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NOVEL UV-SPECTROPHOTOMETRIC METHODS DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF VALACYCLOVIR IN BULK AND PHARMACEUTICAL FORMULATION

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ABSTRACT

A Novel, simple, accurate and precise Zero order derivative spectroscopic method was developed and validated for the estimation of valacyclovir in bulk and pharmaceutical formulation. The stock solution was prepared by weighing 100 mg of standard valacyclovir in 100 ml volumetric flask with Methanol. The stock solution was made to produce 1000 µg/ml with methanol. Further dilutions were prepared as per procedure. The drug solution showed the maximum absorbance at 254 nm. The linearity was found in the concentration range of 2-12 µg/ml. The correlation coefficient was found to be 0.999. The regression equation was found to be Y=0.043x+0.001. The method was validated for linearity, accuracy, precision, ruggedness, robustness, LOD and LOQ. The LOD and LOQ for estimation of valacyclovir were found to be 0.02738 µg/ml and 0.08298 µg/ml respectively. Recovery of valacyclovir was found to be in the range of 99.62-100.62 %. Proposed method was successfully applied for the quantitative determination of valacyclovir in bulk and pharmaceutical formulation.

KEYWORDS: Valacyclovir, Zero order UV- Spectroscopy, Methanol, Accuracy.

INTRODUCTION

Valacyclovir, the L-valyl ester of acyclovir, is an oral prodrug that undergoes rapid and extensive first-pass metabolism to yield acyclovir and the essential amino acid L-valine. Acyclovir, the active antiviral component of valacyclovir, shows good in vitro activity against the herpesviruses herpes simplex virus (HSV)-1, HSV-2 and varicella zoster virus.

The bio availability of acyclovir from oral valacylovir is considerably greater than that achieved after oral acyclovir administration. Thus, valacyclovir delivers therapeutic acyclovir concentrations when administered in a less frequent oral dosage regimen than is required for acyclovir.

It has a molecular formula of C13H20N6O4 and molecular weight of 324.34 g/mol.

The literature survey reveals that various analytical methods have been developed such as UV spectroscopy methods, HPLC methods, HPTLC method and for the estimation of valacyclovir present in alone or in combination with other drugs or in marketed products. Most of the reported UV Spectroscopic methods are Simultaneous estimation of valacyclovir along with other Antiviral drugs, by using several solvents, expensive reagents and often time- consuming. So there is a need to develop novel UV Spectroscopic methods for the estimation of valacyclovir alone in bulk and Pharmaceutical formulation.

A detailed review of the literature regarding the existing methods revealed that there is a need for the development of the spectrophotometric method, which is simple for the estimation of valacyclovir present in bulk and Pharmaceutical formulation. An effort was made in the present method to develop a novel, simple, sensitive, accurate, reliable and reproducible with minimum Relative Standard Deviation (RSD) values for the estimation of valacyclovir in bulk and Pharmaceutical formulation.

MATERIALS AND METHOD

Instrument

A Shimadzu-1800 UV-Vis double beam spectrophotometer connected to a computer loaded with Shimadzu UV Probe software with 1 cm matched quartz cells was used for spectrophotometric measurements in above proposed spectrophotometric methods.

Chemicals
Valacyclovir was given as a gift sample by industry. Tablets of Amlodipine were procured from local market.

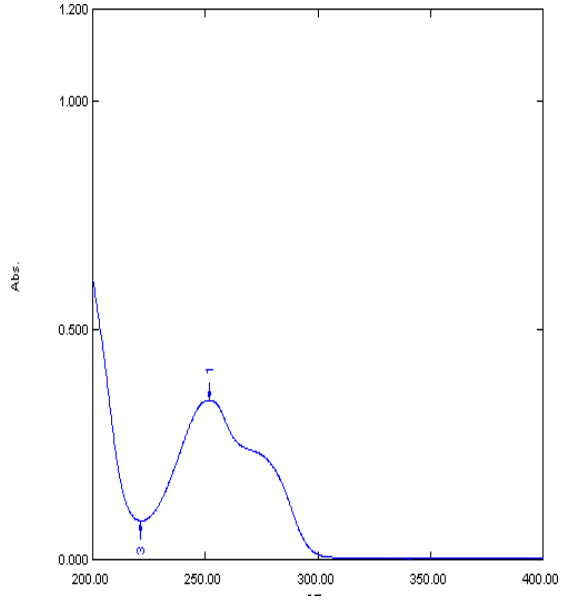
Solvent
Methanol

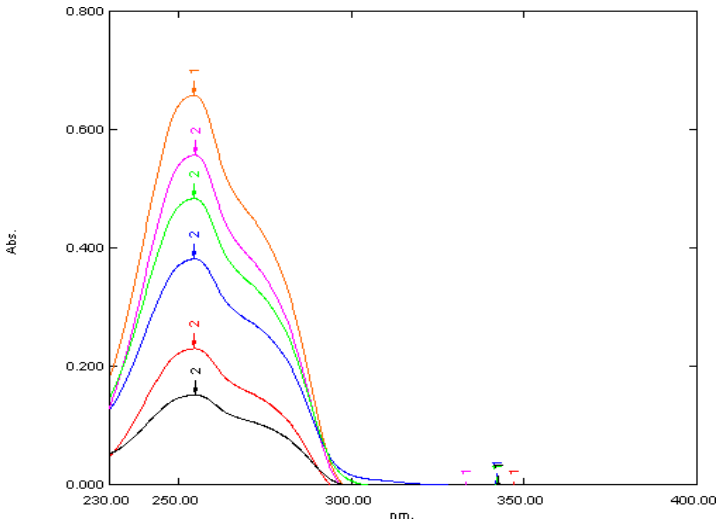
Preparation of stock solutions
Accurately weigh 100mg of Valacyclovir was transferred into 100ml volumetric flask and diluted with Methanol up to the mark. From this pipette out 10ml into 100ml volumetric flask and diluted with Metahnol up to the mark, from this solution pipette out 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2ml into 10ml individual volumetric flask and add Methanol up to the mark, this gives 2, 4, 6, 8, 10 and 12 µg/ml concentrations.

Selection of Analytical Wavelength
Appropriate dilutions were prepared for drug from the standard stock solution and the solution was scanned in the wavelength range of 200-400 nm. The absorption spectra thus obtained were derivatized from Zero order method. It shows maximum absorbance at 254 nm.

Selection of analytical concentration ranges
From the standard stock solution of Valacyclovir, appropriate aliquots were pipetted out in to 10 ml volumetric flasks and dilutions were made with Methanol, Valacyclovir obeys Beer's law in the concentration range of 2-12 µg/ml.

Sample preparation of Valacyclovir
The commercially available Valtrex contains 500 mg of Valacyclovir. From this twenty Tablets were weighed and powdered. The Tablet powder equivalent to100 mg of Valacyclovir was transferred into 100 ml volumetric flask then it was diluted with the Methanol and made up to the mark and the solution was filtered through whatman filter paper NO. 41. From the above solution 10 ml was pipetted out into 100 ml volumetric flask and the volume was made up to the mark with Methanol. The final concentration of Valacyclovir was brought to 6µg/ml.





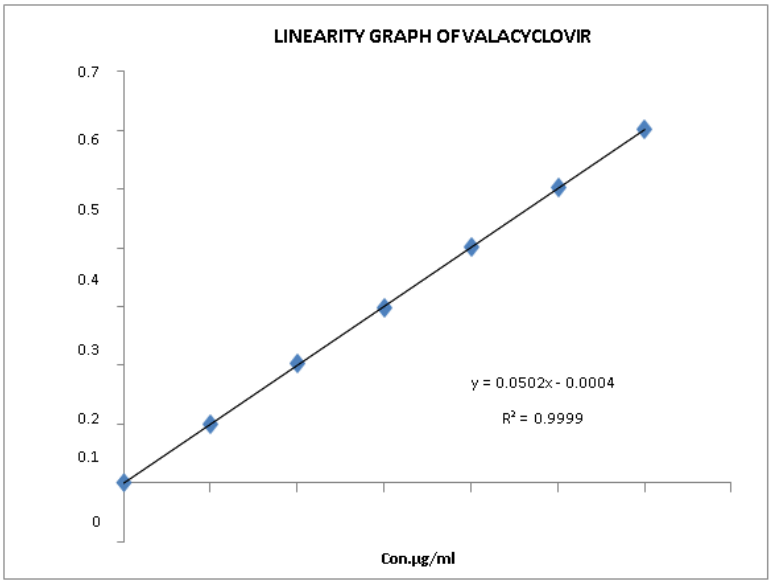
Validation of Spectrophotometric method

1. Linearity The working standard solution were diluted serially with Methanol to obtain the range of 2-12µg/ml. a calibration curve for Methanol was obtained by measuring the absorbance at the λ max of 254 nm and absorbance values are shown and Zero order overlain spectra of Valacyclovir at 254 nm were shown. Calibration graph were presented in Fig.1. Statistical parameters like slope, intercept, coefficient of correlation, and Sandel's sensitivity were determined and presented in Table.

Spectroscopy

Sl. no	Concentration in µg/ml	Absorbance at 254nm±SD
1	2	0.101±0.00173
2	4	0.203±0.00115
3	6	0.298±0.00057
4	8	0.401±0.00
5	10	0.504±0.00115
6	12	0.603±0.001

**Average of Six determinations.



2. Range: The range of analytical method is the interval between the upper and lower levels of analyte that have been demonstrated to be determined within a suitable level of precision, accuracy and linearity.
3. Precision: Precision of the method was studied as intra-day and inter-day precision. Intra- day precision was determined by analysing the 2, 4, 6, 8, 10 and 12µg/ml concentration for three times in same day. Inter-day precision was determined by analysing the same concentration of solution daily for three days. Precision results are shown in Table.

Regression Parameters by Zero order spectroscopy

Optimum Condition	UV Method
λmax(nm)	254nm
Beer's law limits (µg/ml)	2-12
Sandell's sensitivity	0.020 mcg / cm^2
Regression equation (Y*)	Y=0.050x - 0.000
Slope (b)	0.050
Intercept (a)	0.000
Co-relation coefficient(R^2)	0.999

Determination of Precision result for Valacyclovir.

Concentration (µg/ml	Intra-day Absorbance ±SD**	%RSD	Inter-day Absorbance ±SD**	%RSD
2	0.103±0.0020	1.94	0.103±0.0020	1.94
4	0.203±0.0025	1.23	0.204±0.0015	0.73
6	0.297±0.0005	0.16	0.297±0.0015	0.50
8	0.402±0.0015	0.37	0.403±0.0020	0.49
10	0.502±0.0020	0.39	0.502±0.0020	0.39
12	0.601±0.001	0.16	0.606±0.0015	0.24

4. Accuracy: To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i. e, 50%, 100% and 150%. In which the formulation concentration was kept constant and varied pure drug concentration. Accuracy results were shown in Table.

Tablet	Spiked levels	Amount of sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered	% Recovery ±SD**	%RSD
Valcivir 1000 mg	50	4	2	5.89	98.16±0.903	0.98
	100	4	4	7.94	99.25±0.5021	0.50
	150	4	6	9.93	99.30±0.4714	0.47

5. Robustness: Robustness was determined at different wavelengths. The value of %RSD was found to be less than 2 were shown in Table.

Determination of Robustness results for Valacyclovir at 254 nm byZero order Spectroscopy.

Parameter	At 253 nm	At 255 nm
Mean absorbance	0.395	0.390
Standard deviation**	0.001	0.0015
%RSD	0.253	0.393

** Average of six determinations.

6. Ruggedness: Ruggedness was determined between different analysts. The value of %RSD was found to be less than 2 were shown in Table.

Determination of Ruggedness results for Valacyclovir at 254 nm byZero order Spectroscopy.

Analysts	Analyst-1	Analyst-2
Mean absorbance	0.517	0.521
Standard deviation**	0.0020	0.0085
%RSD	0.40	1.63

** Average of six determinations.

7. Limit of detection and Limit of Quantitation: The LOD and LOQ of the present method were calculated based on standard deviation of the Response and slope of linearity curve. LOD and LOQ values of Valacyclovir were found to be 0.02738 µg/ml and 0.08298 µg/ml were shown in Table.

Determination of LOD and LOQ results for Valacyclovir at 249-259nm by AUC Method.

SL.NO	Parameters	Values
1	SD of Intercepts*	0.000473
2	Average of Slopes*	0.0406
3	LOD (3.3×SD of intercepts/average of slopes)	0.0382
4	LOQ (10×SD of intercepts/average of slopes)	0.1165

**Mean value obtained from six calibration curve.

CONCLUSION

In the present investigation, we have developed Novel, simple, accurate and Precise UV- spectrophotometric method like Zero order derivative spectroscopy for the routine estimation of valacyclovir in bulk and pharmaceutical formulation and the method were validated in terms of linearity, accuracy, precision, robustness, ruggedness, LOD and LOQ.

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