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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF VALACYLOVIR BY: REVIEW

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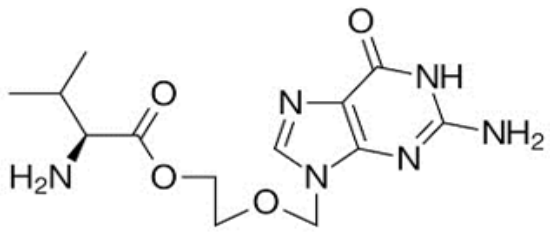
ABSTRACT

Analytical method development and Validation are the continuous and inter-dependent task associated with the research & development, quality control and quality assurance departments. Analytical procedures play a critical role in equivalence and risk assessment, management. It helps in establishment of product-specific acceptance criteria and stability of results. Validations determine that the analytical procedure is suitable for its intended purpose. Literature survey reveals that the analytical methods based on UV spectrometry, The parameters were validated according to ICH guideline in terms of accuracy, precision, robustness, and other components of analytical validation. The developed methods are simple, sensitive and reproducible and can be used for the analysis of Valacylovir.

KEYWORDS: Valacyclovir Hydrochloride, Method Development, UV, HPLC, Validation, ICH Guidelines.

INTRODUCTION

Valacyclovir was approved for medical use in 1995. It is marketed by GlaxoSmithKline under the trade names Valtrex & Zelitrex. Valacyclovir Hydrochloride is a HCL salt of L-valyl ester of acyclovir. It is [(s)-2-[(2-amino-6-oxo-6, 9-dihydro-3H-purin-9yl) methoxy] ethyl-2-amino-3-methylbutanoate] It is an Anti-viral drug used in the treatment of herpes zoster. It inhibits viral DNA synthesis. It is a prodrug intended to increases the bioavailability of acyclovir by increasing lipophilicity. Valacyclovir converted by esterase to active drug acyclovir via hepatic first pass metabolism.[1]



Molecular formula: $C_{13}H_{20}N_6O_4.HCL$
Molecular weight: 360.80

Solubility & Description: White to off white powder with a maximum solubility of water of174 mg/ml at 25°C.

Melting Point: Valacyclovir Hydrochloride has no distinct melting point. It undergoes rapiddecomposition above 200°C.

Pharmacokinetic Data

1	Bioavailability	55%
2	Protein Binding	13-18%
3	Metabolism	Hepatic to (acyclovir)
4	Biological half life	< 30 min. (Valacyclovir) 2.5-3.6 hrs. (acyclovir)

Storage: Stored under cool & dry place.

REVIEW OF LITERATURE

1. **M. Ganesh[2] *et al*:** Have a simple, sensitive, highly accurate UV spectrophotometric method has been developed for the determination of valacyclovir in bulk and tablet dosage form. Solution of valacyclovir in 0.1N HCl shows maximum absorbance at 255 nm. Beer's law was obeyed in the concentration range of 5-25 mcg mL-1 with 1.0910x104 mol-1 cm-1, the slope, intercept, correlation coefficient, detection and quantitation limits were also calculated. The proposed method has been applied successfully for the analysis of the drug in pure and in its tablets dosage forms. Result of percentage recovery and placebo interference shows that the method was not affected by the presence of common excipients. The percentages

assay of valacyclovir HCl in tablet was 99.82%. The method was validated by determining its sensitivity, accuracy and precision which proves suitability of the developed method for the routine estimation of valacyclovir in bulk and solid dosage form.

2. **Sujit Kumar Sahu[6] *et al*:** Two simple, sensitive, accurate, rapid visible spectrophotometric methods (A & B) and one non aqueous potentiometric titration (Method-C) have been developed for the estimation of Valacyclovir in pharmaceutical preparations. They are based on the diazotization of Valacyclovir with sodium nitrite and hydrochloric acid followed by coupling with Orcinol (Method A) to form yellow coloured chromogen, & 8-hydroxyquinolone (Method B) to form red coloured chromogen, (in alkaline medium). The absorption maxima (lmax) were found at 440 & 520nm for method A & B respectively. The colored chromogens formed are stable for more than 2 hours. Beer's law was obeyed in the concentration range of 50-300µg/mL for both the method A & B. Linearity range 5 to 25µg/ml was found for Method – C. The results of all the three methods have been validated statistically and by recovery studies (on the basis of ICH guidelines). The results obtained in the proposed methods are in good agreements with labeled amounts, when marketed pharmaceutical preparations are analyzed.

3. **Ashwini S. Pundkar[3] *et al*:** A Ultra-Violet (UV) and High Performance Liquid Chromatography (HPLC) have been developed for the estimation of Valacyclovir Hydrochloride in bulk drug and pharmaceutical dosage form. The method is carried out using C18 column 150×4.6mm i.e. particle size 5µm and mobile phase consisting of Methanol: Water (70:30), at flow rate of 0.8ml/min. The column temperature is ambient. Eluents were monitored by UV detector set at 252nm. The method was statistically validated in terms of linearity, accuracy, precision and robustness in accordance with ICH guidelines Linear regression analysis data for the calibration plot showed that there was a linear relationship between response and concentration in the range of 10µgm/ml To 50µgm/ml and the correlation coefficient is 0.9998. Literature survey reveals analytical methods for the estimation of Valacyclovir Hydrochloride from pharmaceutical dosage forms and also in biological fluids. The proposed method was found to be simple, precise, accurate, rapid and reproducible for the estimation of Valacyclovir Hydrochloride in bulk drug and tablet.

4. **PS. Kumbhar[4] *et al*:** Several analytical methods such as high performance liquid chromatography (HPLC), Uv- spectrophotometry and colorimetry have been reported for quantitative estimation of Valacyclovir hydrochloride in bulk and pharmaceutical formulations. The aim of this study was to develop simple, easily accessible and economic UV spectrophotometric and newer fluorometric methods. Methods: A simple, rapid, specific and cost effective spectrophotometric method using different solvents like methanol (Method A), ethanol (Method B), water (Method C) and phosphate buffer of pH 7.4 (Method D) and fluorometric method using solvents such as methanol (Method A), water (Method B) and 0.1N HCl (Method C) has been developed to determine the Valacyclovir hydrochloride content in bulk and pharmaceutical dosage formulations. Results: The calibration graph are linear and obeys beer's law in the concentration range of 2-20 µg/mL for all four spectrophotometric methods with a correlation coefficient (r2) of 0.998, 0.996, 0.999 and 0.997, respectively while the calibration graph are linear in the concentration range of 1-10 µg/mL for all three fluorometric methods with a correlation coefficient (r2) of 0.998, 0.999 and 0.999, respectively. The accuracy and precision of the methods were evaluated based on the intra-day and inter-day variations. The accuracy of the methods was further confirmed by standard addition procedure. The other characteristics such as limit of detection (LOD) and limit of quantification (LOQ) values are also reported. Conclusion: The obtained results proved that the developed methods can be employed for the routine analysis of Valacyclovir hydrochloride in bulk as well as in the commercial pharmaceutical formulations.

5. **Dr.K. Bhavya Sri[5] *et al*:** A rapid and sensitive reverse phase high performance liquid chromatography (RP-HPLC) was developed and validated for the analysis of valacyclovir hydrochloride in bulk and pharmaceutical dosage form. A phenomenex C18(250mm×4.6mm, 5µm) provided chromatographic separation using methanol:water (60:40), pH(3.5) adjusted with glacial acetic acid at the flow rate 0.8ml/min with UV detection at 251nm.valacyclovir hydrochloride was eluted at 2.24mins.The method was validated for linearity, precision, accuracy, robustness and recovery. The method was linear in the concentration range of 25-150µg/ml with correlation coefficient 0.9998. limit of detection and limit of quantification were found to be 0.000124µg/ml and 0.0003759µg/ml respectively.

6. **Sheetal Ramya Lahari N.A.[7] *et al* :** A reverse phase high performance liquid chromatography (RP-HPLC) has been developed for the estimation of valacyclovir in bulk drug and pharmaceutical dosage form. The method is carried out using C8 agilent zorbax column 150cm x 4.6mm x 5micron and mobile phase consisting of phosphate buffer at pH 3.0: water : methanol (50:50 % v/v), at flow rate of 1 mL/min. The column temperature is 25°C. Eluents

were monitored by UV detector set at 253 nm. The method was statistically validated in terms of linearity, accuracy, precision, systemsuitability and robustness in accordance with ICH guidelines. Linear regression analysis data for the calibration plot showed that there was a linear relationship between response and concentration in the range of 20-150 mcg/ml and the correlation coefficient is 0.9999.The retention time found to be 2.02min. Literature survey reveals analytical methods for the estimation of Valacyclovir from pharmaceutical dosage forms and also in biological fluids. The proposed method was found to be simple, precise, accurate, rapid and reproducible for the estimation of valacyclovir in bulk drug and tablet.

CONCLUSION

Literature survey suggested that various UV[1-2], RP-HPLC[3-6] and few simultaneous methods were developed and reported. The published methods were validated for various parameters as per ICH guidelines. Statistical analysis proved that the published methods were reproducible and selective. Thus, it can be concluded that the reported and published methods can be successfully applied for the estimation of Valacyclovir Hydrochloride in pure and pharmaceutical dosage form.

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