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

Swapnil R. Patil[1], Anagha P. Patil[2], Prajakta D. Chaudhari[2], Kalpesh V. Sonar[3]
1.Department of Pharmaceutics, Vidya Bharati College of Pharmacy, Amravati University, Amravati (MH) INDIA 444602.
2.Department of Pharmaceutical Chemistry, Arunamai college of Pharmacy, North Maharashtra University, Mamurabad, Jalgaon (MH), INDIA 425001.
3.Department of Pharmaceutical Analysis, KYDSCT'S College of Pharmacy, North Maharashtra University, Sakegaon, Jalgaon (MH), INDIA 425201.

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.

*Corresponding Author Email: patilsp403@gmail.com
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INTRODUCTION

Valsartan is a white crystalline powder with formula $C_{24}H_{29}N_5O_3$ 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].

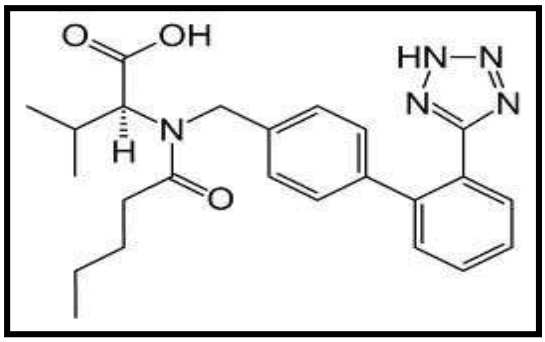

Figure 1: Chemical Structure of Valsartan

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 ƛ 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.

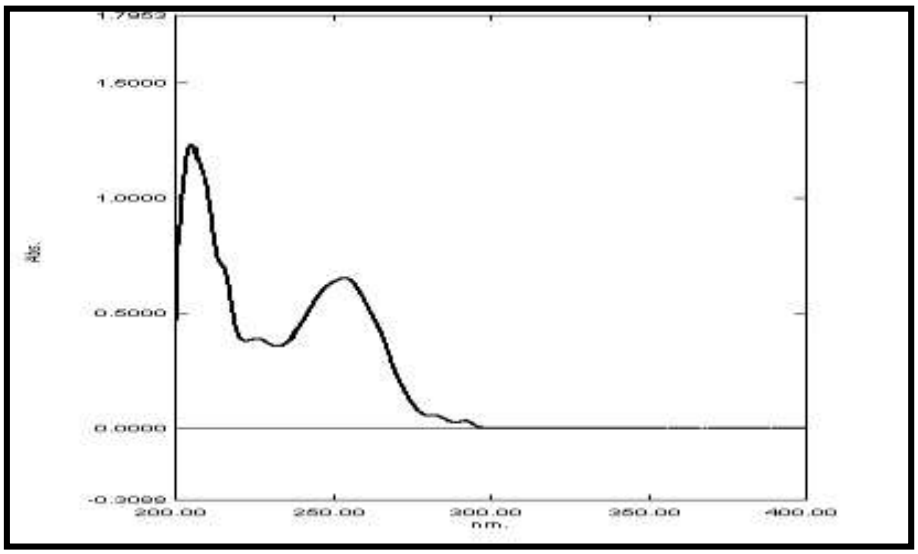

Figure 2: Calibration Curve

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

Torrent Pharma Limited (VALZAAR™ 80 mg)		
Sr. no.	**Sample**	**Absorbance**
1	Blank Solution (Auto zero)	0.0000
2	Standard Solution	0.4745
3	Sample Solution	0.4671

Table 2: Dosage Form Specifications

Sr No	Company	M.D.	E.D.	Batch No.	Average weight (g)	Assay (%)
1	Torrent Pharma Pvt. Ltd (80mg)	08/2018	07/2021	MTN 84251	0.1810	98.40

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

Sr. no.	Sample Concentration	Absorbance
1	10 PPM	0.2371
2	15 PPM	0.3561
3	20 PPM	0.4686
4	25 PPM	0.5895
5	30 PPM	0.7124
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

Spectrophotometric method			
Accuracy (%)	**Qty weighed (mg)**	**Qty found (mg)**	**Recovery (98-102%)**
80	0.8	0.79	98.75
100	1	1.01	101.00
120	1.2	1.19	99.17

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

Sr. No.	Sample Solution	Absorbance
1	Sample Solution 1	0.4651
2	Sample Solution 2	0.4684
3	Sample Solution 3	0.4695
4	Sample Solution 4	0.4674
5	Sample Solution 5	0.4682
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

Sr. No.	Analyst	Results	Mean	% Assay	% RSD
1	Analyst 1	0.4671 0.4682	0.4677	98.57	0.0717

2	Analyst 2	0.4669 0.4695	0.4682	98.67

RESULTS AND DISCUSSION

Solubility of Valsartan

Solubility test was passed as per criteria.

Table 7: Results for solubility studies

Sr. no.	Title	Result
1	Ethanol, Methanol, Acetonitrile	Freely Soluble
2	Water	Sparingly soluble

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.**

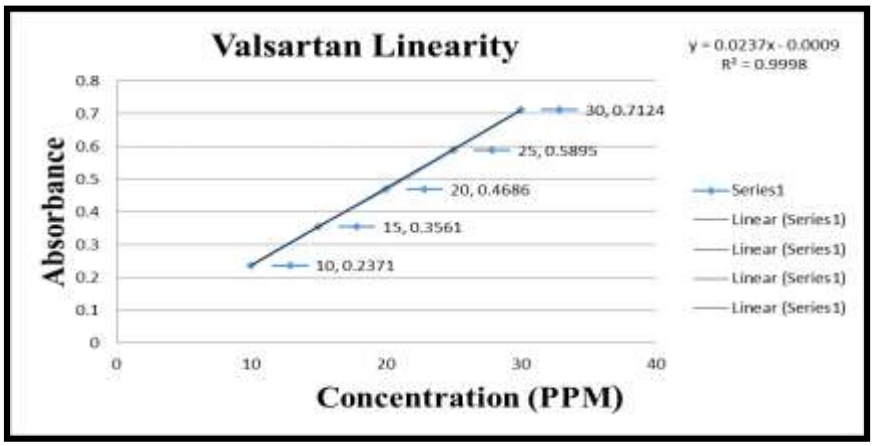

Figure 3: Valsartan Standard Curve

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

1. *en.wikepedia.org/wiki/Valsartan* accessed on 26-11-2019.
2. *https://www.drugbank.ca/drugs/DB00177* accessed on 26-11-2019.
3. Rang HP, Dale MM, Riter MJ, et al. In pharmacology. 6th ed. London: Elsevier Health Sciences; 2007; p. 501–502.
4. Tripathi KD. Essentials of medical pharmacology. 6th ed. New Delhi: Jaypee Brothers Medical Publishers Pvt. Ltd; 2008; p. 549–550, 482, 486, 549, 540, 543,323, 529.
5. Ikuo S, Takao S. Controlled release Nifedipine and Valsartan combination therapy in patients with essential hypertension: the Adalat cr and Valsartan cost effectiveness combination (advance-combi) study. J Hypertens Res. 2006; 29:789–796.

6. Kocyigit-Kaymacoglu B, Unsalan S and Rollas S., Determination and validation of Ketoprofen, Pantoprazole, and Valsartan together in human plasma by high performance liquid schromatography, Pharmazie, 2006, 61,586-589.
7. Daneshtalab N, Lewanczuk RZ and Jamali F., High performance liquid chromatographic analysis of angiotensin-II receptor antagonist Valsartan using a liquid extraction method, J Chromatogr B Analyt Technol Biomed Life Sci., 2002, 766,345-359.
8. Gonzalez L, et al., Fast screening method for the determination of angiotensin II receptor antagonists in human plasma by high performance liquid chromatography with fluroimetric detection, J Chromatogr A, 2002, 949, 49-60.
9. Indian Pharmacopoeia. Ministry of Health and Family Welfare, Indian Pharmacopoeia Commision, Ghaziabad, Vol. III. 2014; p. 2336, 2338, 2339, 2340, 2951, 2952, 2953.
10. Koseki N, et al., Development and validation of a method for quantitative determination of Valsartan in human plasma by liquid chromatography-tandem mass spectrometry, Pharm Biomed Aanal., 2007, 43, 1769-1774.
11. Li H, et al., A liquid chromatography/tandem mass spectrometry method for the simultaneous quantification of Valsartan and Hydrochlorothiazide in human plasma. J Chromatogr B Analyt Technol Biomed Life Sci., 2007, 852,436-442.
12. Selvan PS, et al., Simultaneous determination of fixed dose combination of Nebivolol and Valsartan in human plasma by liquid chromatographic tandem mass spectrometry and its application to pharmacokinetic study, J Chromatogr B Analyt Technol Biomed. Life Sci., 2007, 858,143-150.
13. Macek J, Klima J and Ptacek P., Rapid determination of Valsartan in human plasma by protein precipitation and high-performance liquid chromatography, J Chromatogr B Analyt Technol Biomed Life Sci., 2006, 832,169-172.
14. Hillaert S and Bossche VW., Simultaneous determination of Hydrochlorothiazide and several angiotensin-II receptor antagonists by capillary electrophoresis, J Pharm Biomed Anal., 2003,31,329-339.
15. Satana E, et al., Simultaneous determination of Valsartan and Hydrochlorothiazide in tablets by first-derivative ultraviolet spectrophotometry and LC, J Pharm Biomed Anal, 2001, 25, 1009-1013.
16. Sibel A, Ozakan SE, Gorger N, Altinay S, Zuhre S, Simultaneous determination of valsartan and Hydrochlorothiazide in tablets by first-derivative UV spectrophotometry and LC J. Pharm. Biomed Anal., 2001, 25(5):1009-1013.

17. Gagigal E., Gonzalez L., Alonso R.M. and Jimenez R.M., Experimental design methodologies to optimize the spectrofluroimetric determination of losartan and valsartan in human urine, Talanta, 2001, 54: 1121–1133.
18. Beckeet A. H, Stenlak J. B., "Practical pharmaceutical chemistry edn 4th CBS Publisher & Distribution, New Delhi, 2004, 275-337.
19. Shethi PD. Quantitative Analysis of Pharmaceutical Formulation, 1st edn, 2001, 11.
20. ICH draft Guidelines on Validation of Analytical Procedures: Definitions and Terminology, Federal Register, 60, IFPMA, Switzerland, 1995, pp. 1260.
21. The European Agency for the Evaluation of Medical/Products. ICH Topic Q2BNote for Guideline on Validation of Analytical Procedures: Methodology GPMP/ICH/281/95, 1996.
22. United States Pharmacopoeia. In Validation of Compendial Methods. 26th edn: Pharmacopoeial Convention Inc., Rockville, 2003, pp. 2439-2442.