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A Review Article on Analytical Method on Vericiguat

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Abstract: *Vericiguat is a novel oral soluble guanylate cyclase (sGC) stimulator used in the treatment of chronic heart failure, aimed at reducing hospitalization rates and improving cardiac function by inducing vasodilation. The analysis of Vericiguat in pharmaceutical formulations and biological fluids requires robust and precise analytical methods. High-Performance Liquid Chromatography (HPLC) and UV-Visible Spectrophotometry are the primary techniques employed for this purpose due to their high specificity, sensitivity, and rapid analysis capabilities. This review discusses the development, validation, and application of these analytical methods for Vericiguat. Various HPLC methods have been developed, utilizing different columns, mobile phases, and detection wavelengths to ensure the accurate quantification of Vericiguat in bulk and tablet dosage forms. UV-Visible spectrophotometry has also been employed, offering a simpler and cost-effective alternative for routine analysis. The review consolidates the key parameters and findings of these methods, highlighting their advantages and suitability for the effective analysis of Vericiguat, thereby contributing to quality assurance in pharmaceutical development and therapeutic monitoring.*

Keywords: Vericiguat.

I. INTRODUCTION

Drug	Vericiguat
Synonym	Vericiguat, Véricіguat, Vericiguatum
Category	BCRP/ABCG2 Substrates, Cardiac Therapy, Guanylate Cyclase Stimulators
IUPAC name	Methyl N-[4,6-diamino-2-[5-fluoro-1-[(2-fluorophenyl) methyl] pyrazolo[3,4-b] pyridin-3-yl] pyrimidin-5-yl]carbamate
Molecular Weight	426.328 g /mol
Molecular Formula	$C_{19}H_{16}F_2N_8O_2$
Melting point	149- 158 ^{0} C
pKa	11.84
Log P	2.99

Table 1: Drug Profile[12]

Pharmacodynamics[13]

By directly stimulating the increased production of intracellular cyclic guanosine monophosphate (cGMP), vericiguat causes the relaxation of vascular smooth muscle and vasodilation. Vericiguat has a relatively long half-life (~30h) that

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allows for once-daily dosing. Animal reproduction studies have demonstrated the potential for embryo-fetal toxicity when vericiguat is administered to pregnant females - defects in major vessel and heart formation, as well as spontaneous abortions/resorptions, were observed when vericiguat was administered to pregnant rabbits during organogenesis. The possibility of pregnancy should be excluded prior to beginning therapy with vericiguat, and adequate contraception should be used throughout therapy and for one month following cessation of treatment.

Mechanism of action[14,15]

Heart failure (HF) involves, amongst other morphologic and physiologic changes, the impaired synthesis of nitric oxide (NO) and decreased activity of soluble guanylate cyclase (sGC). Functioning normally, NO binds to sGC and stimulates the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger involved in the maintenance of vascular tone, as well as cardiac contractility and remodeling. Defects in this pathway are thought to contribute to the myocardial and vascular dysfunction associated with heart failure and are therefore a desirable target in its treatment.

Vericiguat directly stimulates sGC by binding to a target site on its beta-subunit, bypassing the need for NO-mediated activation, and in doing so causes an increase in the production of intracellular cGMP that results in vascular smooth muscle relaxation and vasodilation.

Absorption[13]

Following the administration of 10mg of vericiguat by mouth once daily, the average steady-state Cmax and AUC in patients with heart failure is 350 mcg/L and 6,680 mcg•h/L, respectively, with a Tmax of 1 hour. The absolute bioavailability of orally-administered vericiguat is approximately 93% when taken with food - co-administration with meals has been shown to reduce pharmacokinetic variability, increase Tmax to roughly 4 hours, and increase Cmax and AUC by 41% and 44%, respectively.

Analytical techniques in pharmaceutical analysis:

We are discussing analytical techniques used to estimate the concentration of Vericiguat in various contexts. UV/Visible Spectrophotometry and High-Performance Liquid Chromatography (HPLC) are some of the techniques commonly employed for this purpose. These methods are crucial for ensuring the accurate measurement of VER, whether it's in standalone form or in combination with other soluble guanylate cyclase (sGC) stimulators, across different dosage forms.[16]

UV-Visible spectrophotometry:

Spectroscopy, as a scientific discipline, traces its origins back to Isaac Newton's groundbreaking experiments with prisms, which led to the understanding of visible light and the study of color, initially known as optics. Over time, thanks to the work of scientists like James Clerk Maxwell, the scope of spectroscopy expanded to encompass the entire electromagnetic spectrum. At its core, spectroscopy deals with the interaction between electromagnetic radiation and matter. One of the fundamental outcomes of this interaction is the absorption or emission of energy by matter in discrete units known as quanta. These processes occur across the electromagnetic spectrum, from the gamma region, involving phenomena like nuclear resonance absorption or the Mossbauer effect, to the radio region, where nuclear magnetic resonance occurs. Experimental measurement of radiation frequency provides insight into the energy changes involved, allowing for conclusions to be drawn about the discrete energy levels of matter. The practice of spectroscopy involves both the experimental measurement of radiation frequency, whether emitted or absorbed, and the deduction of energy levels from these measurements. This comprehensive approach forms the foundation of spectroscopic analysis.[17]

High-performance Liquid Chromatography:

High Performance Liquid Chromatography (HPLC) has emerged as one of the most potent tools in analytical chemistry, offering the capability to separate, identify, and quantify compounds present in liquid-dissolvable samples. Widely utilized for both quantitative and qualitative analyses of drug products, HPLC operates on the principle of

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injecting a sample solution into a column packed with porous material (stationary phase), while a liquid (mobile phase) is propelled through the column under high pressure. The separation of the sample relies on varying rates of migration through the column, which stem from differing partitioning of the sample between the stationary and mobile phases. HPLC boasts several advantages: Simultaneous Analysis, High Resolution, High Sensitivity, Good Repeatability, Small Sample Size, Moderate Analysis Conditions, Ease of Fractionating and Purifying Samples. Classification of HPLC can be based on various criteria: Scale of operation: Preparative HPLC and Analytical HPLC, Principle of separation: Affinity Chromatography, Adsorption Chromatography, Size Exclusion Chromatography, Ion Exchange Chromatography, Chiral Phase Chromatography, Elution technique: Gradient Separation and Isocratic Separation, Modes of operation: Normal Phase Chromatography and Reverse Phase Chromatography.[18]

Summary of Analytical methods used for Vericiguat:

Table 2: Analytical methods development and validation for Vericiguat in single dosage formed by UV-visible spectroscopy and RP-HPLC

Sr. No.	*Drug*	*Method*	*Description*	*References*
1	*Vericiguat*	*Theoretically guided analytical method development and validation for the estimation of Vericiguat in a Methanol by UV spectrophotometer*	*Wavelength: Vericiguat: 258 nm Solvent: Methanol Linearity: 5-25 µg/mL*	*19*
2	*Vericiguat*	*Development and Validation of a Simple and Sensitive RP-HPLC Method for Determination of Vericiguat in Bulk and Tablet dosage form.*	*RP-HPLC Wavelength: 258 nm Column: Phenomenex Luna C18 column (150 mm × 4.6 mm id; 5 µm particle size) Flow rate: 1ml/min Mobile phase: Acetonitrile: Methanol: Water in 0.1% Triethylamine (50:10:40, v/v/v) Linearity: 20 to 100 µg/ml Retention time: 4.063 min Correlation coefficient: 0.9999*	*20*
3	*Vericiguat*	*Development and Validation of a Simple and Sensitive RP-HPLC Method for Determination of Vericiguat in Bulk and Pharmaceutical dosage form.*	*RP-HPLC Wavelength: 225 nm Column: Symmetry ODS C18 (4.6×250mm, 5µm) Flow rate: 1ml/min Mobile phase: Methanol: Phosphate Buffer (55:45) v/v Linearity: 6 to 14 µg/ml Retention time: 2.252 min.*	*21*
4	*Vericiguat*	*Development and Validation of a Simple and Sensitive HPLC Method for Determination of Vericiguat in Tablet dosage form.*	*HPLC Wavelength: 307 nm Column: Zorbax SB C18 (250mm*4.6mm), 5µm Flow rate: 1ml/min Mobile phase: Phosphate buffer (pH 4.3 adjusted with0.1% OPA): Acetonitrile in ratio of 40:60%v/v Linearity: 150-50 µg/ml*	*1*

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II. CONCLUSION

The analytical evaluation of Vericiguat is critical in ensuring its efficacy and safety in the treatment of chronic heart failure. The robust analytical techniques discussed in this review, specifically High-Performance Liquid Chromatography (HPLC) and UV-Visible Spectrophotometry, demonstrate high specificity, sensitivity, and efficiency in quantifying Vericiguat in pharmaceutical formulations and biological samples.

HPLC, with its various methodologies including different columns, mobile phases, and detection wavelengths, provides precise and accurate quantification of Vericiguat. The high resolution and sensitivity of HPLC make it an indispensable tool in the pharmaceutical analysis of Vericiguat, allowing for effective separation and quantification even in complex matrices. The reviewed HPLC methods exhibit excellent linearity, retention times, and correlation coefficients, underscoring their reliability and applicability in routine quality control and therapeutic monitoring.

UV-Visible Spectrophotometry, while simpler and more cost-effective, also offers reliable analysis for Vericiguat, particularly for preliminary and routine assessments. The method development and validation processes highlighted in this review ensure that these techniques meet stringent regulatory requirements and provide consistent results.

In conclusion, both HPLC and UV-Visible Spectrophotometry are essential analytical methods for the comprehensive analysis of Vericiguat. Their validated protocols ensure accurate and reproducible measurements, contributing significantly to the quality assurance of Vericiguat in pharmaceutical development and clinical applications. These methods support the effective monitoring of Vericiguat, facilitating its therapeutic efficacy and safety in managing chronic heart failure.

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