

SPECTROPHOTOMETRIC METHODS FOR THE ESTIMATION OF VALSARTAN IN BULK AND ORAL DOSAGE FORM

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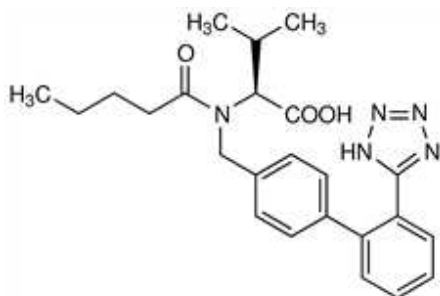
ABSTRACT

Simple precise UV spectrophotometric methods have been developed for the estimation of Valsartan in both bulk and tablet dosage form. Valsartan is well soluble in sodium hydroxide and shows maximum absorption at 249nm. The drug obeyed Beer's law showing linearity in the range of 5-30 μ g/ml with a correlation coefficient of 0.999. Method A is based on standard absorbance, method B involves estimation by Area under curve (AUC) and method C by derivatisation of Zero order spectrum and method D where Q-Absorbance ratio, in wide use of the developed methods were analyzed for specificity, limit of detection (LOD), limit of quantification (LOQ), linearity of response, precision and accuracy. Thus the proposed methods could be adopted for routine analysis of bulk drug and its formulation.

Keywords: Valsartan, First derivative, AUC, LOD and LOQ.

INTRODUCTION

Valsartan¹ is a non-peptide, orally active and specific angiotensin II receptor blocker acting on the AT1 receptor subtype. Valsartan is 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 plasma², Colorimetric estimation³, RP-HPLC⁴ and degradation studies by isocratic HPLC⁵ 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. Method A is the standard absorbance method involving the determination of valsartan in 0.1N sodium hydroxide followed by measuring the absorbance at 249 nm. Method B involves estimation of the drug by Area under curve of the spectrum obtained in method A and method C involves the derivatization of the Zero order spectrum obtained in method A where the first order spectra showed negative maxima at 249 nm for valsartan and method D makes use of Q-Absorbance ratio at selected wavelengths.



Structure⁶

MATERIALS AND METHODS

A Shimadzu model UV-1650 double beam UV-Vis spectrophotometer with a pair of 1cm matched quartz cells was used to measure absorbance. The tablet dosage form was obtained from the local market. All the solutions were freshly prepared just before the analysis, and 0.1N sodium hydroxide used was of analytical grade.

Estimation of valsartan

Aliquot quantity of each standard valsartan was weighed in 100ml volumetric flasks. Dissolved in 10 ml of 0.1N sodium hydroxide and made up to volume with 0.1N sodium hydroxide. Dilutions ranging from 5-30 μ g/ml of standard valsartan solutions were prepared

using 0.1N sodium hydroxide. The final dilutions were scanned in ultraviolet region 200-400nm against 0.1N sodium hydroxide blank. Valsartan showed maximum absorption at 249 nm and it obeyed Beer's law⁷ in the concentration range of 5-30 μ g/ml (fig 1 & 2)

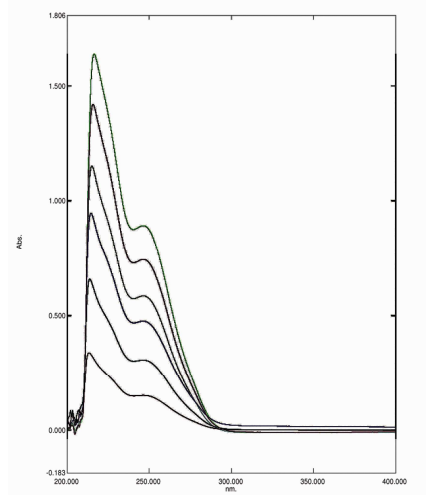


Fig 1: Overlain spectra of valsartan

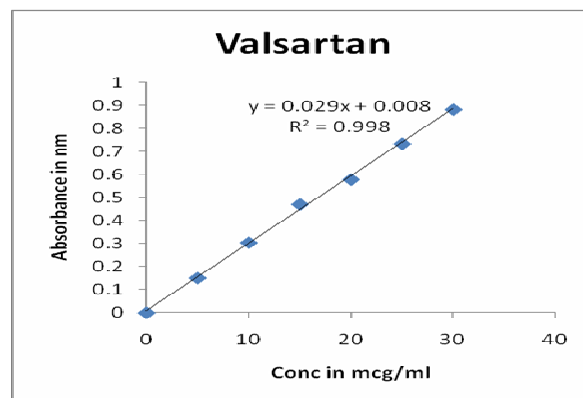


Fig 2: Calibration chart of valsartan

Assay

Method A: Standard absorbance method

Estimation of Valsartan

20 tablets of valsartan was accurately weighed and crushed to fine powder. Tablet powder equivalent to 100mg of the valsartan was weighed in a 100 ml volumetric flask, shaken vigorously with sufficient amount of 0.1N sodium hydroxide for half an hour. Finally the solution was made up to volume with 0.1N sodium hydroxide. Solution was well shaken and filtered through Whatmann filter paper (No.41). The first few ml of the filtrate was discarded and aliquot quantity of the filtrate was diluted to obtain a final concentration of 10µg/ml of valsartan. The absorbance of the resulting solution was measured at 249nm against 0.1N sodium hydroxide blank.

Method B: Area under the curve⁸

The AUC (area under curve) method involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ_1 and λ_2 . The wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. The standard spectra obtained in the linearity characterization and the sample spectra obtained in method A were used. The AUC for valsartan (fig 3) were determined between 238 and 254 nm for both standard and sample. The calibration graph was plotted between AUC and concentration. The sample AUC was interpolated on the respective linearity chart of the AUC and the concentration was determined.

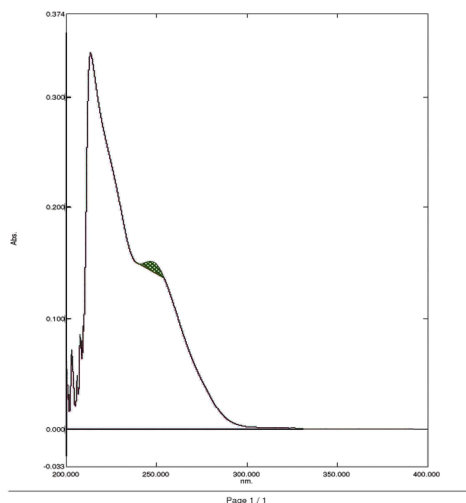


Fig. 3: AUC

Method C: First derivative⁹

Derivative spectrophotometry involves the conversion of normal spectrum to its first, second or higher derivative spectrum. The first derivative (D^1) spectrum is the plot of the rate of change of absorbance with wavelength against wavelength i.e., the plot of the slope of the fundamental spectrum against wavelength or $dA/d\lambda$ vs. λ . Valsartan showed zero cross over point at 249nm (fig 4). The amplitude of the negative maxima were measured and plotted against concentration to determine the linearity. The sample amplitudes were interpolated on the respective linearity chart of the derivative spectra and the concentration was determined.

Recovery studies

The recovery studies were carried out on spiked samples by adding predetermined amount of standard drugs to the respective sample. About 20, 50 and 100% of standard drugs were added to the sample solutions and the absorbance was measured against 0.1N sodium

hydroxide blank. The percentage recovered was calculated. The recovery studies were performed at three levels to confirm the accuracy of the above said methods.

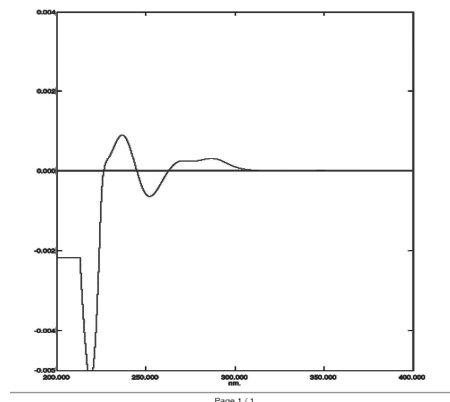


Fig. 4: First derivative

Method D: Q-Absorbance Method¹⁰

Q-Absorbance method depends on the property that, for a substance which obeys Beer's law at all wavelengths, the ratio of absorbances at any two wavelengths is a constant value independent of concentration or pathlength. The wavelengths selected for this method are 235nm and 250nm (fig 5). The ratio of absorbance between these two wavelengths was calculated. The difference in absorbances between these two wavelengths were calculated and plotted against concentration to determine the linearity, the concentration of sample was determined by interpolation. The values obtained by the proposed method are presented.

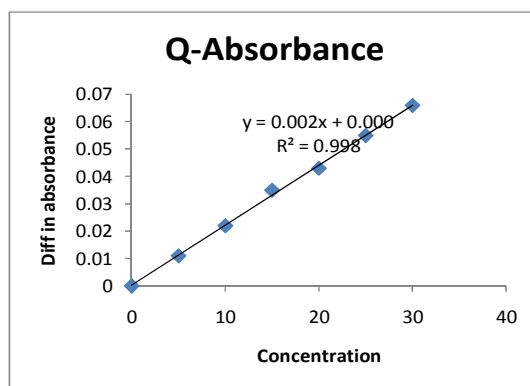


Fig. 5: Q-Absorbance

RESULTS AND DISCUSSIONS

Valsartan was found to obey Beer's law in the concentration range of 5-30µg/ml. Valsartan showed good linearity as indicated by correlation coefficient value of 0.999. The optical parameters of valsartan with respect to all the three methods are presented in table no.1. The percentage of the individual drugs in the formulation according to the four methods were calculated and presented in the table no.2.

The results of the analysis showed that the amount of drugs were in good agreement with the label claim of the formulation. The accuracy of the proposed method was determined by recovery studies. The recovery studies were carried out on spiked samples and calculated for all the three methods. The percentages recovered were found to be in the range of 98-101 represented in table.3 which showed that the excipients in the formulation did not interfere with the analysis.

Table 1: Optical parameters of Valsartan

S.No	Optical Parameter	Method			
		A	B	C	D
1.	Wavelength λ_{max}	249 nm	249nm	249nm	249nm
2.	Molar absorptivity	13056.53	---	---	-----
3.	Beer's law limit $\mu\text{g/ml}$	5-30	5-30	5-30	5-30
4.	Regression equation	$y = 0.029x + 0.008$	$y = 0.014x - 0.004$	$y = 0.063x - 0.025$	$y = 0.063x - 0.000$
5.	Slope	0.029	0.014	0.06	0.063
6.	Intercept	0.008	0.004	0.025	0.00
7.	Correlation coefficient	1.0	0.999	0.998	0.992
8.	Sandell's sensitivity	0.03338	----	----	----
9.	LOD	1.5971	0.5629	---	-----
10.	LOQ	15.97137	5.6299	---	-----

Table 2: Result of Tablet Assay

Drug	Method A		Method B		Method C		Method D	
	% Amount Present \pm SD	RSD %	% Amount Present \pm SD	RSD %	% Amount Present \pm SD	RSD %	% Amount Present \pm SD	RSD %
Valsartan	99.3 \pm 0.82	0.8323	100.92 \pm 1.2	1.1470	100.25 \pm 2.0	2.0	100.58 \pm 1.53	1.5224

Each value is a mean of 3 determinations.

Table 3: Recovery Studies

Drug	Amount of drug added		% Recovery by the proposed methods			
	Sample	Standard	Method A	Method B	Method C	Method D
Valsartan	10 $\mu\text{g/ml}$	2	99.7	100.25	100.25	98.6
		5	99.4	102.26	102.26	99.58
		10	99.4	100.25	101.26	101.93

Each value is a mean of 3 determinations.

CONCLUSION

The above methods developed for the estimation of valsartan were found to possess good linearity of response, specificity and accuracy. The methods are simple, economical and easy to perform. Thus the proposed methods could be applied for routine analysis of these drugs.

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REFERENCES

- Indian Pharmacopeia: Vol 3; 2010. p.2286.
- Nozomu Koski, Hiroto Kwashita, Hisanori Hara, Miyuki Niina, et al Development and validation of a method for the quantitative determination of valsartan in human plasma by LC- tandem MS. J of Pharm and Biomedical Analysis 2007; 43: 1769-1774.
- Narendra Kumar Reddy K, Devalrao G, Sudhakara Sai Babu G. New analytical methods for the estimation of valsartan in pharmaceutical formulations: www.ijrc.com: 2011; 1(3):575-578.
- Thanusha G, Jose Gnana Babu C, Channa Basavaraj KP, Reddy Panditi V, Sharadha Ch. Validated RP-HPLC method for the quantitative estimation of valsartan in bulk and pharmaceutical dosage forms. Int. J.Chem. Tech. Research 2010; 2(2): 1194-1198.
- Bhatia M Sudesh and Kokil S Uttamrao, Determination and validation of valsartan and its degradation products by isocratic HPLC. J. Chem.Metrl. 2009; 3(1):1-12.
- www.drug bank.com
- Manas Chakravarty, Bijank Gupta, Rabindra Debnath et al. New spectrophotometric method development for the determination of rimonabant in bulk and tablets. Int J Pharmacy and Pharm Sci 2009; 1(1): 162-164.
- Niraimathi V, Jerad Suresh A, Nanjappan K Spectrophotometric estimation of Nisoldipine in bulk and tablet dosage formulation. Acta Ciencia Indica 2010; xxxvi C(4):393.
- Smita T.Kumbhar, Swapnil D. Jadhav, Neela M. Bhatia, Manish S. Bhatia. Development and validation of derivative spectrophotometric method for estimation of atorvastatin calcium and amlodipine besylate in tablet dosage form. Int J Pharmacy and Pharm Sci 2011; 3(4): 195-197.
- Priyadarshini J, Giji GP, Niraimathi V, Jerad Suresh A UV spectrophotometric estimation of metaxalone in bulk and tablet dosage form. Int. Journal of Chemical Sciences 2010; 8(2):1041-1045.