STABILITY INDICATING METHOD FOR SIMULTANEOUS ESTIMATION OF MECLIZINE AND CYCLIZINE ON HPLC

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Abstract

Stability-indicating analytical methods play a critical role in pharmaceutical quality assurance by enabling accurate quantification of drug substances in the presence of degradation products. Meclizine and Cyclizine are antihistaminic agents widely prescribed for the management of nausea, vertigo, and motion sickness, and their analytical determination in combined or co-administered formulations is essential for ensuring therapeutic efficacy and product stability. This review provides a comprehensive overview of reported stability-indicating chromatographic and spectrophotometric methods developed for the simultaneous estimation of Meclizine hydrochloride and Cyclizine hydrochloride. The article summarizes analytical advancements in RP-HPLC, HPTLC, UPLC, UV-spectrophotometry, derivative spectrophotometry, and chemometric approaches, focusing on method optimization, chromatographic conditions, detection wavelengths, and separation efficiency. Special emphasis is placed on forced degradation studies under stress conditions such as acid/base hydrolysis, oxidation, photolysis, and thermal exposure, demonstrating the capability of these methods to discriminate active drugs from their degradants in compliance with ICH Q1A(R2) and Q2(R1) guidelines. Challenges associated with co-elution, matrix interference, and simultaneous drug quantification are discussed along with future prospects including green analytical chemistry and hyphenated analytical techniques. This review highlights that validated stability-indicating analytical methods represent an indispensable tool for quality control laboratories and regulatory submissions for pharmaceutical products containing Meclizine and Cyclizine

Keywords-Meclizine, Cyclizine, Stability-indicating method, RP-HPLC, Simultaneous estimation, Forced degradation, ICH guidelines, Analytical validation.

1.0. INTRODUCTION

Quality, safety, and efficacy are paramount considerations for any sector, with particular significance in the pharmaceutical industry. Ensuring quality products is crucial for the effective treatment of various diseases. Quality management ensures that products are produced in accordance with quality standards, and meet the requirements specified by the authorities. Pharmaceutical manufacturers adhere to regulatory guidelines when seeking Food and Drug Administration (FDA) approval to their drugs in United States of America (USA).[1] Unwanted entities present in drug products and drug substance must be identified and reported since they affect the product quality and a safety concern. In this regard, it is necessary to develop new analytical methods to identify & report unwanted entities in drug substances and products. This section was divided into six major topics as follows.[1]

- Definitions
- Classification of Impurities
- Pharmaceutical analysis
- Analytical method validation

- Regulatory Guidelines

1.1 Definitions

Drug products are medicinal forms that contain active drug substances associated with inactive substances. Drug substances are the active pharmaceutical ingredients that are biologically active ingredients of the drug product and produce a deliberate effect.

Any component of a drug substance other than the active ingredient is an impurity.

1.2 Classification of Impurities[1]

According to the International Council for Harmonisation (ICH) Q3 guidelines, impurities are classified into three categories.

A. Inorganic impurities.

B. Residual solvents.

C. Organic impurities.

Inorganic impurities are reagents, catalysts, inorganic salts, ligands, catalysts, and heavy metals. They are known & identified and formed during the manufacturing process. Liquids used in manufacturing processes called residual solvents. They are organic or inorganic liquids. reagents, catalysts, ligands, by-products, starting materials, intermediates, and degradation products are examples of organic impurities. During manufacturing and storage of drug products and drug substances can produce these impurities and they can be identified and unidentified (1- 3).[1]

1.3 Pharmaceutical analysis

In all stages of the product development and manufacturing process, pharmaceutical products are analyzed to determine their physical and chemical properties and impurity profile. To determine whether drug products and drug substances are safe, effective, and stable. There are several types of analytical techniques available for pharmaceutical analysis.

A. Titrimetric techniques

B. Spectroscopic techniques

a. Fluorimetry and phosphorimetry

b. Nuclear magnetic resonance spectroscopy

c. Near-infrared spectroscopy

d. Spectrophotometry

C. Chromatographic techniques

a. Ultra-performance liquid chromatography

b. High-performance liquid chromatography

c. Gas chromatography

d. Thin-layer chromatography (TLC)

e. High-performance thin-layer chromatography (HPTLC)

D. Hyphenated techniques

a. LC-MS

b. GC-MS

c. ICP-MS

d. LC-NMR

1.3.1 Chromatographic techniques

The separation of a mixture by distributing it between two phases is called chromatography. The separation of a mixture by the difference in affinity toward the stationary phase and mobile phase.

Molecules with a greate affinity for the stationary phase tend to spend a longer time within it and elute late, while those with affinity toward mobile-phase elute first.[2]

A. Based on the principle, chromatography is classified into four types:

a) Adsorption chromatography

b) Partition chromatography

c) Ion exchange chromatography

d) Size exclusion or gel permeation chromatography

B. On the basis of the utilization of stationary phase and mobile phase:

a) Liquid chromatography

b) Gas chromatography

High-Performance Liquid Chromatography (HPLC)

High-performance liquid chromatography is the most dependable and extensively employed technique in the pharmaceutical sector. It is used to assess the impurity profile, enatiomeric purity, assay of the compound and cheking the stability of the drug product and drug substances. Based on the polarity, it is classified into two types :[3]

a) Reverse-phase liquid chromatography: stationary phase exhibits polarity, while the mobile phase is non-polar in nature.

b) Normal phase liquid chromatography: stationary phase exhibits non-polar, while the mobile phase is polar in nature.

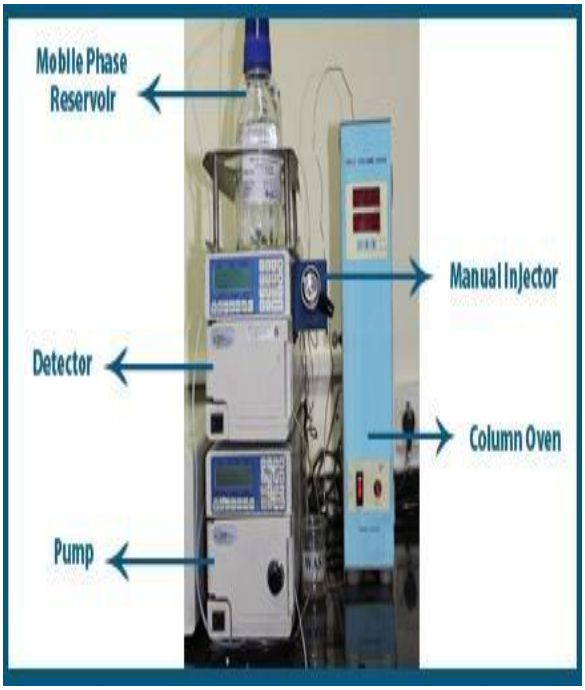

Fig 1.1: HPLC instrument[3]

High-Performance Liquid Chromatography (HPLC) is a widely used analytical technique for separating, identifying, and quantifying components in a mixture. The principle behind HPLC is based on the differential distribution of compounds between a stationary phase (usually packed inside a column) and a mobile phase (liquid solvent). Here's a more detailed breakdown:[3]

A. Stationary Phase :

The stationary phase in HPLC is usually a column packed with fine particles of silica or polymer materials. These particles are typically chemically modified to interact with different components of the sample. The most common stationary phase is non-polar, but polar and other specialized phases are also available.[3]

B. obile Phase:

The mobile phase is a liquid solvent (or mixture of solvents) that moves through the column. It carries the sample through the stationary phase. The choice of

solvent or solvent mixture (aqueous, organic solvents, etc.) depends on the nature of the sample being analyzed.[3]

C. Separation Principle:

When a sample is injected into the HPLC system, it is carried by the mobile phase through the column. Components of the sample interact with the stationary phase to different extents. Some compounds interact more strongly and move slowly (they are retained longer in the column), while others interact weakly and move more quickly. This differential interaction causes the components to separate over time as they travel through the column. The result is that different components of the mixture exit the column at different times.[4]

D. Detection:

As the components exit the column, they are detected by various detectors (such as UV- Vis, fluorescence, or refractive index detectors). The detector records a signal (usually intensity vs. time) which is then plotted as a chromatogram. Each peak in the chromatogram represents a compound, and the area under the peak is proportional to its concentration.[4]

E. Retention Time:

The time it takes for a particular compound to pass through the column and reach the detector is called its retention time. Retention time is a key parameter in identifying compounds, as each compound typically has a unique retention time under set conditions.[4]

F. Factors Affecting Separation:[4]

- Flow Rate: The speed at which the mobile phase moves through the column affects the resolution and separation efficiency.
- Column Temperature: Temperature can influence the interactions between the sample and the stationary phase.
- Mobile Phase Composition: The ratio of solvents used in the mobile phase can be adjusted to optimize separation.
- Particle Size of the Stationary Phase: Smaller particles provide better separation, but they also cause higher backpressure.

1.2 HPLC Method Development

Developing an HPLC method is a structured and systematic process that requires a detailed understanding of the chemical nature of the analytes, the desired separation, and the final purpose of the analysis. Method development typically involves optimizing various parameters, such as the mobile phase, stationary phase, flow rate, temperature, detection wavelength, and more.[5]

A. Introduction to HPLC Method Development

High-Performance Liquid Chromatography (HPLC) is one of the most widely used techniques for the qualitative and quantitative analysis of complex mixtures. In method development, the goal is to design and optimize a chromatographic procedure that ensures the effective separation of the components in a sample.[5]

Key Objectives of Method Development:

- **Separation:** Achieving good resolution between different components.
- **Sensitivity:** Ensuring low detection limits for analytes.
- **Reproducibility**: Making sure that the method produces consistent results across different runs.
- **Specificity**: The method should be able to accurately detect and identify the target analytes without interference.

B. General Steps in HPLC Method Development

The development of an HPLC method involves several essential steps, as outlined below:

a. Define the Goal of Analysis

Before beginning method development, it's crucial to understand the requirements of the analysis. Some questions to consider include:
What is the purpose of the analysis (e.g., quality control, research)?

What type of sample will be analyzed (e.g., pharmaceutical, environmental)? What is the target analyte, and how complex is the sample matrix?

Selection of Detection Technique

The choice of detector depends on the nature of the analytes and the sensitivity requirements. Common detectors include: UV-Vis Detector: Suitable for compounds that absorb UV or visible light. Fluorescence Detector: For compounds that exhibit fluorescence. Refractive Index (RI) Detector: Useful for non-UV-absorbing compounds like sugars or polymers. Mass Spectrometry (MS): High specificity and sensitivity, often coupled with HPLC for complex sample analysis.[5]

b. Preliminary Selection of Column and Stationary Phase

The choice of stationary phase plays a key role in separation. Common column types include:

- Reverse-Phase Columns (e.g., C18): Widely used for organic compounds.
- Normal-Phase Columns: Used when polar compounds need to be separated.
- Ion-Exchange Columns: Used for charged species.
- Size-Exclusion Columns: Suitable for separating large molecules like proteins or polymers.

c. Choice of Mobile Phase

The mobile phase is a critical factor in method development. It's selected based on the polarity of the analytes. Inreverse-phase chromatography, the mobile phase typically consists of water (often with an acid or base) and organic solvents like methanol or acetonitrile. In normal- phase chromatography, solvents like hexane or chloroform are often used.[5]

d. Determining Initial Conditions

Start with standard conditions, and then modify the parameters to optimize the method:

- Flow Rate: Typically, between 0.5 and 2 mL/min, depending on the column dimensions.
- Column Temperature: Temperature control can help improve separation efficiency.

e. Injection Volume: The sample injection volume should be optimized based on sample concentration and column capacity.[5]

f. Method Development for Different Types of Samples

Different samples require different method development approaches. Here, we'll cover the development for some common sample types. Pharmaceutical Samples Pharmaceutical applications often require the separation of active pharmaceutical ingredients (APIs) from

excipients.[5]

The method must ensure:

- Selectivity: Ability to separate APIs from other substances like excipients, preservatives, and degradation products.
- Linearity: For accurate quantification over a range of concentrations.
- Robustness: Tolerance to small variations in method parameters like temperature or mobile phase composition.[5]

g. Optimization of Chromatographic Conditions

Once initial conditions have been set, the next step is optimization, which involves adjusting various parameters to improve separation and enhance peak resolution.

Mobile Phase Optimization

The composition and pH of the mobile phase can significantly influence separation:

- pH Adjustment: pH can alter the ionization state of analytes, influencing their retention on the column.
- Solvent Strength: Changing the ratio of solvents (e.g., water:acetonitrile) can affect retention times and separation.

h. Flow Rate and Column Temperature

- Flow Rate: A lower flow rate increases separation time but improves resolution. A faster flow rate decreases analysis time but can reduce separation quality.
- Temperature: Raising the column temperature can enhance the separation by increasing the diffusion rate of analytes.[6]

i. Gradient vs. Isocratic Elution

- Isocratic Elution: Involves using a constant composition of the mobile phase throughout the analysis.
- Gradient Elution: Involves changing the mobile phase composition during the analysis to improve the separation of compounds with a wide range of polarities.

j. System Suitability Testing (SST)

System Suitability Testing (SST) is critical in method development to ensure that the HPLC system is operating as expected and the developed method is reliable. Parameters like resolution, peak asymmetry, theoretical plates, and tailing factor are monitored.[6]

- Resolution is defined as the degree to which two analytes are separated. A resolution greater than 1.5 is generally considered acceptable for routine analysis.
- Peak asymmetry is undesirable as it can indicate poor separation or interaction with the stationary phase. Aim for symmetric, Gaussian-shaped peaks.

1.5 Validation of the HPLC Method

HPLC (High-Performance Liquid Chromatography) method validation is a critical process to ensure the reliability and accuracy of results obtained from HPLC analysis, especially in pharmaceutical and related fields. It involves demonstrating that the method is suitable for its intended purpose by assessing its performance characteristics and establishing its limitations. This process is crucial for quality control, stability studies, and regulatory compliance.[6]

a. Precision

Precision is a key component in the validation of an HPLC method and refers to the degree to which repeated measurements under the same conditions produce consistent results. High precision indicates that the method can reliably give the same result every time it is used to

analyze a sample.[6]

Precision in validation is typically divided into three categories:

i. Intra-day Precision (Repeatability)

➢ Intra-day precision is the variation observed when multiple injections of the same sample are made on the same day, under the same conditions.

How It's Measured:

- Analyze multiple (typically 6) replicates of the same sample during a single day.
- Calculate the mean and standard deviation of the peak areas or retention times for these replicates.
- Acceptance Criteria: The relative standard deviation (RSD) of the results should be less than 2% for acceptable precision.[6]

ii. nter-day Precision (Intermediate Precision)

➢ Inter-day precision is the variation observed when the same sample is analyzed over multiple days by the same or different analysts, using the same equipment. To assess if the method remains consistent over different days or shifts in analytical conditions.[6]

How It's Measured:

- Multiple (typically 6) replicates of the same sample are analyzed across 2-3 different days.
- Data from these days are pooled, and the overall precision is calculated by determining the mean and RSD of the results.
- Acceptance Criteria: RSD values should again be below 2% for a method to be considered precise.[6]

iii. Reproducibility (Inter-laboratory Precision)

➢ This refers to the variation between different laboratories or different instruments used to conduct the same method. This is sometimes less commonly tested in routine validation, but it is important for method transfer or multi-laboratory comparisons. To evaluate how well the method can be applied in different settings.[7]

How It's Measured:

- Samples are analyzed in different laboratories or with different instruments and analysts.
- The results are compared to determine consistency across these variables.

b. Acceptance Criteria: The RSD should typically be ≤ 2-5%, depending on the complexity of the analysis and the number of laboratories involved.

c. Accuracy

Accuracy in HPLC is a critical parameter in method validation, which measures how close the results of the HPLC analysis are to the true value or known reference of the analyte in the sample. In other words, accuracy assesses whether the HPLC method correctly measures the quantity or concentration of a compound in a sample without bias or significant error.[7]

How to Evaluate Accuracy in HPLC

Use of Standard Reference Materials (SRMs) or Certified Reference Materials (CRMs):

- Standard reference material with a known concentration of the analyte is analyzed using the developed HPLC method. Measured concentration obtained from the HPLC system is compared to the known value (the reference or true value).

➢ Recovery is used to assess the accuracy of

an HPLC method by spiking known amounts of a standard analyte into the sample and measuring how much is recovered during the analysis.

- The difference between the known amount added and the amount measured gives an indication of the accuracy of the method.

d. Sensitivity

Sensitivity in HPLC refers to the ability of the system to detect and quantify small amounts of the analyte in the sample. It measures the system's ability to respond to low concentrations of the analyte, with minimal interference from background noise. High sensitivity is essential for detecting trace amounts of substances in complex mixtures, and it plays a significant role in both qualitative and quantitative analysis. It is often quantified as the limit of detection (LOD) and limit of quantification (LOQ), which indicate the smallest concentrations of the analyte that can be reliably detected and quantified, respectively.[8]

Sensitivity Parameters in HPLC

The sensitivity of an HPLC method can be quantified using the following parameters:

i. Limit of Detection (LOD)

The LOD is the lowest concentration of an analyte that can be detected, but not necessarily quantified, with acceptable accuracy and precision.

ii. Limit of Quantification (LOQ)

The LOQ is the lowest concentration of an analyte that can be reliably quantified with acceptable accuracy and precision, typically defined as the concentration where the signal-to-noise ratio is 10:1.

e. Robustness

Robustness in HPLC refers to the ability of the method to remain unaffected by small, deliberate variations in method parameters, while still delivering reliable and consistent results. It is a measure of how well an analytical method can perform under different, yet controlled, conditions, without significant changes in the output (such as retention time, peak shape, or quantification). This characteristic is particularly important when the method is used in different laboratories, with different analysts, or over extended periods.[8]

Importance of Robustness in HPLC

- Method Reliability: Robustness ensures that the method will produce reliable results even when small variations occur in day-to-day operations (e.g., slight changes in temperature, mobile phase composition, or flow rate).[8]
- Real-world Applications: In a production environment or when methods are transferred between laboratories, small fluctuations in environmental or operational conditions are inevitable. Robustness helps ensure that results stay consistent despite these variations.[8]
- Regulatory Compliance: Robustness is often a requirement in method validation, especially for regulatory submissions (e.g., FDA, EMA). It proves that the method is reliable under practical conditions.[8]

Testing Robustness in HPLC

To assess the robustness of an HPLC method, several method parameters are deliberately varied within defined ranges to check how these variations affect the chromatographic results. This is typically done by conducting a robustness study.

Steps to Perform a Robustness Test.[8]

Identify Key Parameters:

First, identify the critical method parameters that could affect the method's performance (e.g., mobile phase composition, flow rate, column temperature, etc.).[8]

i. Design the Study:

Select a set of deliberate variations in the identified parameters. Typically, these are small changes, such as ± 5-10% variations from the method's optimal conditions. For example:[8]

✓ Mobile phase pH: ± 0.1 pH units

✓ Flow rate: ± 5% of the method's nominal flow rate

✓ Temperature: ± 5°C from the nominal column temperature

ii. Perform the Experiment:

Analyze the same sample or standard under these different conditions, and record the results for each condition. Conduct the experiment across a range of variations for each parameter.

For example, if varying the mobile phase composition, test at different solvent ratios.[8]

iii. Analyze the Results:

Evaluate the impact of each variation on the following:

➢ Retention Time: Small changes in retention time could indicate that the method is sensitive to that parameter.

➢ Peak Resolution: The ability to resolve two or more analytes should be consistent despite parameter variations.

➢ Peak Shape: Observe whether peak symmetry is maintained under different conditions.

➢ Quantitative Results: Check if the area or height of the peaks remains consistent, ensuring that the method can consistently quantify the analyte.[8]

iv. Determine Acceptability:

A method is considered robust if small changes in the parameters do not result in significant deviations in chromatographic performance, such as peak area, retention time, or resolution. The standard deviation or relative standard deviation (RSD) of the measurements should remain within acceptable limits (typically, an RSD < 2% for quantitative analysis).[9]

2.0. LITERATURE REVIEW:

- **Foroughbakhs H et .al (2025)** reported a simple, selective, and sensitive analytical method for the estimation of Apremilast in both bulk drug and tablet dosage forms. The study focused on developing a validated method that adheres to regulatory guidelines, ensuring accuracy, precision, and reproducibility. Their method demonstrated high sensitivity and specificity, making it suitable for routine quality
control and pharmaceutical analysis. The findings highlight the method's potential utility in industrial and laboratory settings due to its efficiency and reliability.
- **K. xiong et .al, (2024)** developed and validated a High-Performance Liquid Chromatographic (HPLC) method for the quantitative estimation of Apremilast in bulk drug and its pharmaceutical formulations. The method was designed in compliance with ICH guidelines, ensuring parameters such as linearity, precision, accuracy, specificity, and robustness were thoroughly evaluated. The study confirmed that the HPLC method is highly

effective for routine analysis of Apremilast in quality control laboratories due to its reliability, reproducibility, and accuracy.

- **Chaudhari et.al, (2023)**[13] developed and validated spectrophotometric methods for the simultaneous estimation of Apremilast in bulk drug and dosage form. The proposed methods were reported to be simple, accurate, and cost-effective, making them suitable for routine analysis in pharmaceutical laboratories. The study confirmed good accuracy and precision, with acceptable validation parameters as per standard analytical guidelines. This method offers a practical alternative to more complex techniques for the estimation of Apremilast.
- **Prashansha Mullick, et. al. (2022)** developed a simple, precise, and accurate Reverse Phase High-Performance Liquid Chromatography (RP-HPLC) method for the estimation of Apremilast in both bulk drug and pharmaceutical formulations. The method was validated as per ICH guidelines, demonstrating satisfactory results in terms of linearity, accuracy, precision, and robustness. Due to its reliability and reproducibility, the method is considered suitable for routine quality control and analysis of Apremilast in pharmaceutical industries.

3.0. AIM: To develop and validate Stability indicating method for simultaneous estimation of meclizine and cyclizine on HPLC.

3.1. OBJECTIVES:

The objectives of present analytical work are:

- To develop an HPLC method for the simultaneous separation and quantification of Meclizine and Cyclizine with good resolution, peak symmetry, and acceptable retention times.
- To optimize chromatographic conditions (mobile phase composition, flow rate, detection wavelength, column type, etc.) for best separation efficiency.
- To validate the developed method as per ICH guidelines (Q2(R1)) for parameters such as:

✓ Linearity

✓ Accuracy

✓ Precision (intra-day and inter-day)

✓ Specificity

✓ Limit of Detection (LOD)

✓ Limit of Quantification (LOQ)

✓ Robustness

- To perform forced degradation studies (acidic, basic, oxidative, thermal, and photolytic conditions) to evaluate the stability-indicating capability of the developed method.
- To ensure the method can separate degradation products from the active pharmaceutical ingredients (APIs), confirming its specificity and suitability as a stability-indicating method.
- To apply the validated method for the analysis of Meclizine and Cyclizine in marketed pharmaceutical formulations.

- **4.0 MATERIALS & METHODS**:

Table 4.1 : Name Of Equipment

Sr. No.	Name Of Equipment	Make& Mode

1	ligh Performance Liquid Chromatogra hy	AGILENT 1100
2	HPLC Column	ARP-C18 (25 mm X 4.6 mm) 5µ column
3	UV-Visible Spectrophoto meter	SHIMADZU 1800
4	Sonicator	LAB MAN Tech.
5	Electronic Balance	CITIZON
6	PH METER	LABTRONICS

4.1. Methodology

A. Materials and Reagents

Standards: Meclizine hydrochloride and Cyclizine hydrochloride (working standards with known purity)
Pharmaceutical Formulation: Marketed tablets/capsules containing Meclizine and Cyclizine Chemicals & Solvents:

- HPLC-grade Acetonitrile
- HPLC-grade Methanol
- Water (Milli-Q or double distilled)
- Analytical grade buffers (e.g., potassium dihydrogen phosphate)
- Hydrochloric acid, sodium hydroxide, hydrogen peroxide (for degradation studies)

B. Chromatographic Conditions (to be optimized during method development)

C. Preparation of Solutions

a. Standard Stock Solutions

- Dissolve an accurately weighed quantity of Meclizine and Cyclizine separately in methanol or mobile phase to get stock solutions (e.g., 1000 µg/mL).
- Prepare mixed standard solution from stock to contain working concentrations (e.g., 10–100 µg/mL).

b. Sample Preparation (Formulation)

- Weigh and finely powder tablets or capsules.
- Transfer an equivalent amount of Meclizine and Cyclizine to a volumetric flask.
- Extract using mobile phase or suitable solvent.
- Filter and dilute to desired concentration.

D. Method Development

- Optimize mobile phase, pH, column type, flow rate, and detection wavelength.
- Evaluate system suitability parameters: retention time, theoretical plates, resolution, tailing factor.

E. Method Validation (As per ICH Q2(R1))

- Linearity: Prepare standard solutions at different concentrations (e.g., 5–100 µg/mL). Plot calibration curves.
- Accuracy (Recovery Studies): Spike known amounts of standards into placebo or pre- analyzed samples.
- Precision:
- Intra-day (repeatability) – multiple injections on the same day

- Inter-day (intermediate precision) – different days, different analyst (optional)
- Specificity: Ensure no interference from excipients or degradation products.
- LOD & LOQ: Based on standard deviation of response and slope.
- Robustness: Slight variation in flow rate, mobile phase ratio, detection wavelength.

F. Forced Degradation (Stability-Indicating Capability)

G.5.0 PLAN OF WORK:

1. Selection of drug candidate and reference standard from literature and market survey, suitable drug and information will be selected on the basis of physicochemical parameters and potential of drug.
2. Selection of Marketed formulation.
3. Review of the literature.
4. Procurement of drugs, chemical reagents.
5. Selection of analytical techniques.
6. High Performance Liquid Chromatography (HPLC) method
7. Estimation of formulation by RP- HPLC method involving following steps:

- Drug solubility.
- Selection of wavelength.
- Selection of stationary and mobile phase.
- Selection and optimization of chromatographic conditions.
- Preparation of solutions and linearity study by RP-HPLC.
- Validation of proposed RP- HPLC method.
- Data Compilation

Achievable targets	Period o study
Literature survey	0-3 months
Procurement of dru and other chemicals	1 month
Selection of techniques any studies	2 months
Result and Conclusion	1 month
Thesis Writing an submission	1 month

6.0 Scope of the Study/ Expected Outcome

The scope of this study encompasses the development, optimization, and validation of a stability-indicating High-Performance Liquid Chromatography (HPLC) method for the simultaneous estimation of Meclizine and Cyclizine in bulk drugs and pharmaceutical formulations. The method will be designed to separate and quantify both active pharmaceutical ingredients (APIs) in the presence of their degradation products, ensuring its applicability for quality control and stability testing in compliance with regulatory standards. Specifically, the study will cover:

6.1. Method Development:

- Designing an HPLC method capable of accurately separating Meclizine and Cyclizine.
- Optimization of chromatographic parameters (mobile phase composition, flow rate, detection wavelength, etc.) for best performance.

6.2. Method Validation:

Comprehensive validation of the method as per ICH guidelines (Q2(R1)), including:

- Linearity
- Precision
- Accuracy
- Specificity
- Limit of Detection (LOD) and Limit of Quantification (LOQ)
- Robustness

6.3. Forced Degradation Studies:

✓Subjecting both drugs to various stress conditions (acidic, basic, oxidative, thermal, and photolytic) to induce degradation.

✓ Ensuring the developed method can detect and separate degradation products from the parent compounds, proving it is stability-indicating.

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