ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IX September 2025

"Review on Development and Validation of RP-HPLC Method, And Techniques for Vorasidenib in Bulk Drug and Pharmaceutical Dosage Forms"

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DOI: https://doi.org/10.51244/IJRSI.2025.120800247

Received: 21 Sep 2025; Accepted: 27 Sep 2025; Published: 02 October 2025

ABSTRACT

Vorasidenib, a novel dual inhibitor of mutant isocitrate dehydrogenase 1 and 2 (IDH1/2), has gained considerable attention for its therapeutic potential in the treatment of low-grade gliomas and other IDH-mutant malignancies. Accurate and reliable analytical methods are essential for the quantitative estimation of Vorasidenib in bulk drug and pharmaceutical dosage forms to ensure quality, safety, and efficacy. Among the available analytical techniques, Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) has emerged as the method of choice due to its sensitivity, selectivity, reproducibility, and cost-effectiveness. This review highlights the development and validation strategies of RP-HPLC methods for Vorasidenib, focusing on critical parameters such as selection of stationary and mobile phases, optimization of chromatographic conditions, and detection wavelength. Method validation is discussed in accordance with ICH guidelines, covering accuracy, precision, linearity, specificity, robustness, limit of detection (LOD), and limit of quantitation (LOQ). Furthermore, the review emphasizes the application of validated methods in routine quality control and stability studies of pharmaceutical formulations. Overall, the article provides comprehensive insights into RP-HPLC method development for Vorasidenib, serving as a valuable reference for researchers and pharmaceutical analysts engaged in drug analysis and regulatory submissions.

Keywords:. Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) Vorasidenib,limit of detection (LOD)

INTRODUCTION

Human life starting from birth to death mostly depends on medicines like vaccines, pharmaceutical dosages, drugs, vitamin tablets, mineral supplements, energy drinks, boosters etc. The word medicine is drawn from Latin "ars medicina" which means "the art of healing"1 . Because of advent development of the medical and pharmaceutical sciences were now leading a long span of healthy life. Medicines enhanced the life expectancy of humans and are considered to be the most important necessity of mankind which plays a vital role in curing the diseases and health issues. People who are suffering with hypertension, diabetes etc. are completely depending on the medicines throughout their tenure of life. Thus, the medicine is basically concerned with the health and welfare of the human2 .

During our ancestor's period pollution was low, food habits are hygiene, lot of physical work was involved, no significant mental stress or work pressures etc., and hence their health was not affected much with various kinds of diseases. But today, rapid increase of population, change of food habits, lack of physical work, extensive work pressure, mental stress, various kinds of pollutions etc., are causing the diseases and health problems. As the increase of diseases, the usage of medicines is also enormously increased. For the effective treatment of various diseases and health issues, proper medicines or pharmaceutical dosages in the right combinations are required. Medicines are there since from the ancient times and most of them are prepared by using herbals, natural ingredients and by the other home remedy methods. Preparation of the medicines is mainly concerned with the efficiency of the drug and the existing technology. The medicines should maintain certain requirements - like purity, effective reaction time, lack of side effects etc.

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Pharmaceutical companies look at qualitative and quantitative analysis to verify the quality of final product and to check that their raw materials meeting their indeed specifications3 . Qualitative analysis concerns with the identification of elements, functional groups or compounds in a sample, whereas the quantitative analysis helps in the determination of amount of a particular element, species or compound in the given sample4 , which enable us to maintain permissible limits of impurities in the sample.

Importance of Analytical Chemistry

The modern day medicinal research focusing towards decreasing the side effects of the drugs and keeping our lives even more secure6 . Many analytical techniques and instrumental methods were invented and developed to ascertain the standards of the drugs so as to serve the purpose of the pharmaceutical drugs safely7 . These techniques and methods play an important role in maintaining and assuring the quality of drugs and critical components of quality assurance (Q.A) or quality control (Q.C)8

Pharmaceutical analysis is an important branch of analytical chemistry which involves series of process for the identification, determination, quantitation and purification of drugs. It is mainly used for the separation of the components in a mixture and also for the determination of the structure of chemical compounds9 . Analytical method development for a newly manufactured product is so crucial because the chemical formulation does not available in any pharmacopoeias. The newly introduced analytical techniques were suggestive in order to determine the chemical quality standards of the medicine10 .

Analytical Techniques

For the qualitative and quantitative analysis of various drug products the following analytical techniques are readily available.

Titrimetric Techniques

Titrimetric analysis implies in the determination of concentration of a standard solution to react quantitatively with a measured volume of a solution of the substance to be determined11. It is also used for the determination of degradation products of the pharmaceuticals.

Spectroscopic Techniques

Spectroscopy is the study of absorption, emission, or scattering of electromagnetic radiation with matter12 .

Electrochemical Techniques

These techniques are concerned with the interaction between electricity and chemistry for the measurements of electrical quantities such as electric current, voltage or potential, charge and their relationship with the chemical parameters12 .

Kinetic method of Analysis

Chemical kinetics provides a major tool for the study of chemical mechanisms, and the detailed account of how reactions take place. The basic concept of the reaction kinetics is “law of mass action” and it states that the rate of a chemical reaction is proportional to the active masses of the reacting substances each raised to the power of its coefficient in the stoichiometric equation13

Electrophoresis Techniques

The principle of electrophoresis is very simple, namely that a charged ion or group migrates towards one of the electrodes when placed in an electric field and this technique operates on a principle which is different from the principle of chromatography and is alternative technique for separating the closely related charged substances, and after electrophoresis the substances are located as a number of separate discrete zones14 .

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Flow injection analysis and Sequential injection analysis In flow injection analysis (FIA) definite volume of the liquid sample is injected into a moving, non-segmented continuous carrier stream of a suitable liquid15. The injected sample forms a zone, which is then moves towards a detector that continuously records the changes in absorbance, electrode potential, or other physical parameter resulting from the passage of the sample through the flow cell15 . The flow injection technique is used as an automated solution handling system for went chemical analysis16 , sensors and electrodes17 , chromatography18, atomic absorption spectrometry19 etc. Sequential injection analysis (SIA) is the development of flow injection analysis and it provides a robust methodology than the traditional flow injection16 .

Hyphenated technique

Hyphenation involves the union of two or more instrumental methods in a single run with the help of proper interface20 . A significant preglen have been noticed in past two decades which has broadened their applications in the analysis of biomaterials, especially natural products21 . Hyphenated analytical methods provide more compatible information in less time leading to faster and accurate results. Here the combinations include separationseparation, separation-identification and identification-identification techniques22 .

Chromatography

Chromatography is unique in the history of analytical methodology and is probably the most powerful, versatile and widespread technique available in the modern chemical analysis. It plays a vital role in the advancement of chemistry, biology, medicine and the other similar fields of science. It can be used together with detection systems such as electrochemical, photometric and mass spectrometry due to its simplicity and ease of operation. Chromatography is extensively used for the separation and identification of complex chemical mixtures23 . Advanced methods of spectroscopy and chromatography are accelerating the method developments in the discovery of new drugs. The pharmaceutical industry still at demand for advanced products to improve quality of life24 .

Chromatography was discovered in 1903 by a Russian botanist Tswett during the separation and isolation of various plant pigments25 . Tswett called his newly discovered phenomena as “Chromatography” which is derived from Greek which means “color writing”26 . This chromatographic method was not recognized earlier until L.S.Palmer and C.Dhere independently published about the similar separation process 27 . Chromatography can be achieved by distributing the chemical components of a mixture through a moving mobile phase and a stationary phase in which the mobile phase (liquid or a gas) flows through the stationary phase (solid, or a liquid supported on a solid) and carries the components with it. The components which have stronger interactions with the stationary phase move slowly than the components having weaker interactions through the column. This difference in flowrates causes the separation of components in the mixture.

HPLC Method Development:

A method is a set of experimental conditions designed to create a good analysis of the given sample. HPLC method development and validation plays a prominent role in the discovery, development and manufacture of pharmaceuticals and agro chemical products. Understanding the physical and chemical characteristics of the drug helps us to select the most appropriate method development. By the method development, information such as molecular mass, structure and functionality, pKa values, UV spectra, solubility of the compound should be compiled. The requirement of removal of insoluble impurities by filtration, centrifugation, dilution or concentration, extraction (liquid or solid phase), derivatization for detection etc. should be checked28 . For pure compound, the sample solubility (soluble in water or organic solvent) should be identified, as it helps to select the best mobile phase and column in the method development28 .

In developing the HPLC method for the quantitative analysis, the following steps are to be followed; □

Literature Survey □

Selection of Mode □

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue IX September 2025

Selection of detection wavelength □

Selection of chromatographic techniques □

Selection of chromatographic conditions

Sample injection and Analysis □

Method Validation

METHOD VALIDATION

“Performing a thorough and suitable method validation may be tedious, but the consequences of not doing it are considerably effective, which results waste of time, money and the other resources.”

The suitability of a method for its intended purpose can be demonstrated by analytical method validation. Validation is a process by which a method is tested for reliability, stability, accuracy and preciseness. The testing process includes acceptance of raw materials, release of the drug substances/ products, testing for quality assurance, and establishment of the expiry duration. All methods should be validated and designed for ruggedness or robustness. Every Method should be reproducible when it is used by other analysts/ on other equivalent equipment/ on other days or locations. If the method used to generate the data for acceptance, release, stability, or pharmacokinetics is reliable then only the generated data is trustworthy29

Requirements prior to Method Validation □

Instruments / Equipment are to be validated and calibrated □

Reference Standards and Reagents are to be standardized

Trained and qualified analysts □

Availability of Test methods,

glassware's, Specifications etc. □

Availability of test material □

Approved protocols.

Parameters for the validation of HPLC method

The following parameters are considered for the validation of HPLC method29

□ Accuracy □

Detection and Quantitation Limit

□ Linearity □

Precision

Specificity □

Range □

Ruggedness

Robustness □

System Suitability

Sample Solution Stability

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