



SIMPLE METHOD DEVELOPMENT AND VALIDATION OF VALSARTAN IN BULK AND TABLET
DOSAGE FORM

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ABSTRACT

A simple, economic UV Spectroscopic method has been developed and validated for estimation of Valsartan in bulk and tablet dosage form. The λ_{max} for Valsartan in methanol showed at 249nm and in phosphate buffer pH 6.8 showed at 250nm. Calibration plots were plotted over the concentration range 2 to 10 $\mu\text{g/ml}$ with correlation coefficient 0.9991 in methanol and 10 to 50 $\mu\text{g/ml}$ with correlation coefficient 0.9999 in phosphate buffer pH 6.8. Validation was performed as per ICH Q2 (R1) guidelines for linearity, accuracy, precision and robustness. The limit of detection for Valsartan in methanol and phosphate buffer pH 6.8 was found to be 0.47 $\mu\text{g/ml}$ and 0.57 $\mu\text{g/ml}$ and limit of quantification for Valsartan in methanol and phosphate buffer pH 6.8 was found to be 1.44 $\mu\text{g/ml}$ and 1.75 $\mu\text{g/ml}$. The percent purity of Valsartan in tablet dosage form was 98.8%. Results of validation found to be significant acceptable limit. The developed UV Spectroscopic method can be used for routine estimation of Valsartan in bulk and dosage form, using both water and phosphate buffer pH 6.8 as a solvent.

Keywords: Valsartan, UV Spectroscopy, Validation

INTRODUCTION

Valsartan is chemically N-(1-Oxopentyl)-N-[(2'-(1H-tetrazol-5-yl) (1, 1'- biphenyl)-4-yl) methyl]-L-Valine¹. It is a white crystalline powder with formula $C_{24}H_{29}N_5O_3$ and molecular mass 435.52 g/mol. It is used as a potent angiotensin receptor blocker used as an antihypertensive i.e., used at high BP Conditions and also can be used in treatment of congestive heart failure (CHF) Post myocardial infarction^[1-3], Literature survey revealed that few analytical methods reported for estimation of Valsartan alone and combination with other drugs UV-Spectrophotometric^[4-6], RP-HPLC^[7-8], The objective of present work was to develop and validate simple, economical UV-Spectroscopic method for routine estimation of Valsartan in bulk and tablet dosage form by using separately methanol & phosphate buffer PH 6.8 solvent.

MATERIALS AND METHODS:

Instrumentation, Reagents & Chemicals:

Instruments used were UV-Visible spectrometer Shimadzu 1700, analytical balance FCOSET FX-300. Valsartan pure drug (99.99%) was obtained as a gift sample from Cipla, Pvt. Ltd. Kurkumbh. Batch no. B130339. All chemicals and reagents used were of analytical grade

Selection of media:

Main criteria for selection of media solubility and stability i.e., drug should be soluble as well as stable for sufficient time in selected media. Solubility studies of Valsartan were performed by adding excess amount of Valsartan to water, methanol and buffer solutions having different pH (1.2, 6.8, and 7.4) buffers contained in vials. The solutions were shaken for 24 hours using orbital rotator. The solutions were filtered through Whatman filter paper No 41 and filtrate was diluted

with respective solutions. The absorbances were recorded at 250 nm, which was the absorption maxima and drug concentration were determined. Valsartan was slightly soluble in distilled water and was freely soluble in methanol and was considerably stable.

Preparation of standard stock solution in methanol:

A stock solution of Valsartan was prepared by dissolving 100 mg of Valsartan in methanol, final volume was made upto 100ml with same solvent to obtain standard stock solutions (A1), of known concentration (1000 $\mu\text{g}/\text{ml}$) from which desired concentrations solution were prepared.

Preparation of standard stock solution in Phosphate Buffer pH 6.8:

100 mg of drug was weighed accurately and transferred to 100 ml volumetric flask. Then phosphate buffer pH 6.8 was added to dissolve the drug completely with the help of sonication. Then final volume was made with same solvent to obtain standard stock solution (A2), of known concentration (1000 $\mu\text{g}/\text{ml}$) from which desired concentrations solution were prepared.

Determination of λ_{max} of Valsartan in Methanol:

A solution of 10 $\mu\text{g}/\text{ml}$ was valsartan was prepared and scanned in UV range of 200- 400nm and spectrum was obtained. The maximum absorbance was found to be at 249 nm. Hence this is considered as absorbance maxima (λ_{max}) shown in fig.1.

Determination of λ_{max} of Valsartan in Phosphate Buffer pH 6.8: A solution of 10 $\mu\text{g}/\text{ml}$ was valsartan was prepared and scanned in UV range of 200- 400nm and spectrum was obtained.

The λ_{max} of Valsartan in Phosphate Buffer pH 6.8 was found to be 250nm shown in fig.2.

Preparation of calibration curve in methanol:

Standard stock solution was suitably diluted with methanol to obtain concentrations ranging from 2-10 $\mu\text{g/ml}$. Absorbance of these solutions was measured at 249nm (λ_{max} valsartan) using UV, calibration curve was obtained by plotting graph between concentration and absorbance shown in figure.2.

Preparation of calibration curve in phosphate buffer pH 6.8:

Standard stock solution was suitably diluted with methanol to obtain concentrations ranging from 2-10 $\mu\text{g/ml}$. Absorbance of these solutions was measured at 249nm (λ_{max} valsartan) using UV, calibration curve was obtained by plotting graph between concentration and absorbance shown in figure.3.

Method Validation in methanol

The objective of method validation is to demonstrate that the method is suitable for its intended purpose. The method was validated for linearity, precision, accuracy, robustness, ruggedness, LOD, LOQ, and specificity as per ICH guidelines.

1. Linearity: From the standard stock solution, the various dilutions in the concentration of 2, 4, 6, 8, and 10 $\mu\text{g/ml}$ were prepared. The solutions were scanned at 249 nm and the absorbance was recorded, given in table 1. From this calibration curve was obtained by plotting absorbance versus concentration of valsartan and the linearity graph was represented in figure 2. The correlation coefficient was found to be 0.9991.

2. Precision:

Intra-day precision was determined by checking the absorbance of (10 $\mu\text{g/ml}$) on the same day. Inter-day precision was determined by checking the absorbance of (10 $\mu\text{g/ml}$) on three different days. The %RSD was found to be 1.02% for intra-day and 1.7 % inter-day as shown in table 3&4.

3.Accuracy:

Accuracy study was conducted by spiking at three different concentration levels (80%, 100%, 120%). At each level samples were scanned and from the absorbance recovery percentage was determined and presented in table 7.

4.Robustness:

To determine robustness of the method 10 $\mu\text{g/ml}$ sample prepared from standard stock solution A1 then absorbance of this solution measured two different wavelengths. No significant difference was found in the absorbance and hence the proposed method was considered as robust which is shown in table 4.

5. Limit of detection and Limit of quantification:

Limit of detection is the lowest amount of an analyte in a sample that can be detected, but not necessarily quantified, under the stated experimental conditions. Limit of quantification is the lowest amount of analyte in a sample that can be quantified under stated experimental conditions. The LOD and LOQ for valsartan was found to be 0.47 $\mu\text{g/ml}$, 0.44 $\mu\text{g/ml}$.

6. Assay of Valsartan tablet:

Weigh accurately 3 tablets and crush in to mortar. Take quantity of powder containing 100 mg of Valsartan dissolve in small amount of methanol first then sonicate this solution for 15 min. Then final volume was adjusted with methanol up to the mark. Then solution was kept for 2 hours for

stable, and then filtered through whattmann filter paper (No. 41) and volume adjusted with the solvent. From this further dilution was made to get final concentration of 10ug/ml. The results were presented in table 13.

Validation in phosphate buffer pH 6.8:

1. Linearity:

From the standard stock solution, the various dilutions in the concentration of 10, 20, 30, 40, and 50 $\mu\text{g/ml}$ were prepared. The solutions were scanned at 250 nm and the absorbance was recorded, given in table 1. From this calibration curve was obtained by plotting absorbance versus concentration of valsartan and the linearity graph was represented in figure 2. The correlation coefficient was found to be 0.9999.

2. Precision:

Intra-day precision was determined by checking the absorbance of (10ug/ml) on the same day. Inter-day precision was determined by checking the absorbance of (10ug/ml) on three different days. The %RSD was found to be 1.6% for intra-day and 1.2 % inter-day as shown in table 5&6.

3. Accuracy:

Accuracy study was conducted by spiking at three different concentration levels (80%, 100%, 120%). At each level samples were scanned and from the absorbance recovery percentage was determined and presented in table 8.

4. Robustness:

To determine robustness of the method 10 $\mu\text{g/ml}$ sample prepared from standard stock solution

A1 then absorbance of this solution measured two different wavelengths. No significant

difference was found in the absorbance and hence the proposed method was considered as

robust which is shown in table 11-12.

RESULT AND DISCUSSION:

1. Analytical method:

Determination of λ_{max} :

The UV absorption spectrum was found to be λ_{max} at 249 nm and 250 nm for methanol and phosphate buffer pH 6.8 respectively as shown in fig.1

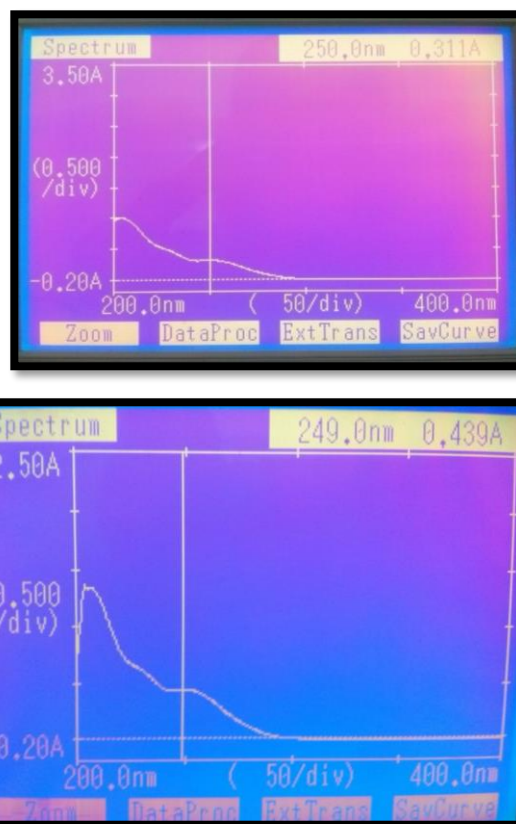


Fig. 1: UV absorption spectra of valsartan in phosphate buffer pH 6.8, λ_{max} 250 nm (upper) and in methanol, λ_{max} 249 nm (lower)

2. Calibration curve:

Calibration curve was obtained by plotting absorbance versus concentration of valsartan and the linearity graph was represented in figure 2. The correlation coefficient was found to be 0.9991 and 0.9999 in methanol and phosphate buffer respectively.

Fig 2: Calibration Curve for Valsartan in Methanol

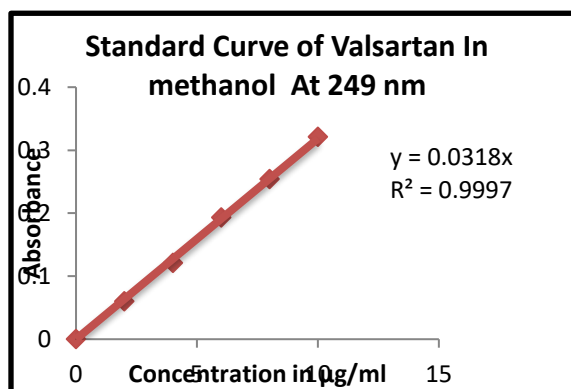


Table 1: Standard Curve of Valsartan in Methanol

Sr. No.	Concentration In ($\mu\text{g/ml}$)	Absorbance
1	0	0
2	2	0.060
3	4	0.121
4	6	0.193
5	8	0.254
6	10	0.321

Table 2: Standard Curve of Valsartan in Phosphate Buffer pH 6.8

Sr. No.	Conc. In $\mu\text{g/ml}$	Absorbance
1	0	0.0
2	10	0.311
3	20	0.631
4	30	0.935
5	40	1.247
6	50	1.580

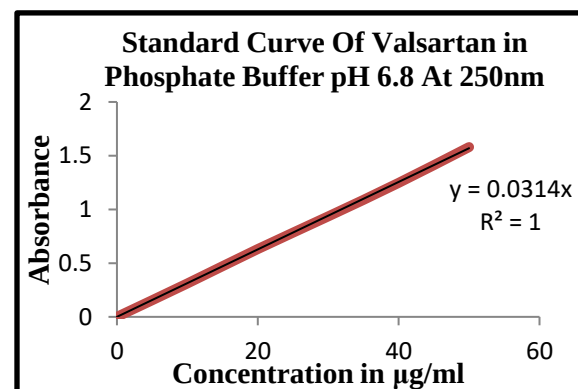


Fig.2: Calibration Curve for Valsartan in Phosphate Buffer pH 6.8

3. Precision:

The % RSD for intraday and interday precision of Valsartan, in methanol was shown in table no.3,4 and in Phosphate buffer pH 6.8 was shown in table 5&6

Sr. No.	Conc.	Wavelength	Abs	Abs2	Abs3
			1st day	2nd day	3rd day
1	10µg/ml	249 nm	0.447	0.451	0.458
2	10µg/ml	249 nm	0.447	0.453	0.468
3	10µg/ml	249 nm	0.449	0.452	0.476
4	10µg/ml	249 nm	0.453	0.46	0.48
5	10µg/ml	249 nm	0.459	0.449	0.472
6	10µg/ml	249 nm	0.449	0.457	0.462
		Mean	0.4506667	0.45366667	0.4693333
		S.D	0.0046332	0.004082483	0.0083586
		% RSD	1.0280799	0.899886019	1.7809577

Table 3: Intraday precision of Valsartan in methanol

Sr. No.	Conc.	λ max	Absorbance
1	10 µg/ ml	249 nm	0.447
2	10 µg/ ml	249 nm	0.449
3	10 µg/ ml	249 nm	0.459
4	10 µg/ ml	249 nm	0.447
5	10 µg/ ml	249 nm	0.453
6	10 µg/ ml	249 nm	0.449
		Mean	0.45066667
		S.D	0.004633213
		%RSD	1.028079903

Table 4: Inter-Day Precision of Valsartan in methanol

Sr. No.	Conc.	λ max	Absorbance
1	10 μ g/ ml	250 nm	0.325
2	10 μ g/ ml	250 nm	0.325
3	10 μ g/ ml	250 nm	0.321
4	10 μ g/ ml	250 nm	0.320
5	10 μ g/ ml	250nm	0.329
6	10 μ g/ ml	250 nm	0.335
		Mean	0.32583333
		S.D	0.005528713
		%RSD	1.696791692

Table5. Intraday precision of Valsartan in phosphate buffer PH.6.8

Sr. No.	Conc.	λ max	Abs	Abs2	Abs3
			1st day	2nd day	3rd day
1	10 μ g/ml	250 nm	0.325	0.36	0.368
2	10 μ g/ml	250 nm	0.325	0.36	0.372
3	10 μ g/ml	250 nm	0.321	0.361	0.372
4	10 μ g/ml	250 nm	0.320	0.363	0.362
5	10 μ g/ml	250 nm	0.329	0.362	0.366
6	10 μ g/ml	250 nm	0.335	0.368	0.365
		Mean	0.32583333	0.362333333	0.3675
		S.D	0.005528713	0.003011091	0.0039875
		% RSD	1.696791692	0.831027767	1.0850287

Table 6: Inter-Day Precision of Valsartan in phosphate buffer

4. Accuracy:

Result of accuracy of Valsartan in methanol and phosphate buffer shown in table no.7,8

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	80%	249 nm	0.384	0.381833	0.002317	0.606706
2	80%	249 nm	0.381			
3	80%	249 nm	0.380			
4	80%	249 nm	0.385			
5	80%	249 nm	0.379			
6	80%	249 nm	0.382			
1	100%	249 nm	0.470	0.469833	0.005811	1.236802
2	100%	249 nm	0.472			
3	100%	249 nm	0.477			
4	100%	249 nm	0.474			
5	100%	249 nm	0.462			
6	100%	249 nm	0.464			
1	120%	249 nm	0.571	0.572	0.004817	0.84207
2	120%	249 nm	0.577			
3	120%	249 nm	0.572			
4	120%	249 nm	0.577			
5	120%	249 nm	0.564			
6	120%	249 nm	0.571			

Table 7: Accuracy of valsartan in methanol

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	80%	250 nm	0.286	0.281333	0.004509	1.602814
2	80%	250 nm	0.281			
3	80%	250 nm	0.277			
1	100%	250 nm	0.33	0.334667	0.004041	1.207605
2	100%	250 nm	0.337			
3	100%	250 nm	0.337			
1	120%	250 nm	0.388	0.390333	0.004041	1.035385
2	120%	250 nm	0.395			
3	120%	250 nm	0.388			

Table 8: Accuracy of valsartan in phosphate buffer

5. Robustness:

To determine robustness of the method 10 μ g/ml sample prepared from standard stock solution then absorbance of this solution measured two different wavelengths. % RSD was within limit indicates developed method was robust shown in table no.9,10 ,11,12.

a. Absorbance at λ max – 2 nm (247 nm):

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	10 μ g/ ml	247 nm	0.453	0.456	0.0026458	0.5802086
2	10 μ g/ ml	247 nm	0.458			
3	10 μ g/ ml	247 nm	0.457			

Table 9: Robustness at λ max – 2 nm (247 nm) in methanol

b. Absorbance at λ max + 2 nm (251 nm):

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	10 μ g/ ml	251 nm	0.462	0.4553333	0.0090738	1.9927756
2	10 μ g/ ml	251 nm	0.459			
3	10 μ g/ ml	251 nm	0.445			

Table 10: Robustness at λ max + 2 nm (251nm) in methanol**a. Absorbance at λ max – 2 nm (248 nm):**

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	10 μ g/ ml	248 nm	0.337	0.3366667	0.0015275	0.4537204
2	10 μ g/ ml	248 nm	0.335			
3	10 μ g/ ml	248 nm	0.338			

Table 11: Robustness at λ max – 2 nm (248 nm) in Phosphate buffer**b. Absorbance at λ max + 2 nm (252 nm):**

Sr. No	Conc.	λ max	Absorbance	Mean	S. D.	%RSD
1	10 μ g/ ml	252 nm	0.33	0.3306667	0.0011547	0.3492038
2	10 μ g/ ml	252 nm	0.33			
3	10 μ g/ ml	252 nm	0.332			

Table 12: Robustness at λ max + 2 nm (252nm) in Phosphate buffer**6. Limit of Detection and Limit of Quantification (LOD& LOQ):**

The LOD for Valsartan in methanol & phosphate buffer was found to be 0.47 μ g/ ml & 0.57 μ g/ ml respectively.

The LOQ for Valsartan in methanol & phosphate buffer was found to be 1.44 μ g/ ml & 1.75 μ g/ ml respectively.

8. Assay of Valsartan tablet:

Sample	Label claim (mg)	Amount found (mg)	% Recovered
Diovan	10mg	9.88mg	98.8%

Table13. Assay of Valsartan tablet

CONCLUSION:

The method was developed and validated as per ICH guidelines. Developed UV Spectrophotometric method was simple, accurate, precise, linear, robust, economical can be applied for routine analysis of Valsartan in bulk and pharmaceutical dosage form by using methanol as well as phosphate buffer pH 6.8.

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