"Development and Validation of a UV- Visible Spectrophotometric Method for Quantitative Analysis of Valsartan in Bulk and Tablet Dosage Forms"

Kunal Gaikwad, Dr.Varsha Tegeli, Irfan Dalwale, Soheb Tamboli, Mohammed Saud

Department of Pharmaceutics, D.S.T.S. Mandal's College of Pharmacy, Solapur

Abstract:

Objectives:A novel, cost-effective UV spectrophotometric method was developed for the quantification of Valsartan in pure and tablet forms. **Method**: The analysis utilized methanol as the solvent, with a wavelength of 260 nm, using a Systronics 2201 UV-Visible double beam spectrophotometer. The method was validated per ICH guidelines**. Results**: Validation included parameters such as linearity (10-50 µg/ml), accuracy (recovery between 98.5% and 99.7%), precision, robustness, limit of detection (LOD), and limit of quantification (LOQ). The percentage relative standard deviation (%RSD) was below acceptable limits. **Conclusion**: The developed UV spectroscopic method is accurate, precise, stable, linear, specific, and simple, making it suitable for routine analysis of Valsartan in both bulk and tablet forms.

Keywords: Valsartan, UV-Visible spectrophotometric method, Method Validation.

Introduction

Chemically Valsartan is a (S)-3-methyl-2-(N-{[2'-(2H-1,2,3,4-tetrazol-5-yl) biphenyl-4-yl] methyl}pentanamido) butanoic acid[1].Valsartan (VAL) is a specific blocker of the angiotensin II receptor, exhibiting a strong affinity for the angiotensin type I receptor. It is commonly utilized in the management of hypertension, post-myocardial infarction, and congestive heart failure[2]. Classified as a BCS class IV weak acid drug, Valsartan has low solubility and permeability[3], which means that its systemic exposure is influenced by both these factors, as well as its release from the dosage form, resulting in a bioavailability of 23%[4,5].It exhibits greater solubility in specific organic solvents, including ethanol, methanol, and dimethyl sulfoxide (DMSO). Recent research has presented various UV spectrophotometric techniques for the quantification of Valsartan, utilizing a solvent mixture of methanol and water.

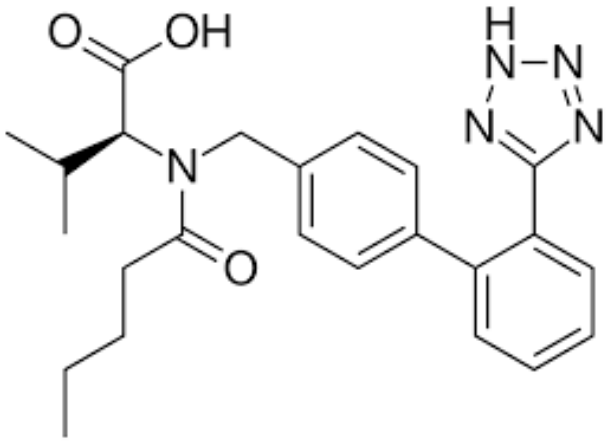

Fig.1: Structure of Valsartan

The investigation focused on the determination of valsartan in biological fluids using high-performance liquid chromatography (HPLC)[6, 7].High-performance liquid chromatography (HPLC) was also used to simultaneously analyse valsartan and hydrochlorothiazide in tablet formulations[8].This study was conducted with the aim of developing a straightforward, rapid, accurate, economical, precise, and robust UV method for the estimation of Valsartan in both bulk and tablet dosage forms, utilizing methanol as the solvent.

Materials and method

Chemicals and reagents: Valsartan is supplied by Smruthi Organics Pvt. Ltd in Solapur as a gift sample. Valsartan marketed formulation which was used as reference standard.All chemicals and reagents utilized are of analytical grade.

Instruments: The analysis was conducted using a Systronics 2201 UV-Visible double beam spectrophotometer, employing standard cuvettes with a path length of 10 mm. Ultrasonicator (microclean-103) was utilized to sonicate the formulation sample, electronic analytical balance, volumetric flask, Pipette, etc.

Preparation of the Valsartan standard stock solution

A precise quantity of 10 mg of the standard medication Valsartan was measured and placed into a 10 ml volumetric flask. An adequate volume of methanol was then added, followed by sonication for a duration of 15 minutes. Subsequently, the solution was adjusted to the mark with the same solvent, resulting in a stock solution with a concentration of 1000 µg/ml. From this stock solution, 1 ml was further diluted to a final volume of 10 ml, yielding a concentration of 100 µg/ml of Valsartan.

Determination of absorption maxima (λmax)

To ascertain the appropriate wavelength for measurement, a Valsartan solution (10µg/ml) was analyzed within the wavelength range of 200-400nm, using methanol as a blank reference. The wavelength corresponding to the peak absorption of the drug was identified, with Valsartan exhibiting maximum absorption at 260nm.

Preparation of calibration curve

The calibration curve was established using Stock-2 to create five distinct calibration standards corresponding to concentrations of 10, 20, 30, 40, and 50 µg/mL. The absorbance for each calibration standard was measured at a wavelength of 260 nm, employing a fixed wavelength measurement mode. The resulting calibration curves, illustrating the relationship between concentration and absorbance, were plotted using Microsoft Excel 2016.

Method Validation

The ultraviolet (UV) method established for the quantification of Valsartan underwent validation concerning various parameters, including linearity, range, precision, robustness, ruggedness, accuracy, limit of quantification (LOQ), and limit of detection (LOD). This validation was conducted utilizing predefined calibration standards, as detailed below.

Linearity and Range:

The linearity of the proposed UV method was determined through the use of five distinct calibration standards. By analysing these calibration standards, calibration curves were created, plotting absorbance against concentration, and subsequently analysed using linear least squares regression. The R-squared value was deemed a critical factor in confirming the linearity of the proposed method. The range of the proposed UV method was defined as the interval between the upper and lower concentration limits that exhibited acceptable linearity.

Intra-day and Inter-day Precision

The precision of the assay method was evaluated by examining its repeatability through seven independent assays of the ritonavir test arrangement, with the percentage relative standard deviation (% RSD) calculated for intra-day measurements. To assess the

intermediate precision of the method, the same procedure was conducted over three consecutive days.

Stability Study

A stability study was conducted in which samples designated for the repeatability assessment were stored at room temperature for a duration of 24 hours. These samples were subsequently analysed the next day to evaluate their short-term stability.

Robustness

Robustness refers to the ability of a system to maintain its performance despite minor, intentional changes in method parameters, serving as an indicator of its reliability under standard operating conditions. The assessment of robustness was conducted using two distinct instruments and involved the participation of two different analysts. In the present investigation, the absorption maxima exhibited a decrease and an increase of 1 nm, with the procedure conducted using a standard solution of 30 µg/ml. The percentage relative standard deviation (% RSD) was determined.

Limit of Detection (LOD)

In the development of UV methods, the Limit of Detection was established using the equation

$LOD = 3.3 \times SD/S,$

Where SD represents the standard deviation of the Y-intercepts and

S denotes the slope.

Limit of Quantification (LOQ):

In the development of UV methods, the Limit of Quantification was established using the equation below:

$LOQ = 10 \times SD / S$

Where S represents the slope and SD denotes the standard deviation of the Y-intercepts.

Estimation of Valsartan content in marketed formulation:

A developed and pre-validated UV-Vis method was effectively employed to determine the Valsartan content in a commercially available formulation. For this study, Valzaar tablets were acquired from the local market in Solapur, and the tablet contents were collected, followed by appropriate dilutions using a pre-optimized solvent system. The prepared

samples were then analysed using the pre-validated UV method, and the results were expressed as the average percent assay.

Results and Discussion:

The identification of the wavelength corresponding to maximum absorbance is essential for conducting quantitative UV analysis. A solution exhibiting an absorbance value of less than 1 is typically deemed appropriate for determining the wavelength of maximum absorbance. In light of this requirement and suitability, the maximum wavelength for a Valsartan solution (100 µg/mL) was determined utilizing the full scan mode of a UV-Visible spectrophotometer (refer to Figure 2). The full scan was executed using UV software, which facilitated the identification of λmax. The maximum absorbance wavelength for Valsartan was established at 260 nm.

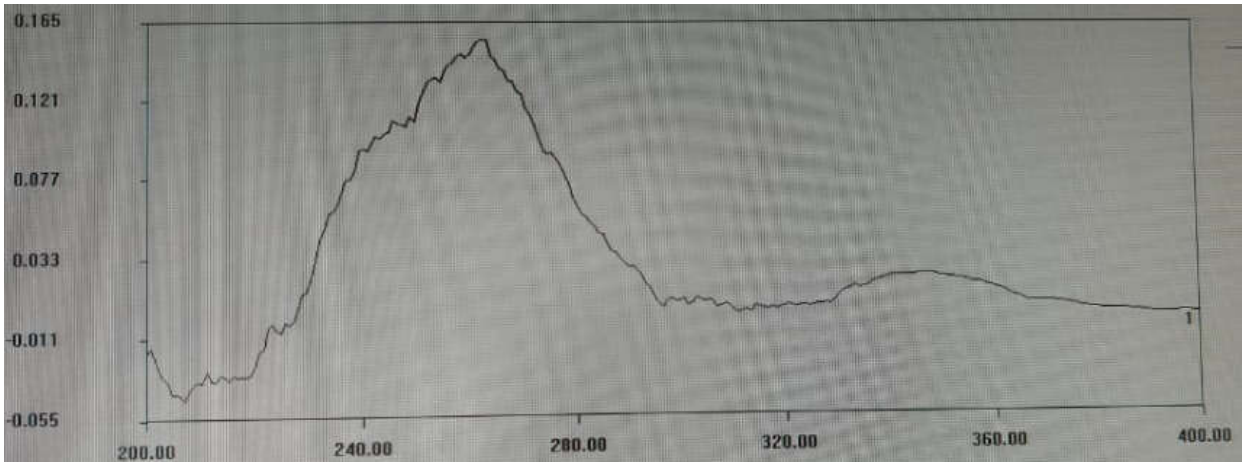

Fig. 2: The identification of λmax for Valsartan using a UV spectrophotometer.

Preparation of Calibration Curve:

The quantification of unknown samples utilizing a UV-Visible spectrophotometer or any other instrumental analytical method necessitates the establishment of a reproducible calibration curve, along with an equation that defines the correlation between concentration and the measured response. Compared to graphical methods, the aforementioned approach is widely recognized and demonstrates reproducibility. In light of the importance of quantitative analysis for Valsartan, a calibration curve was constructed using five distinct calibration standards. The absorbance values for these standards were measured at 260 nm using the

fixed wavelength mode of the UV-Visible spectrophotometer. The calibration curve was generated three times, with the results presented in Table 1.

Table 1:Calibration curve results at 260 nm

Sr.no.	Concentration (µg/ml)	Absorbance
1	10	0.159
2	20	0.261
3	30	0.331
4	40	0.414
5	50	0.503

Method Validation

Linearity and Range

The proposed method aims to achieve optimal performance, with particular emphasis on linearity and range. A five-point calibration curve for Valsartan was established within a concentration range of 10-50 µg/ml. The concentrations and their corresponding mean absorbance values are shown in Table 1. The calibration curve was analyzed using least squares regression, yielding the equation y = 0.008x + 0.081, with a correlation coefficient of 0.997, as depicted in Figure 3. The linearity assessment confirmed that the developed UV method is linear within the specified concentration range of the calibration standards.

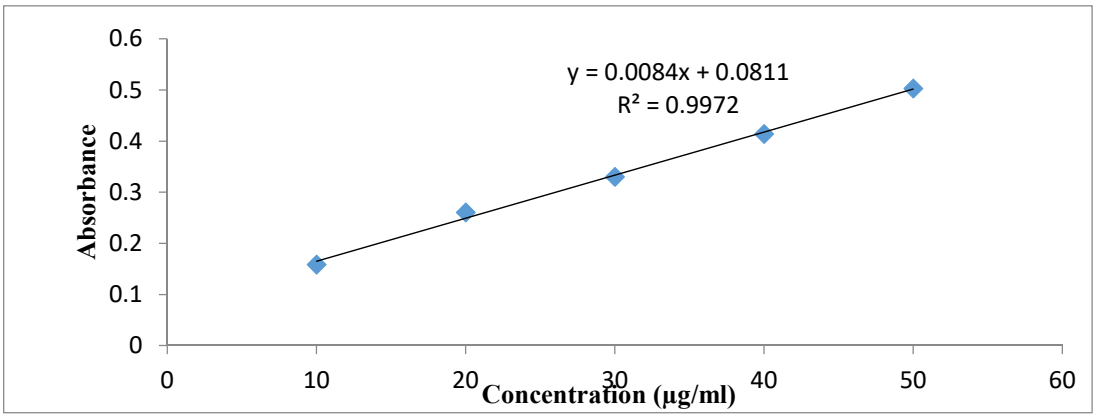

Fig.3 Calibration curve for the standard solution of Valsartan.

Table 2: Accuracy data of UV method for Valsartan

Recovery Level (%)	Concentration of sample (µg/ml)	Amount added (µg/mL)	% Recovery
50	10	7	98.5
100	30	40	99.2
150	50	70	99.7

Precision:

Precision serves as an indicator of the extent of variability in measurements. It reflects the consistency of the results obtained. An effective analytical method is anticipated to yield outcomes that are consistently reproducible. A precise analytical approach contributes to the generation of accurate results. Recognizing the significance of achieving both reproducibility and accuracy, the intra- and inter-day precision of the established UV method was assessed at a concentration of 10µg/ml. The results obtained were within the acceptable range, showcasing a relative standard deviation (RSD) of under1%.

Table 3: Intra-day precision data of UV method for Valsartan

Sr no	Concentration	Absorbance
1	10(µg/ml)	0.158
2		0.159
3		0.161
4		0.159
5		0.160
	Mean	0.1594
	SD	0.00114
	RSD	0.715

Table 4: Inter day precision data of UV method for Valsartan

Sr. No	Concentration	Absorbance (1st Day)	Absorbance (2nd Day)
1	10(µg/ml)	0.158	0.159

2		0.160	0.162
3		0.161	0.160
4		0.159	0.161
5		0.160	0.162
	Mean	0.1596	0.1606
	SD	0.00102	0.00114
	RSD	0.631	0.710

Robustness

Robustness refers to the ability of a method to maintain its performance despite minor, intentional changes in method parameters, serving as an indicator of its reliability under typical conditions. The assessment of robustness was conducted using two distinct instruments and involved two different analysts. This characteristic is crucial, as inadvertent variations in elements like solvent composition or pH may occur during routine procedures, which could compromise the effectiveness of the method. It is anticipated that such variations will not substantially impact the analytical method's performance. Consequently, there is a significant demand for a reliable analytical method. Robustness indicates that the absorption level of the Valsartan solution in methanol exhibits minimal variation across different wavelengths (±2nm).

Table 5: Robustness data of UV method for Valsartan

Sr.no	**Absorbance at 258**	**Absorbance at 262**
1	0.158	0.157
2	0.160	0.159
3	0.159	0.158
SD	0.001	0.001
%RSD	0.628	0.632

Limit of Quantitation (LOQ) and Limit of Detection (LOD)

The Limit of Quantification (LOQ) denotes the minimum concentration that can be measured with satisfactory accuracy and precision. Typically, the LOQ serves as the initial calibration standard. In the proposed UV method, the Limit of Detection (LOD) and LOQ were determined to be 0.448 and 1.3902 µg/ml, respectively, as presented in the table. The lower LOQ value suggests that the proposed method is appropriate for analyzing samples with even minimal amounts of Valsartan.

Table 6: LOD & LOQ data for UV method for Valsartan

LOD	0.448 (µg/mL)
LOQ	1.3902 (µg/mL)

Estimation of Valsartan:

The established UV method was effectively utilized for the determination of Valsartan concentration in Valzaar Tablet 80 mg. The average percentage assay of the Valsartan tablet was determined to be 96.7%.

Conclusion:

The suggested UV spectroscopic technique has been demonstrated to be accurate, precise, stable, linear, specific, and straightforward for the quantitative determination of Valsartan in both bulk and tablet dosage forms. The method demonstrated robustness and resilience, proving effective for the estimation of Valsartan.

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Conflict of Interest: No conflict of interest**.**

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