obtained as 10µg/mL, 20µg/mL, 30µg/mL, 40µg/mL, 50µg/mL and 60µg/mL.

The absorbance of each solution was measured at 249 nm against ethanol as blank. The readings were recorded, shown in the Table No. 01 and figure No. 3.

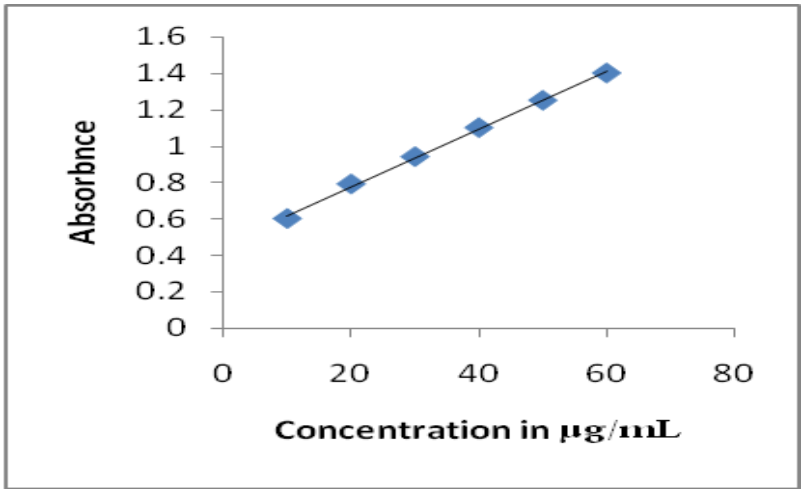

Figure 3: Linearity of Valsartan.

Table No. 1: Linearity Study.

S. No.	Concentration µg/mL	Absorbance
1.	10	0.65
2.	20	0.79
3.	30	0.94
4.	40	1.10
5.	50	1.25
6.	60	1.40

Accuracy

Preparation of accuracy test solutions:

Accurately weighed quantities of tablet powder equivalent to about 15mg, 30mg and 45mg of Valsartan was transferred to 50mL volumetric flask, shaken with ethanol and diluted up to the mark with ethanol to get stock solutions of various concentrations. The contents were filtered through Whatman filter paper No: 1. Aliquot portions were further diluted with ethanol to get concentration of 15µg/mL,30µg/mL and 45µg/mL of Valsartan. The absorbance of the final solutions was read at selected wavelength in triplicate.

Table No. 2: Accuracy Study.

ACCURACY					
TEST SOLUTION	**ABS**	**Assay**	**Average**	**SD**	**%RSD**
50% Accuracy Solution-01	0.475	99.68			
50% Accuracy Solution-02	0.482	101.14	99.82	1.26	1.26
50% Accuracy Solution-03	0.47	98.63			
100% Accuracy Solution-01	0.949	99.57			
100% Accuracy Solution-02	0.958	100.51	100.48	0.89	0.89
100% Accuracy Solution-03	0.966	101.35			
150% Accuracy Solution-01	1.428	99.89			
150% Accuracy Solution-02	1.433	100.23	100.33	0.49	0.49
150% Accuracy Solution-03	1.442	100.86			

Method Precision& Intermediate Precision

Method precision& intermediate precision of the proposed method was determined by analysis of samples by taking from homogeneous batch by different analysts and under similar operational and environmental conditions.

Table No. 3: Method Precision & Intermediate Precision.

METHOD PRECISION					
	ABSORBANCE	% ASSAY	AVERAGE	SD	% RSD
Standard	0.953		% w/v		
Test Solution -1	0.949	99.57			
Test Solution -2	0.944	99.05			
Test Solution -3	0.948	99.47	99.43	0.73	0.74
Test Solution -4	0.936	98.21			
Test Solution -5	0.955	100.20			
Test Solution -6	0.954	100.09			
INTERMEDIATE PRECISION					
	ABSORBANCE	% ASSAY	AVERAGE	SD	% RSD
Standard	0.964		% w/v		
Test Solution -1	0.958	99.37			
Test Solution -2	0.957	99.89			
Test Solution -3	0.964	100.72	99.91	1.35	1.35
Test Solution -4	0.94	97.50			
Test Solution -5	0.948	100.84			
Test Solution -6	0.959	101.15			

Table No. 4: Method & Intermediate Precision combinedly.

METHOD PRECISON & INTERMEDIATE PRECISON COMBINEDLY				
METHOD PRECISION	INTERMEDIATE PRECISION	AVERAGE	SD	% RSD
99.57	99.37			
99.05	99.89			
99.47	100.72	99.67	1.07	1.07
98.21	97.50			
100.20	100.84			
100.09	101.15			

Percentage assay was calculated using the following formula.

$$\%ASSAY = \frac{Abs\ test}{Abs\ standard} \times \frac{weight\ of substance}{50} \times \frac{5}{100} \times \frac{diluted\ to}{Eq.Wt.of\ tablets\ taken} \times \frac{100}{5} \times \frac{potency}{100}$$

RESULTS AND DISCUSSION

Method validation:

The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as per the earlier adopted procedure given in the experiment.

Linearity studies:

The linear regression data for the calibration curves showed good linear relationship over the concentration range 10–60µg/mL for ValsartanFigure3. Linear regression equation was found to be $Y = 0.0343X + 0.0294$ ($r^2 = 0.999$).

Accuracy:

The solutions were analysed by the proposed method and the results of recovery studies are reported in Table 2 which showed that the % amount found was between 95.0% and 103.0% with % RSD not more than 2.

Precision:

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These results show reproducibility of the assay. The % RSD values found to be less than 2 that indicate this method precise for the determination of both the drugs in formulation (Table 3).

Ruggedness: (Method & Intermediate Precision)

The absorption was measured for same concentration solutions at six times. The results are within the acceptable range. The results are given in Table 4. The result showed that the % RSD was less than 2%.

CONCLUSION

This UV-spectrophotometric technique is quite simple, accurate, precise and reproducible. The UV method has been developed for quantification of Valsartan in tablet formulation. The validation procedure confirms that this is an appropriate method for their quantification in the formulation and can and can be used for routine analysis. The developed method can also be used for estimation of valsartan in other dosage forms also by making slight modifications in extraction procedures.

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ABBREVIATIONS

ICH : International Conference on harmonization
RSD : Relative Standard Deviation
UV : Ultra violet
API : Active Pharmaceutical Ingredient

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