International Journal of Advances in Pharmaceutics
E-ISSN: 2320-4923; P-ISSN: 2320-4931
Journal DOI: https://doi.org/10.7439/ijap
Journal home page: http://ssjournals.com/index.php/ijap
Research Article

Estimation of Valsartan in Pharmaceutical Formulation by Area under Curve Spectrophotometric Method

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***Article History:**
Received: 04/01/2018
Revised: 28/01/2018
Accepted: 29/01/2018
DOI: https://doi.org/10.7439/ijap.v7i1.4550

Abstract

For estimation of Valsartan in pharmaceutical dosage form, a simple, accurate and precise area under curve spectrophotometric method was developed. The area under two points on the mixture spectra is directly proportional to the concentration of the component of interest is the AUC curve. The area selected for estimation of Valsartan was between 238.20 to 254.40 nm. The method represented regression coefficient (r2 = 0.996) at concentration rang 2-10 µg/ml. Estimation of the drugs was found up to 100 % representing the accuracy of the method. The recovery of the Valsartan was found up to 100 %. Validation of the proposed method was carried out for its accuracy, precision and specificity according to ICH Q2 (R1) guidelines. The developed methods can be successfully applied in routine work for the estimation of Valsartan in its pharmaceutical dosage form.

Keywords: Valsartan; UV; AUC.

1. Introduction

Valsartan1 is a non-peptide, orally active and specific angiotensin II receptor blocker acting on the AT1 receptor subtype. Valsartan in chemically described as N-(1-oxopentyl)-N-[2'(1H-tetrazol -5 yl)[1,1'biphenyl]4-yl methyl]L-valine. Valsartan is used for treatment of hypertension, can be used alone or in combination with other antihypertensive drugs. Only LC-MS in human plasma, Colorimetric estimation, RP-HPLC and degration studies by isocratic HPLC has been reported so far. The aim of this work is to develop simple, accurate, precise spectrophotometric methods for the routine determination of valsartan in bulk and tablet dosage form.[1-8,11]

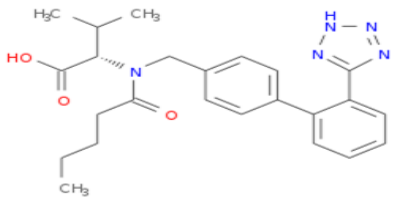

Figure 1: Chemical structure of Valsartan

2. Materials and methods

2.1 Chemicals

Valsartan was supplied by Chempure Pharmaceuticals Ltd., Mumbai, India. Tablet of Valsartan 10 mg (DIOVAN 40 mg) was procured from local pharmacy. 0.1N Sodium hydroxide was obtained from S.D. Fine Chemicals, Mumbai, India. All chemicals and reagents were of analytical reagent (AR) grade.

2.2 Instrumentation

A Shimadzu (Kyoto, Japan) model UV-1800 double beam UV-Visible spectrophotometer attached with computer operated software UV probe 2.0 with spectral width of 2 nm, wavelength accuracy of 0.5 nm and pair of 1 cm matched quartz cells was used to measure absorbance of the resulting solutions. Analytical balance, Mettler Toledo (Model JL1503-C).

2.3 Preparation of Standard and Sample Stock Solution

Transfer accurately weighed quantity of Valsartan (10 mg) to a separate 100 ml volumetric flask, dissolved and diluted up to the mark with 0.1N Sodium hydroxide to

get standard solution having concentration 100 µg/ml of Valsartan. Successive dilutions were carried out to get 10 µg/ml of Valsartan which was scanned in the UV-region i.e. 400 to 200 nm. In UV– Spectrophotometric method, two wavelengths 238.20 nm and 254.40 nm were selected for estimation of area under curve (AUC) of Valsartan. For Sample solution, Valsartan tablet was taken, 10 mg was transferred into 10 ml volumetric flask and make up the volume with distilled water. 1 ml from above solution was taken into 10 ml volumetric flask and make up volume with distilled water to get a final concentration of 100 µg/ml.

2.4 Area under Curve:

The AUC (area under curve) method was applicable where there is no sharp peak or when broad spectra are obtained. It involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ1 and λ2. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observation so as to get the linearity between area under curve and concentration. The above mentioned spectrums were used to calculate AUC. Thus, the calibration curve can be constructed by plotting concentration versus AUC.[9]

2.5 Method Validation:

The method was validated as per the ICH guidelines.

2.5.1 Linearity

Standard solution of Valsartan (1.25, 2.5, 3.75, 5 and 6.25 ml) was pipette out in to a separate series of 25 ml volumetric flask. The volume was adjusted to the mark with distilled water and mixed. The area under curve for solutions was measured between 238.20 to 254.40 nm against distilled water as blank. From using this area, the 'X' value of the drug was determined at the selected AUC range.[10]

2.5.2 Precision

Precision of the method was verified by repeatability and intermediate precision studies. Repeatability studies were performed by analyses solution (5-25 µg/ml) on the same day. The %RSD of six determinations was calculated. Intermediate precision of the method was checked by repeating studies on two different days. The %RSD of determinations was calculated.[10]

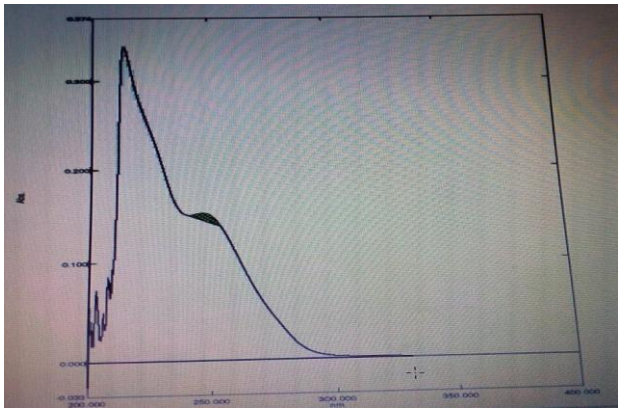

Figure 2: Area between 238.20-254.40 nm selected for valsartan tablet formulation (10 µg/ml)

Table 1: Calibration Curve Data of Valsartan

Conc.(ppm)	AUC
2	0.090
4	0.152
6	0.227
8	0.304
10	0.349
12	0.433

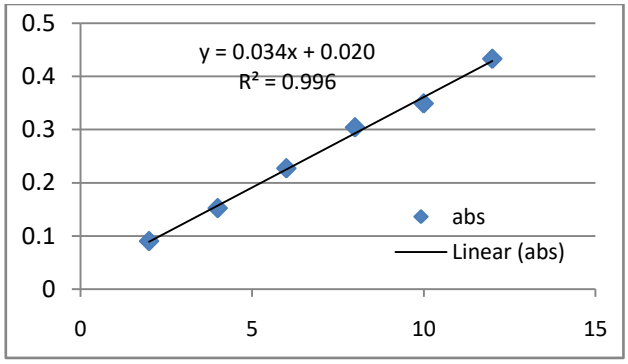

Figure 3: calibration curve of Valsartan

2.5.3 Sensitivity

The sensitivity of the method was determined in terms of limit of detection (LOD) and limit of quantitation (LOQ). The LOD and LOQ were calculated by using the formula, LOD = 3.3 × σ/S and LOQ = 10 × σ/S,

Where, σ is standard deviation of regression line and S is slope of corresponding regression line.[10]

2.5.4 Recovery

To study the accuracy of the proposed methods and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by the standard addition.[10]

Table 2: Regression Analysis Data for Valsartan by the Area under Curve

Method Parameter	AUC
Wavelength range	238.20-254.40 nm
Concentration range(µg/ml)	2-12
Slope (m)	0.034
Intercept (c)	0.020
Correlation coefficient (r2)	0.996

Table 3: Results of Intra and Inter Day Precision

Parameter	±SD*	%RSD*
Interday	**0.05**	**1.84**
Intraday	**0.01**	**0.73**

*n=6

Table 4: Data of Recovery Studies

Level of Mean Recovery (%)	% Mean	Recovery SD*	% RSD
80%	99.65	0.5760	0.5802
100%	99.97	0.5482	0.5497
120%	99.75	0.7019	0.7068

*n = 3

Table 5: Assay Results for the Estimation of Valsartan in Pharmaceutical Formulation

Parameter	Labeled Claim (mg/tab)	Amount Found (mg/tab)	% Labeled Claim
AUC	40	39.999	99.97%

Table 6: Summary Data of Validation Parameters

Sr. No.	Parameter	AUC Method
1	Linearity range	2-12
2	Regression equation	Y=0.034x+0.020
3	Correlation co-efficient	R2=0.996
4	LOD(µg /ml)	0.14
5	LOQ (µg /ml)	0.448
6	Precision	
	Intra day	0.73
	Inter day	1.84
7	% recovery	0.5760-0.7068

2.5.5 Assay Procedure

Twenty tablets (Valsartan) containing 10 mg of Valsartan weighed, average weight calculated and triturated to fine powder and then weight equivalent 10 mg of Valsartan transferred into 10 ml volumetric flask and dissolved in water and diluted up to the mark with water to get a solution containing of 1000 µg/ml from the 2.5 ml was transferred to 25 ml volumetric flask and diluted up to the mark with water to get Valsartan solution containing 100 µg/ml of Valsartan. From above solution 2.5 ml was transferred to 25 ml volumetric flask and diluted up to the mark with water and to produce 10 µg/ml solution of Valsartan. 10 µg/ml of Valsartan which was scanned in the UV-region i.e. 400 to 200 nm.

3. Results and discussion

The area under the curve spectra for Valsartan was recorded at the wavelength of 238.20-254.40 nm.

3.1 Linearity and Range

Under the experimental conditions described, the graph obtained for area under the curve spectra showed linear relationship (Figure 3). Regression analysis was made for the slope, intercept and correlation-coefficient values. The regression equations of calibration curves were y = 0.034x-+0.020 (r2 = 0.996) at 238.20-254.40 nm for area under the curve spectrophotometry. The range was found to be 2-12 µg/ml for area under the curve spectrophotometric method (Table 1).

3.2 Precision

To determine the precision of the method, an Valsartan solution at a concentration 10 µg/ml was analyzed each six times for area under the curve spectrophotometric method. Solutions for the standard Curves were prepared fresh everyday (Table 3).

3.3 Sensitivity

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using the equations LOD = 3 x σ / S and LOQ = 10 x σ /S, where σ is the standard deviation of intercept, S is the slope. The LOD and LOQ were found to be 0.14 µg/ml and 0.448 µg/ml respectively for area under the curve method.

3.4 Recovery

To study the accuracy of the proposed methods and to check the interference from excipients used in the dosage forms, recovery experiments were carried out by thestandard addition method. This study was performed by addition of known amounts of Valsartan to reanalyzed solutions of commercial dosage form (Table 4).

3.5 Analysis of Marketed Formulation

There was no interference from the excipients. The drug content was found to be 99.97 % for area under the curve spectrophotometric method. It may therefore be inferred that degradation of Valsartan had not occurred in the marketed formulations that were analyzed by this method. The low % R.S.D. value indicated the suitability of this method for routine analysis of Valsartan (Table 5).

4. Conclusion

No any spectrophotometric methods have been described for AUC estimation of Valsartan. Therefore, simple, fast and reliable area under curve spectrophotometric method was developed for the routine analysis of Valsartan. The developed method can be concluded as accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

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