Development and Validation of UV Spectroscopic Method for Estimation of Valsartan In Tablet Dosage Form

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ABSTRACT

To develop and validate simple, rapid, linear, accurate, precise and economical UV Spectroscopic method for estimation of Valsartan in tablet dosage form. The drug is freely soluble in analytical grade Ethanol, Methanol and Acetonitrile. The drug was identified in terms of solubility studies and on the basis of melting point done on Melting Point Apparatus of Equiptronics. It showed absorption maxima were determined in diluent Methanol: Water (50:50) ratio. The drug obeyed the Beer’s law and showed good correlation of concentration with absorption which reflect in linearity. The UV spectroscopic method was developed for estimation of Valsartan in tablet dosage form and also validated as per ICH guidelines. The drug is freely soluble in analytical grade Ethanol, Methanol, Acetonitrile and sparingly soluble in water. So, the analytical grade Methanol: water (50:50) is used as a diluent in method. The melting point of Valsartan was found to be 115-116˚C (uncorrected). It showed absorption maxima 250 nm in Methanol: Water (50:50) ratio. On the basis of absorption spectrum the working concentration was set on 20µg/ml (PPM). The linearity was observed between 10-30 µg/ml (PPM). The results of analysis were validated by recovery studies. The recovery was found to be 98.75, 101.00 and 99.17% for three levels respectively. The % RSD for precision was found to be 0.35%. A simple, rapid, linear, accurate, precise and economical UV Spectroscopic method has been developed for estimation of Valsartan in tablet dosage form. The method could be considered for the determination of Valsartan in quality control laboratories.

Keywords: Valsartan, Development, UV Spectrophotometer, Melting Point, Assay Method, Validation, Accuracy, Linearity, Ruggedness, Precision.
INTRODUCTION

Valsartan is a white crystalline powder with formula C_{24}H_{29}N_{5}O_{3} and molecular mass 435.52 g/mol [1, 2]. Valsartan is an ARB that selectively inhibits the binding of Angiotensin II to AT1, which is found in many tissues such as vascular smooth muscle and the adrenal glands [3]. Chemical name of valsartan is [1-4],N-[p-(o-1H-Tetrazol-5-ylphenyl) benzyl]-N-valeryl-L-valine1(Figure-1) [2]. This effectively inhibits the AT1-mediated vasoconstrictive and Aldosterone-secreting effects of Angiotensin II and results in a decrease in vascular resistance and blood pressure [4]. Valsartan belongs to a class of antihypertensive agents called Angiotensin II receptor blockers (ARBs) [5]. Valsartan is a specific and selective type-1 Angiotensin II receptor (AT1) antagonist which blocks the blood pressure increasing effects Angiotensin II via the renin Angiotensin-Aldosterone system (RAAS) [6].

![Figure 1: Chemical Structure of Valsartan]

RAAS is a homeostatic mechanism for regulating hemodynamics, water and electrolyte balance. During sympathetic stimulation or when renal blood pressure or blood flow is reduced, renin is released from granular cells of the juxtaglomerular apparatus in the kidneys [7, 8]. Valsartan is official in Indian Pharmacopoeia [9].

From literature review it's found that few HPLC [6-8], LC-MS [10-12], Protein precipitation [13], Capillary electrophoresis [14], Simultaneous UV spectrophotometric methods [15, 16], Spectrofluorimetric method was developed for determination of losartan and valsartan in human Urine [17] is reported for estimation of Valsartan alone or in combination. But no method was found on estimation of Valsartan in tablet dosage form for UV spectroscopic method. This indicates that so far no UV method exists for the estimation and determination of Valsartan in tablet dosage forms in single without combination.

MATERIALS AND METHOD

**Instruments :**

Shimadzu double beam UV-visible spectrophotometer 1700 Ultra with matched pair
Quartz cells corresponding to 1 cm path length and spectral bandwidth of 1 nm, Bath sonicator and citizen weighing balance. Melting point apparatus of Equiptronics were used.

**Materials:**
Valsartan was obtained as a gift sample. Valsartan tablets were procured from local pharmacy. Water used was of analytical grade. Glass double distilled analytical grade water and analytical grade methanol were used throughout the experiment. Freshly prepared solutions were employed.

**Diluent:**
Mixture of Water and Methanol is used as a diluent in 50:50 proportions.

**Method development [18, 19]:**

**Determination of $\lambda_{\text{max}}$ (20 PPM)**

100 mg weighed amount of Valsartan was dissolved into 100 ml of volumetric flask with diluent. Pipette out 2 ml and added in 100 ml of volumetric flask, dissolved and diluted up to the mark with diluent. This solution was subjected to scanning between 200-400 nm and absorption maximum was determined.

![Figure 2: Calibration Curve](image)

**Preparation of Working concentration**

**Preparation of Standard stock solution:**
Standard stock was prepared by dissolving 100 mg of Valsartan in 100 ml of diluent to get concentration of 1000 µg/ml (PPM).

**Preparation of Standard solution:**
Pipette out 2 ml from standard stock solution and diluted up to 100 ml with diluent to get concentration of 20 µg/ml (PPM).
Procedure for UV reading

Blank Solution: (For Auto zero)

Fill the cuvette with Diluent. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Standard Solution:

Fill the cuvette with standard solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Sample Solution:

Fill the cuvette with sample solution. Wipe it with tissue paper properly then placed inside the chamber. Note down the reading.

Procedure for sample preparations

For analysis of commercial formulations; twenty tablets are taken weighed it and powdered. The powder equivalent to 100 mg of Valsartan was accurately weighed and transferred into the 100 ml of volumetric flask, added 60 ml of diluent; the solution was sonicated for 20 min. After sonication cool the flask and diluted upto 100 ml with diluent. Filtered the solution through whatmann filter paper. Pipette out 2 ml of the above solution and diluted up to 100 ml with diluent. The absorbance was measured at 250 nm. The absorbance was recorded:

Table 1: Absorbance of Dosage Form

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Sample</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Blank Solution (Auto zero)</td>
<td>0.0000</td>
</tr>
<tr>
<td>2</td>
<td>Standard Solution</td>
<td>0.4745</td>
</tr>
<tr>
<td>3</td>
<td>Sample Solution</td>
<td>0.4671</td>
</tr>
</tbody>
</table>

Table 2: Dosage Form Specifications

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Company</th>
<th>M.D.</th>
<th>E.D.</th>
<th>Batch No.</th>
<th>Average weight (g)</th>
<th>Assay (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Torrent Pharma Pvt. Ltd (80mg)</td>
<td>08/2018</td>
<td>07/2021</td>
<td>MTN 84251</td>
<td>0.1810</td>
<td>98.40</td>
</tr>
</tbody>
</table>

Method of validation [19, 20, 21, 22]

The proposed method was developed by using linearity, accuracy, precision and ruggedness as per ICH guidelines, 1996.

Linearity:

The linearity of the proposed assay was studied in the concentration range 10 - 30 PPM at 250nm. The calibration data showed a linear relationship between concentrations.
Table 3: Linearity Studies

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Sample Concentration</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 PPM</td>
<td>0.2371</td>
</tr>
<tr>
<td>2</td>
<td>15 PPM</td>
<td>0.3561</td>
</tr>
<tr>
<td>3</td>
<td>20 PPM</td>
<td>0.4686</td>
</tr>
<tr>
<td>4</td>
<td>25 PPM</td>
<td>0.5895</td>
</tr>
<tr>
<td>5</td>
<td>30 PPM</td>
<td>0.7124</td>
</tr>
</tbody>
</table>

**Correlation coefficient** 0.9998

Accuracy:
To ensure the accuracy of the method, recovery study was performed by preparing 3 sample solutions of 80, 100 and 120% of working concentration and adding a known amount of active drug to each sample solution and dissolved in 100ml of volumetric flask with analytical grade water and measuring the absorbance at 250nm.

Table 4: Accuracy Studies

<table>
<thead>
<tr>
<th>Spectrophotometric method</th>
<th>Accuracy (%)</th>
<th>Qty weighed (mg)</th>
<th>Qty found (mg)</th>
<th>Recovery (98-102%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80</td>
<td>0.8</td>
<td>0.79</td>
<td>98.75</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>1</td>
<td>1.01</td>
<td>101.00</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>1.2</td>
<td>1.19</td>
<td>99.17</td>
</tr>
</tbody>
</table>

Precision:
The precision of the method was demonstrated by inter-day and intra-day variation studies. Five sample solutions were made and the %RSD was calculated.

Table 5: Precision studies

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Sample Solution</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sample Solution 1</td>
<td>0.4651</td>
</tr>
<tr>
<td>2</td>
<td>Sample Solution 2</td>
<td>0.4684</td>
</tr>
<tr>
<td>3</td>
<td>Sample Solution 3</td>
<td>0.4695</td>
</tr>
<tr>
<td>4</td>
<td>Sample Solution 4</td>
<td>0.4674</td>
</tr>
<tr>
<td>5</td>
<td>Sample Solution 5</td>
<td>0.4682</td>
</tr>
</tbody>
</table>

Mean 0.4677
SD 0.0016
% RSD 0.3518

Ruggedness:
Ruggedness is a measure of the reproducibility of a test result under normal, expected operating condition from instrument to instrument and from analyst to analyst.

Table 6: Results for Ruggedness Studies

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Analyst</th>
<th>Results</th>
<th>Mean</th>
<th>% Assay</th>
<th>% RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Analyst 1</td>
<td>0.4671</td>
<td>0.4677</td>
<td>98.57</td>
<td>0.0717</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

Solubility of Valsartan
Solubility test was passed as per criteria.

Table 7: Results for solubility studies

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Title</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ethanol, Methanol, Acetonitrile</td>
<td>Freely Soluble</td>
</tr>
<tr>
<td>2</td>
<td>Water</td>
<td>Sparingly soluble</td>
</tr>
</tbody>
</table>

Melting point of Valsartan
The melting point of Valsartan was found to be 115-116°C (uncorrected).

Results for linearity for assay method of Valsartan
The linearity of method was determined at concentration level ranging from 10 to 30 μg/ml (PPM). The correlation coefficient value was found to be \( R^2 = 0.9998 \).

Results for accuracy for assay method of Valsartan
The accuracy of the method was determined by recovery experiments. The recovery studies were carried out and the percentage recovery were calculated and represented in Table - 4. The high percentage of recovery indicates that the proposed method is highly accurate. Accuracy results were found within acceptance criteria that are within 98-102%.

Results for precision for assay method of Valsartan
The % RSD for different sample of precision was found to be 0.3518 and it is within acceptance criteria represented in Table - 5.

Results for ruggedness for assay method of Valsartan
The %RSD for different sample of ruggedness was found to be 0.0717 and it is within acceptance criteria represented in Table - 6.

CONCLUSION

A method for the estimation of Valsartan in tablet form has been developed. From the spectrum of Valsartan, it was found that the maximum absorbance was 250 nm in diluent. A good linear relationship was observed in the concentration range of 10-30 µg/ml (PPM). The high percentage recovery indicates high accuracy of the method. This demonstrates that the developed spectroscopic method is simple, linear, accurate, rugged and precise for the estimation of Valsartan in solid dosage forms. Hence, the method could be considered for the determination of Valsartan in quality control laboratories.

Abbreviations

1. PPM - Parts per Million
2. nm - Nanometer
3. HPLC - High Performance Liquid Chromatography
4. UV - Ultra violet
5. HBV - Hepatitis B virus
6. DNA - Deoxyribonucleic acid
7. ARB - Angiotensin II receptor blockers
8. RAAS - Renin Angiotensin-Aldosterone system
9. HIV - Human Immunodeficiency Virus
10. ICH - International Council for Harmonization
11. RSD - Relative Standard Deviation
12. SD - Standard Deviation
13. Qty - Quantity
14. C - Celsius
15. M.D. - Manufacturing Date
16. E.D. - Expiry Date

REFERENCES


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