



Original Article

A Comprehensive Review of Analytical Methods for the Estimation and Quantification of Ranolazine in Pharmaceutical and Biological Samples

Corresponding Author:

Riyaz Ahmad

Bhavdiya Institute of
Pharmaceutical Sciences and
Research, Ayodhya, UP

Email-

khansoban93@gmail.com

Riyaz Ahmad¹, Abhay Pandey¹, Soban Khan^{1*}

Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, UP

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ABSTRACT

Ranolazine is a clinically important anti-anginal drug widely prescribed for the management of chronic stable angina. The increasing therapeutic use of Ranolazine has created a growing need for reliable, accurate, and validated analytical methods for its quantitative determination in pharmaceutical formulations and biological samples. Various analytical techniques have been developed and employed for the estimation of Ranolazine, including UV-visible spectrophotometry, reverse-phase high-performance liquid chromatography (RP-HPLC), liquid chromatography-mass spectrometry (LC-MS), and stability-indicating analytical methods. The estimation of Ranolazine, with emphasis on method development, validation parameters, and pharmaceutical applications. The principles, advantages, limitations, and analytical performance of UV spectrophotometric and chromatographic methods are critically discussed. Attention is given to RP-HPLC methods because of their high sensitivity, specificity, precision, and suitability for stability studies and impurity profiling.

Keywords: Ranolazine, UV-visible spectrophotometry, Reverse-Phase High-Performance Liquid Chromatography (RP-HPLC), Liquid Chromatography-Mass Spectrometry (LC-MS).

INTRODUCTION

Ranolazine is a novel anti-anginal drug widely used in the management of chronic stable angina (Chaitman et al., 2004). Unlike conventional anti-anginal agents that primarily affect heart rate or blood pressure, Ranolazine acts by inhibiting the late sodium current in cardiac cells, thereby improving myocardial oxygen efficiency and reducing ischemic symptoms (Ferrari & Ford, 2008; Fihn et al., 2012). Due to its clinical importance and widespread use, accurate estimation of Ranolazine in pharmaceutical formulations and biological samples is essential for ensuring product quality, safety, efficacy,

and regulatory compliance (Ermer & Miller, 2005; Ravisankar et al., 2015). Analytical methods play a critical role throughout the pharmaceutical product lifecycle, from drug development and formulation studies to quality control and stability assessment (Skoog, Holler, & Crouch, 2018; Ermer & Miller, 2005). Regulatory authorities require analytical methods to be reliable, precise, accurate, and validated according to established guidelines (EURACHEM, 2014; Ermer & Miller, 2005). Consequently, considerable research has been directed toward developing and validating analytical procedures for the quantitative determination of Ranolazine in pharmaceutical dosage forms and biological matrices (Kamble et al., 2018; Saxena & Gupta, 2016). Ranolazine is necessary for the development of sensitive bioanalytical methods used in therapeutic drug monitoring and bioavailability assessment (Jerling, 2006).

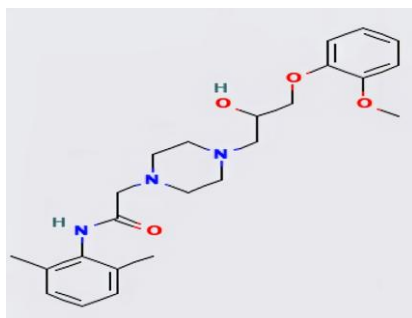


Fig 1.1: Structure Of Ranolazine

Physicochemical and Pharmacological Profile of Ranolazine

Ranolazine is a therapeutic agent approved for the management of chronic stable angina (Chaitman et al., 2004). Its unique mechanism of action differentiates it from traditional anti-anginal therapies. The drug improves myocardial relaxation and reduces ischemia by selectively inhibiting the late inward sodium current in cardiac myocytes (Ferrari & Ford, 2008). The therapeutic effectiveness of Ranolazine has led to increased demand for reliable analytical methods capable of monitoring drug content in pharmaceutical formulations (Ferrari & Ford, 2008). Knowledge of its physicochemical properties, including solubility characteristics, stability profile, and degradation behavior, is essential during analytical method development (Drug Bank, 2024; Dong, 2019). These properties influence the selection of solvents, chromatographic conditions, detection wavelengths, and sample preparation procedures (Dong, 2006; Dong, 2019). Understanding the pharmacokinetic and metabolic profile of Ranolazine is equally important for developing bioanalytical methods used in pharmacokinetic, bioavailability, and therapeutic monitoring studies (Di Piro et al., 2014; Kamble et al., 2018).

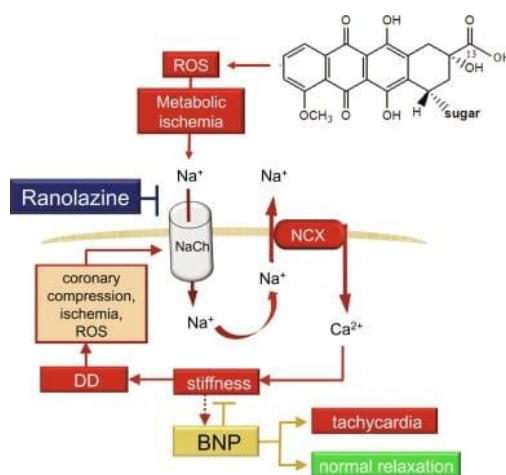


Fig 1.2: Pharmacological effect Of Ranolazine on Heart

Need for Analytical Method Development

Analytical method development is a fundamental requirement in pharmaceutical sciences because it ensures that medicinal products consistently meet predefined quality standards (Skoog et al., 2018; Ermer & Miller, 2005). Accurate determination of drug concentration is necessary to guarantee dosage accuracy, patient safety, and therapeutic effectiveness (Ermer & Miller, 2005; Ravisankar et al., 2015). For Ranolazine, analytical methods are required for assay determination of pharmaceutical formulations, quality control testing, stability studies, dissolution studies, impurity profiling, pharmacokinetic investigations, and bioavailability and bioequivalence studies (Dong, 2019; Dong & Hussain, 2010). The increasing emphasis on regulatory compliance has further highlighted the importance of validated analytical procedures

capable of generating reproducible and reliable results (Dong & Hussain, 2010; EURACHEM, 2014; Ermer & Miller, 2005).

UV Spectrophotometric Methods for Ranolazine Estimation

UV-visible spectrophotometry is one of the simplest and most economical analytical techniques used in pharmaceutical analysis (Ewing, 1985; Day & Underwood, 2007). The method is based on the absorption of ultraviolet radiation by the analyte at a specific wavelength (Ewing, 1985). Several researchers have reported UV spectrophotometric methods for the estimation of Ranolazine in pharmaceutical dosage forms (Tripathi & Saxena, 2014; Rao et al.). These methods generally involve dissolving the drug in a suitable solvent and measuring absorbance at the wavelength corresponding to maximum absorption (Tripathi & Saxena, 2014). Such procedures are attractive because of their simplicity, rapidity, and low operational cost (Tripathi & Saxena, 2014). Despite these benefits, UV methods have certain limitations. They may lack specificity in the presence of impurities, degradation products, or formulation excipients (Shukla & Verma, 2017; Deshmukh & Patil, 2018). UV spectroscopy is suitable for routine assay determination, it may not always be appropriate for stability-indicating applications (Deshmukh & Patil, 2018). UV spectrophotometric methods continue to be preferred in many laboratories because they require minimal sample preparation and relatively inexpensive instrumentation (Patel & Raj, 2015). Visible and chromogenic spectrophotometric approaches have been explored to improve the selectivity of Ranolazine estimation, particularly in complex sample matrices (Bhavya Sri et al., 2026). Spectrophotometric techniques are especially useful during preliminary formulation studies where rapid analysis and cost-effectiveness are important considerations (Pravalika et al., 2025).

The major advantages of UV spectrophotometric methods include:

- Simple instrumentation
- Rapid analysis
- Cost-effectiveness
- Minimal sample preparation
- Suitability for routine quality control

RP-HPLC Methods for Ranolazine Estimation

Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) is among the most widely used analytical techniques for pharmaceutical drug analysis (Dong, 2006; Dong, 2019). The technique offers excellent sensitivity, specificity, precision, and reproducibility (Dong, 2006; Ermer & Miller, 2005). Numerous studies have focused on the development of RP-HPLC methods for Ranolazine estimation (Arora & Bhatt, 2015; Sharma et al.). During method development, chromatographic parameters such as column type, mobile phase composition, pH, flow rate, and detection wavelength are systematically optimized to achieve efficient separation and accurate quantification (Arora & Bhatt, 2015; Dong, 2006). RP-HPLC methods provide high analytical sensitivity, excellent selectivity, superior precision, better reproducibility, and the capability to separate degradation products and impurities (Saxena & Gupta, 2016; Sharma et al.). Furthermore, RP-HPLC methods have gained broad regulatory acceptance in pharmaceutical analysis (Dong & Hussain, 2010; Ermer & Miller, 2005). Compared with UV spectrophotometric techniques, RP-HPLC offers significantly improved analytical performance and is therefore considered a preferred method for pharmaceutical quality control and stability studies (Shukla & Verma, 2017; Deshmukh & Patil, 2018). RP-HPLC remains the most frequently reported analytical technique for Ranolazine estimation because it offers excellent resolution, accuracy, and reproducibility for both bulk drug and pharmaceutical formulations (Patel & Raj, 2015).

The widespread acceptance of RP-HPLC in pharmaceutical industries is attributed to its ability to separate active pharmaceutical ingredients from impurities and degradation products within a single analytical run (Pravalika et al., 2025). Studies have demonstrated that optimized RP-HPLC methods can achieve excellent linearity, low detection limits, and high recovery values, making them suitable for routine quality control applications (Bhavya Sri et al., 2026).

Stability-Indicating Analytical Methods

Stability testing is a critical component of pharmaceutical development because it provides information regarding the behavior of a drug under various environmental conditions (EURACHEM, 2014). Stability-indicating analytical methods are specifically designed to distinguish the active pharmaceutical ingredient from its degradation products (Saxena & Gupta, 2016). Researchers have developed and validated several stability-indicating methods for Ranolazine that demonstrate high specificity and resolution (Saxena & Gupta, 2016). Forced degradation studies generally involve exposing Ranolazine to acidic, alkaline, oxidative, thermal, and photolytic stress conditions to evaluate the stability profile of the drug (Deshmukh & Patil, 2018). Stability-indicating analytical methods play a vital role in evaluating the degradation behavior of Ranolazine under stress conditions such as acid, alkali, oxidation, heat, and light exposure (Patel & Raj, 2015). Forced degradation studies contribute to the identification of potential degradation pathways and assist in establishing appropriate storage conditions for pharmaceutical products (Bawane & Bhavsar, 2026). Chromatographic techniques are

generally preferred for stability studies because they provide effective separation between the parent drug and degradation products (Gowsami et al., 2026). These studies help establish degradation pathways and confirm the ability of the analytical method to accurately quantify the drug in the presence of degradation products (Saxena & Gupta, 2016). Stability-indicating RP-HPLC methods have proven particularly effective because of their superior separation capability and ability to resolve degradation impurities from the active drug substance (Deshmukh & Patil, 2018).

Forced degradation studies generally involve exposing Ranolazine to:

- Acidic conditions
- Alkaline conditions
- Oxidative conditions
- Thermal stress
- Photolytic stress

LC-MS and Advanced Analytical Techniques

Liquid Chromatography–Mass Spectrometry (LC–MS) represents one of the most advanced analytical tools available for pharmaceutical analysis (Dong, 2019). The technique combines the separation efficiency of liquid chromatography with the sensitivity and selectivity of mass spectrometry (Dong, 2006). Researchers have reported LC–MS methods for the determination of Ranolazine in biological samples (Kamble et al., 2018). These methods have been successfully employed in pharmacokinetic evaluations, bioavailability studies, and therapeutic monitoring applications (Di Piro et al., 2014). The major advantages of LC–MS include extremely high sensitivity, excellent selectivity, detection of trace-level analytes, structural identification capability, and suitability for biological matrices (Kamble et al., 2018). Although LC–MS instrumentation is expensive and requires specialized expertise, it remains the preferred choice for advanced bioanalytical investigations (Dong, 2019).

Analytical Method Validation

Analytical method validation is a documented process that demonstrates the suitability of an analytical procedure for its intended purpose (Ermer & Miller, 2005). Regulatory agencies recommend that pharmaceutical analytical methods be validated according to internationally accepted guidelines (EURACHEM, 2014; Dong & Hussain, 2010). Successful validation ensures that the developed method consistently produces reliable and reproducible results under defined operating conditions (Ermer & Miller, 2005; EURACHEM, 2014). Analytical method validation is a systematic and documented process used to demonstrate that an analytical procedure is suitable for its intended purpose. In pharmaceutical analysis, validation provides scientific evidence that a method consistently generates accurate, precise, and reliable results when applied to the analysis of drug substances and pharmaceutical products. Regulatory authorities worldwide require analytical methods to be validated before their use in routine quality control, stability testing, and regulatory submissions. The primary objective of method validation is to ensure that analytical data generated during pharmaceutical development and manufacturing are scientifically sound and trustworthy (Ermer & Miller, 2005; ICH, 2024). The importance of analytical method validation has increased significantly with the growing emphasis on pharmaceutical quality assurance and regulatory compliance. Modern pharmaceutical products must meet stringent quality standards throughout their lifecycle, from drug development to commercialization. Consequently, analytical procedures used for identification, assay determination, impurity profiling, dissolution testing, and stability studies must demonstrate adequate performance characteristics before implementation in routine laboratory operations. Validation ensures that analytical methods remain fit for purpose and capable of generating reproducible results under defined operating conditions (Ermer & Miller, 2005; EURACHEM, 2014). International regulatory agencies such as the International Council for Harmonization (ICH), the United States Food and Drug Administration (FDA), and the European Medicines Agency (EMA) have established guidelines that describe the principles and requirements of analytical method validation. The ICH Q2 guideline serves as the globally accepted framework for validating analytical procedures and outlines the performance characteristics that should be evaluated during validation studies. These characteristics include specificity, accuracy, precision, linearity, range, detection limit, quantitation limit, robustness, and system suitability. The selection of validation parameters depends on the intended application of the analytical procedure (ICH, 2024; FDA, 2024).

For Ranolazine analysis, validation studies commonly evaluate the following parameters:

- Specificity
- Accuracy
- Precision
- Linearity
- Range
- Robustness
- Ruggedness
- Limit of Detection (LOD)

- Limit of Quantification (LOQ)
- System suitability

Specificity

Specificity is the ability of an analytical method to accurately measure the analyte in the presence of impurities, degradation products, excipients, and other potential interfering substances. It is considered one of the most critical validation parameters because it directly affects the reliability of analytical results. A specific method can distinguish the analyte from all other components present in the sample matrix. In pharmaceutical analysis, specificity is particularly important for stability-indicating methods where degradation products must be separated and quantified independently of the active pharmaceutical ingredient (ICH, 2024).

Accuracy

Accuracy refers to the closeness of agreement between the experimentally determined value and the true or accepted reference value. It indicates the degree to which an analytical method measures the actual concentration of an analyte without systematic error. Accuracy is typically assessed through recovery studies in which known quantities of the analyte are added to the sample matrix and subsequently measured. Recovery values close to 100% indicate excellent method of accuracy. Accurate analytical methods are essential for ensuring dosage uniformity and maintaining pharmaceutical product quality (FDA, 2024; Ermer & Miller, 2005).

Precision

Precision describes the degree of agreement among individual test results obtained from repeated measurements of the same homogeneous sample under prescribed conditions. Precision is generally evaluated at three levels: repeatability, intermediate precision, and reproducibility. Repeatability assesses variation under identical conditions over a short period, whereas intermediate precision evaluates variability within the same laboratory under different conditions such as different analysts, instruments, or days. Reproducibility examines variation between laboratories. Low relative standard deviation (%RSD) values indicate good method precision and analytical consistency (ICH, 2024).

Linearity and Range

Linearity is the ability of an analytical method to generate test results that are directly proportional to analyte concentration within a specified range. It is typically evaluated by analyzing standard solutions at different concentration levels and constructing calibration curves. A strong correlation coefficient indicates a linear relationship between concentration and analytical response. The analytical range represents the interval between the upper and lower concentrations of analytes that can be determined with acceptable accuracy, precision, and linearity. Establishing linearity and range is particularly important for quantitative pharmaceutical assays (ICH, 2024; EURACHEM, 2014).

Limit of Detection and Limit of Quantitation

The Limit of Detection (LOD) is defined as the lowest amount of analytes that can be detected but not necessarily quantified accurately. In contrast, the Limit of Quantitation (LOQ) represents the lowest concentration that can be quantified with acceptable accuracy and precision. These parameters are especially important for impurity analysis and trace-level determinations. Sensitive analytical methods with low LOD and LOQ values are preferred for detecting minute quantities of degradation products and related substances (ICH, 2024).

Robustness

Robustness is the capacity of an analytical method to remain unaffected by small but deliberate variations in method parameters. During robustness studies, factors such as flow rate, mobile phase composition, pH, column temperature, and detection wavelength may be slightly altered to determine their effect on analytical performance. A robust analytical method consistently produces reliable results despite minor experimental variations and is therefore more suitable for routine quality control applications (EURACHEM, 2014; ICH, 2024).

System Suitability Testing

System suitability testing is an integral component of validated analytical procedures. It is performed before routine sample analysis to verify that the analytical system is functioning properly and capable of producing acceptable results. Common system suitability parameters include retention time, theoretical plates, tailing factor, resolution, and repeatability of injections. These tests ensure that chromatographic systems maintain consistent performance throughout the analytical process (ICH, 2024).

Comparative Evaluation of Analytical Methods

Table.1; Different analytical methods possess unique strengths and limitations.

Parameter	UV Spectrophotometry	RP-HPLC	LC-MS
Cost	Low	Moderate	High
Sensitivity	Moderate	High	Very High
Specificity	Moderate	High	Excellent
Precision	Good	Excellent	Excellent
Analysis Time	Short	Moderate	Moderate
Stability Studies	Limited	Excellent	Excellent
Routine QC	Highly Suitable	Highly Suitable	Limited
Bioanalysis	Not Suitable	Limited	Excellent

Chromatographic methods have been found superior for impurity profiling and stability evaluation, whereas UV methods remain attractive for routine quality control because of their simplicity and affordability (Shukla & Verma, 2017; Deshmukh & Patil, 2018).

Regulatory and Quality Assurance Considerations

Validated analytical methods are essential components of pharmaceutical quality assurance systems (Skoog et al., 2018). Regulatory agencies expect analytical procedures to be scientifically sound, reproducible, and appropriately documented (Dong & Hussain, 2010). Studies involving pharmaceutical analytical methods have emphasized the importance of regulatory compliance and analytical reproducibility in ensuring consistent product quality (Ravisankar et al., 2015). Method validation not only satisfies regulatory requirements but also enhances confidence in analytical data generated during routine quality control, stability testing, and product release activities (Dong & Hussain, 2010; Ravisankar et al., 2015). Future research is expected to focus on greener analytical methodologies, advanced bioanalytical techniques, and highly sensitive methods suitable for complex pharmaceutical and biological matrices (Yadav et al., 2025).

CONCLUSION

The development of reliable analytical methods for Ranolazine has attracted significant attention due to the drug's growing therapeutic importance. Among the available techniques, UV spectrophotometry offers a simple and economical approach for routine quality control, while RP-HPLC provides superior accuracy, precision, selectivity, and stability-indicating capability. LC-MS remains the method of choice for highly sensitive bioanalytical applications. Validated analytical methods are indispensable for ensuring the quality, safety, efficacy, and regulatory compliance of Ranolazine pharmaceutical products.

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