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A Review on Stability Testing Guidelines of Pharmaceutical Products [With Case Studies]

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ABSTRACT
Stability studies require to be conducted in a systematic way and in compliance with the guidelines provided by the International Conference on Harmon the World Health Organization, and/or other authorities. The primary objective of stability testing is to develop techniques that producing pharmaceutical goods and their packaging that, when stored and used in compliance with label directions, have the appropriate physical, chemical, and microbiological properties for a certain shelf life.
To ensure the quality, safety, and efficacy of a pharmaceutical product, stability studies must be conducted in accordance with ICH, WHO, and other significant guidelines. This reviewdiscusses the importance of stability testing, various methods of testing, and the types of thestability of pharmaceutical substances, guidelines issued to test the stability of pharmaceutical.
KEY WORDS: Stability studies, ICH guidelines, Pharmaceutical products, Protocol for stability testing

I. INTRODUCTION [1-8]

In order to produce pharmaceutical products with efficacy, quality, and safety, a significant amount of time, money, use, and scientific experience are needed for the complex process collection known as pharmaceutical product stability.[1]

Researchers and regulatory bodies examining pharmaceutical stability have an interest in any modification that takes place in a pharmaceutical product after it has been generated that might result in an adverse effect on a patient's fitness for use or the product's quality. [2]

The capacity of a specific formulation in a certain container/closure system to remain its physical, chemical, microbiological, toxicological, protective, and informative specifications is known as the pharmaceutical product's stability.[2]

Pharmaceutical analysis and stability studies, which are necessary to determine and ensure the identity, potency, and purity of ingredients as well as those of the manufactured products, among the most important steps during the developmental stages.[3]

One technique used in the pharmaceutical industry to analyse stability samples is the stability-indicating assay. [4, 1]

During in the drug development process, the formulation and stability of active ingredients is examined.[5]

The reactions to chemical degradation, including oxidation, reduction, hydrolysis, and racemization, depend effectively on the stability of chemical products.Thestability of pharmaceutical products also affects raw materials, pH, radiation, catalyst concentration, raw material concentration, and the time interval between product development and usage. Drug stability can also be impacted by physical alterations produced on by collisions, abrasions, and temperature variations like freezing or shearing, which can result in the loss of the active ingredients.[6]

A pharmaceutical product stability test evaluates the efficacy, safety, and quality of active drug substances and dosages, as well as the shelf life or expiration date to verify product states.7

Carefully carried out stability studies must comply with to laws governed by the World Health Organization (WHO), the International Council for Harmonization (ICH), and other similar organizations.[8]

IMPORTANCE OF STABILITY TESTING[9-14]

1. Understanding the processing and shelf life requirements for the manufacturing of new products.
2. Active drugs may decompose and produce toxic products.
3. To maintain the manufacturer's reputation, ensure that the product is effectively acceptable and fit for use for the duration of its market presence.

International Journal of Pharmaceutical Research and Applications
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4. To prevent any changes to production or formulation procedures that may affect product stability.
5. It provides a database that might be useful for currently available product growth when selecting on formulations, excipients, and container closing techniques.
6. Understanding API deterioration and its impact on pharmaceutical product quality.
7. This is only way to ensure the drug complies with acceptable standards.

FACTORS AFFECTING ON DRUG STABILITY [15-17]

- Temperature –

The changes in temperature affect the stability of a drug substance; when the temperature rises, the hydrolysis rate of pharmaceuticals increases.

- Moisture –

When water-soluble substances are absorbed into a moist surface, their physical and chemical properties may alter.

- pH –

pH affects the deterioration rate of hydrolyzed solution pharmaceutical productswhich lowers the effectiveness of drugs developed with buffers at the pH of their optimal stability.

- Excipients –

Excipients such as starch and povidone increase the water content of formulations, affecting their stability. Furthermore, chemical interactions between excipients and medications can reduce instability.

- Oxygen –

Some products oxidize more easily when there is oxygen present. Products that decompose quickly can be stabilized by replacing oxygen with carbon dioxide and nitrogen in storage containers.

- Light –

When exposed to light, the deterioration rate increases. Drugs with photosensitivity can be tested for stability when exposed to light or stored in darkness.Photosensitive medications should be stored in a glass amber bottle in a dark environment.

TYPES OF STABILITY OF DRUG SUBSTANCE[18, 9]

1. Physical Stability
2. Chemical Stability
3. Microbiological Stability
4. Therapeutic Stability
5. Toxicological Stability

1. Physical Stability

Physical stability is crucial for drug safety and efficacy, as it influences consistency and release rate.[18] Physical features include size, palatability, homogeneity, dissolution, and suspension.[9]

2. Chemical Stability

Pharmaceuticals' chemical stability decreases as they deteriorate. The chemical purity and labelled strength of each active component are within specified limitations.[18, 9]

3. Microbiological Stability

Antimicrobial drugs maintain their effectiveness within certain limits and can also be used to sterilize or inhibit the growth of microorganisms in accordance with established parameters.[18]

4. Therapeutic Stability

The therapeutic impact will remain the same.

5. Toxicological Stability

There is no significant raise in toxicity.

METHODS OF STABILITY TESTING

1) Real-time stability testing
2) Accelerated stability testing
3) Retained sample stability testing
4) Cyclic temperature stress testing

1.Real-time Stability Testing

Real-time stability testing is typically conducted over a longer period who were responsible for product degradation during mentioned storage conditions.[19]

The stability of the product, which clearly shows that it is neither deteriorated nor broken down over an extended period of time due to inter-assay variance, determines how long the product test will last. Samples are taken at regular intervals throughout the testing procedure as to ensure that data is collected at the appropriate frequency and the analyst is able to identify daily deterioration.[3, 20]

International Journal of Pharmaceutical Research and Applications
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2.Accelerated Stability Testing

The heating input required for the failure of the product is determined at elevated temperatures (higher than ambient). This test is carried out to make the product condition worse. The purpose of this data is to compare and predict the stability of different formulation options. Early product quality assessment reduces development time and improves efficiency.

The stress conditions used in accelerated stability testing include humidity, heat, turbulence, weight, pH, and packing. Because the analysis period is limited, the samples are strained, cooled, and then evaluated concurrently, which reduces the possibility of measurement instability as compared to real-time stability testing. Furthermore, in accelerated stability testing, the unstressed product compared with the stressed material, and the affected sample recovery is presented as an unpressured proportion of the sample recovery.[21, 22] The concept of accelerated stability testing depends on Arrhenius equations 1 and 2

Ink = InA +ΔE/RT
Where,
K= Specific rate constant
A= Frequency factor
ΔE= Activation energy
R= Real gas constant
T= Absolute temperature

The link between degradation rate and storage temperature is defined by these equations. The stability projection of the degradation rates found for certain degradation processes at hightemperature is determined by the Arrhenius equation. At lower temperatures, the rate of degradation can be determined at "stress temperature."[23, 24, 25]

3.Retained sample stability testing

This is routine for all marketed products that require stability data. This study selects stability samples suitable for at least one batch per year of storage. If more than 50 batches are marketed, it should be considered to collect stability samples from two of them. When introducing a product to the market for the first time, stability samples may be taken from each batch. Later on, this may be reduced to 2% to 5% of marketed batches. This study tests stability samples at specified intervals. For example, a product with a shelf life of 5 years is often tested at 3, 6, 9, 12, 18, 24, 36, 48, and 60 months.

Stability testing using market samples is a modified method that evaluates stability properties based on samples already available in the market. Adequate testing challenges the product not only in ideal storage settings, but also in real-world scenarios.[26]

4. Cyclic temperature stress testing

For products that are marketed, this is not the usual testing procedure.[27]

Cyclic temperature stress tests simulate market storage conditions based on product knowledge.

The everyday cycle on Earth lasts 24 hours, thus marketed drugs are likely to undergo the same pattern during storage. Cyclic stress testing requires selecting both minimum and maximum temperatures based on the product, taking into careful consideration storage temperatures, physical characteristics, and chemical degradation. Also, the test typically consists of 20 cycles.[28]

GUIDELINES FOR STABILITY TESTING

Table 1: Codes and titles used in ICH guidelines[29, 30]

Sr. No.	ICH Guideline Code	Title
1.	Q1A	Stability testing of new drug substances and products
2.	Q1B	Stability testing : Photostability testing of new drug substances and products
3.	Q1C	Stability testing of new dosage forms
4.	Q1D	Bracketing and matrixing design for stability testing of drug substances and products
5.	Q1E	Evaluation of stability data
6.	Q1F	Stability data package for registration applications in climatic zone III and IV
7.	Q5C	Stability testing of biotechnological/biological products

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In 1980, these guidelines were issued then harmonized by the ICH to improve marketing and registration in other nations. Regulatory authorities in several nations require producers to submit stability information in order to guarantee molecules and products are produced with optimized stability, distributed, and provided to patients. These guidelines aim to promote consistency in testing.

The guidance documents describe test con ditions for APIs, drug products, dosage forms, and excipient. [13]

Table 1 shows the codes and names for stability res earch that are included under the ICH criteria.

Q1A (R2): Stability testing of new drugs substance and products

According to these standards, information about new molecular entities and related drug products needs to be included in the registration application. The purpose of testing for stability is to establish a retest or shelf life for drug substances or drug products and to suggest storage conditions. It also attempts to provide evidence of how the quality of the drug substances or drug product changes over time under the influence of various environmental factors, such as temperature, light, and humidity. [19, 31]

Q1B: Photostability testing of new drug substances and products

Considered to the parent guidelines, the ICH Harmonized triple guideline on novel drug substances and stability of products testing states that the most important component of stress testing need to be simple testing.

This paper deals with the photostability evaluation guidelines and is an article to the parent guideline. One batch of carefully chosen materials goes through to photostability testing in accordance with the parent specifications.[32]

Q1C: Testing for stability of new dosage forms

These suggestions respond to a recommendation from the first applicant related to the stability of new dosages that developed after the original application for novel pharmaceutical substances and goods.
A new dosage form is a pharmaceutical product that has the same active ingredient as an existing drug product that has been approved by the regulatory body but differs in the delivery system (e.g., tablet to modified tablet immediately release), the route of administration (e.g., oral to parental), and the form of administration of the same dosage route (e.g., capsule to tablet, a solution to suspension). The idea of stability for a new dosage need to be the parent stability guideline.[33]

Q1D: Bracketing and matrixing design

The use of bracketing and matrixing instability studies is suggested by this guideline. The term of bracketing provides a schedule for stability, wherein only specimens are subjected to rigorous testing associated with design parameters like strength, container capacity, and entire design filling.

Also, the structure requires that the stability of the test endpoints corresponds to any intermediate level of stability. The process for developing a stability plan that calls for the testing of particular sample groups at a later date and the testing of subsets of the total number of samples for all possible combinations of factors at a predetermined time point is known as matrixing. [34, 35]

Q1E: Evaluation of stability data

This guideline describes when and how to use estimation to recommend a new evaluation length for a pharmaceutical substance or product shelf life that exceeds the period covered by "long-term storage conditions information available from stability studies." Official stabilization research design and performance must comply with parent guidelines.

The stability research tries to establish guidelines for retesting and storing future batches of drug substances or items under similar conditions. This is based on testing at least three batches. The different characteristics of individual batches affects the degree of assurance that subsequently manufacturing batches will meet acceptance requirements during retesting or shelf life. [36]

Q1F: Stability data package for registration applications in climatic Zone III and IV

The ICH establishes the storage conditions for stability testing in nations in Climatic Zones III (hot and dry) and IV (hot and humid), which are not covered by ICH Q1 A (R2).
Q1 F Stability Data Package for Registration Applications in Climatic Zones III and IV. To improve medicine availability and reduce storage options, ICH Q1 F established global stability testing criteria. WHO examined member states to

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1258-1269 www.ijprajournal.com ISSN: 2456-4494

agree on 30°C/65% RH as the ideal for extended storage temperature for hot and humid regions. [37]

Q5C: Stability testing for biotechnological/biological products

This guidance is applicable to well-defined polypeptides and proteins, as well as their products and derivatives, extracted from fluids from the body, tissues, cell cultures, or r-DNA technologies.

This document covers the stability of various products, including cytokines (interferon, interleukins, colony-stimulating factors, and tumor necrosis factors), erythropoietin, and plasminogen activating agents, blood plasma components, growth hormones, insulin, monoclonal antibodies (MA), and vaccines with well-characterized proteins or polypeptides. [38, 39]

STORAGE CONDITIONS

Table 2: Stability test storage conditions for drug products

Types of Stability Studies	Storage Condition	Minimum Time Period (Months)
Long-term	25±2°C and 60 ±5% RH or 30±2°C and 65±5%RH	12
Intermediate	30±2°C and 65±5%RH	6
Accelerated	40±2°C and 75±5%RH	6

Table 3: Drug substances intended for storage in a refrigerator

Types of Stability Studies	Storage Condition	Minimum Time Period (Months)
Long-term	5°C ± 3°C	12
Accelerated	25±2°C and 60 ±5% RH	6

Table 4: Drug substances intended for storage in a freezer

Types of Stability Studies	Storage Condition	Minimum Time Period (Months)
Long-term	-20°C ± 5°C	12

STABILITY TESTING EQIPMENT [3, 13]

The stability chamber is the device used for stability testing. It is an environmental specialist chamber that can stimulate conditions of storage and real-time stability, accelerated stability, and for a long time regulations, as well as evaluate the stability of the product. The rooms are capable of both reach-in and walk-in types. Small chambers are selected for quick testing due to their shorter product storage periods, whereas walk-in chambers are preferred for long-term testing. Because of the requirement for years of continuous usage, these chambers are anticipated to be dependable, strong, and equipped with beneficial recording, safety, and alarm systems. In addition, picture stabilization chambers can be utilized with or without temperature and moisture control, two types light source is used.

1. Cool white and near-UV fluorescent light bulbs are mixed together.
2. Daylight artificial lighting (such as metal halide or xenon)

CLIMATIC ZONES FOR STABILITY TESTING

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In 1972, Futscher and Schumacher proposed categorizing the planet into four temperature and humidity zones: Zone I (temperature, climate), Zone II (subtropical in nature and Mediterranean climates),and Zone III (hot and dry the atmosphere), and Zone IV (hot and humid weather). [25]

The WHO stability testing guidelines cover four climate zones and storage conditions. The stability testing evaluation suggestions are based on the parent guidelines as well as WHO guidelines. The parent guideline for climatic Zones I and II, as well as Zones III and IV, specifies the stability data package for tripartite ICH zones (European ,Union, Japan, as well as and the US).[40]In order to simplify and standardize global stability testing, the world has been divided into four climate zones .These long-term stability data have been used to derive stability in real-time and accelerated conditions for testing of stability.[41]

Table 4 : Conditionsfor climatic zone

Climate Zone	Type of Climate	Countries	Long Term Testing Temperature (°C)	Long Term Testing Relative Humidity (*RH*)
I	Temperate	United Kingdom, Northern Europe, Russia, United States	21 °C	45%
II	Subtropical and Mediterranean	Japan, Southern Europe	25 °C	60%
III	Hot and dry	Iraq, India	30 °C	35%
IVa	Hot and humid	Iran, Egypt	30 °C	65%
IVb	Hot and very humid	Brazil, Singapore	30 °C	75%

PROTOCOL FOR STABILITY TESTING

The stability testing protocol is a written document that describes the key elements of an under control and monitored stability test. It is required prior to initiating the test. The protocol is specific to the drug substance or product, taking consideration of intrinsic stability, dosage form, and container closure. It's possible to identify if the medicine is newly developed or currently on the market. Stability tests are used to evaluate a pharmaceutical product's expiry date and shelf life.[42]

The stability protocol should consist of the following information:

1. Number of batches
2. Containers and closures
3. The orientation of storage of containers
4. Sampling time points
5. Sampling plan
6. Test storage conditions
7. Test parameters
8. Test methodology
9. Acceptance criteria

1. Number of batches

Stability studies at the level of development are often conducted on a single batch, whereas registration studies for new or unstable products are conducted on the first three manufacturing batches. Stable and well-developed batches can be tested on two batches. If the initially collected data is not from a full-scale production batch, the first three batches of post-approval drug products should undergo long-term studies following the same protocol as the approved application. Data from small-scale batches obtained during the manufacturing process are not considered primary stability data, but rather provide supporting information. Batch selection should be based on a random sampling of pilot or production batches.[43]

2. Containers and closures

Tests are conducted on materials in immediate containers or marketing closures. Materials for packaging consist of aluminum strips, aluminum packs, blister packets, high density polyethylene bottles, and secondary packs. Transporters are not required. Before distribution and marketing, products must be evaluated separately in each type of container or closure.
Prototype containers can be tested for large quantities if the packing is stimulated.[44]

3. The orientation of storage of containers

To conduct stability investigations, samples of solution, dispersed process, and semi-

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1258-1269 www.ijprajournal.com ISSN: 2456-4494

solid medication materials should be kept upright and positioned reversed or downwards to ensure full contact with the container closure. The mentoring concept is responsible for determining whether the connection between the interaction of pharmaceutical materials or solvents with closures removes chemical compounds or adsorbs product components in the container.[13, 42]

4. Sampling time points

The frequency of testing should be sufficient to determine the stability profile of the new therapeutic substance. For products with a shelf life of at least 12 months, the duration of testing for prolonged storage should be every 3 months for the first year, every 6 months for the second year, and annual subsequent until expiration. For accelerated storage, it's recommended to record at least three time intervals (0, 3, and 6 months), including the start and finish points.

A minimum of four tests should be conducted at the intermediate stage of storage due to major modifications at the accelerated storage state.

Acceptable test points include initial and final time points, such as 0, 6, 9, and 12 months.

When evaluating various products with varying strengths and sizes, reduced stability testing strategies can be developed to minimize the number of test points. The simplified testing plans depend on bracketing and matrixing statistical designs. Bracketing involves designing a stability schedule that only tests samples on the extremes of specific design characteristics, such as strength and package size, at all-time points, similar to a full design. Matrixing tests a subset of all potential combinations at a given time point. Next, a selection of samples for all factor combinations is evaluated.

5. Sampling plan

The technique of sampling requires stability testing, which involves preparing many samples in a stabilization chamber and evaluating the charged batch during the study. To carefully examine all test parameters, determine sampling duration and number at each stage. To conduct long-term or rapid stabilization investigations, approximately 100 tablets (10 for hardness and moisture detection, 6 for disintegration and dissolution, and 50 for friability) should be used. This is the total number of pills required for the study multiplied by the number of outcomes. The sample plan establishes an unequal selection of containers to represent complete batches.[45]

6. Test storage conditions

Storage requirements should be establish based on the climatic zone where the product will be distributed or whether regulatory approval is required. The ICH, CPMP, and WHO have issued general guidelines for storage conditions.[46]

7. Test parameters

The stability test technique should include specific criteria for analyzing stability samples. Following storage choice, a stability test is performed to evaluate efficiency, purity, capacity, and identity.

Routine tests for samples being tested include presentation, manufacturing, material deterioration, dissolution, humidity, and microbiological analysis. Batches used for stability testing must meet all test criteria, including heavy metals, residual solvents, and traces of combustion. Some tests are necessary for product release, but not for continuous stability testing. ICH advice covers additional Q6A criteria such as enantiomeric purity, polymorphic form, and particle size.[46]

8. Test methodology

The adherence to the procedures outlined in official compendia is crucial for improved acceptance of test results. When using alternative procedures, they must be adequately tested. A drug test should use a stability indicator technique developed through tests conducted on a material under forced decomposition. The method should be assessed for linearity, reliability, accuracy, and precision within the context of the drug's expected stability. Validated systems should include limits of detection and quantification for product degradation analysis. After testing reproductivity and conducting basic validation, such as linearity, range, and so on, utilize the procedure described in the documentation. [42]

9. Acceptance criteria

Validation of all analytical procedures is necessary prior to starting stability research. Similarly, criteria for approving analytical results as well as requirements should be defined in anticipation of the presence of degrading compounds. The acceptability criteria for stability analysis include numerical limits for output terms

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1258-1269 www.ijprajournal.com ISSN: 2456-4494

like moisture collection, viscosity, degradation, assay, and particle size, as well as qualitative tests like odor, color, appearance, microbial growth, and cracking. The approval standards for both individual and whole products of degradation must include maximum restrictions.

"ICH Guideline Q3B (R2)" targets contamination in new medicinal products and their degradation in formulations. Once the suggested limits has been achieved, the active ingredient products of degradation, excipients, and container materials must be approved, detected, and/or eligible. The contaminant reporting level depends on the desired dose. The daily maximum dose is 0.1% if it is less than or equal to 1 g, and 0.05% if it exceeds 1 g. The impurity criteria for daily doses of 1 mg or 2 mg is 1.0 to 0.1%.[28]

DIFFERENT WAYS TO INCREASE DRUG STABILITY [47]

- pH adjustment:

Changes in pH can have an impact on the stability of pharmaceutical preparations. Raising the pH can improve stability in some cases, but lowering it may be essential in others.

- Use of antioxidants:

Antioxidants can help reduce the oxidation of drugs by collecting free radicals and reactive oxygen species that could cause oxidation.

- Use of stabilizers:

Stabilizers can be used into medication formulations to stop degradation. These might include substances like proteins, carbohydrates, or amino acids that help stabilize the drug molecule.

- Freeze-drying:

In the freeze-drying process, a drug solution is frozen and then dried under vacuum. By removing water, this can help to stabilize the medication by lowering the chance of degradation.

- Packaging:

Appropriate packaging can also boost a medicine's stability. One way to prevent moisture from entering and causing deterioration is to store medications in sealed containers with desiccant inside.

- Chemical modification:

Occasionally, altering a drug's substance can improve its stability. This could include adding functional groups that can prevent deterioration or changing the formulation to make it more stable.

CASE STUDY

Case Study 1 : Stability Testing of Solid Oral Dosage Forms[48]

Context	Approach	Findings
Tablets and capsules are among the most common forms of drug products, and their stability must be evaluated under various storage conditions.	A study on a new tablet formulation included testing under long-term (25°C/60% RH) and accelerated (40°C/75% RH) conditions for up to 12 months. Analytical methods such as high-performance liquid chromatography (HPLC) were used to assess the drug content, dissolution rate, and presence of degradation products.	The tablet formulation remained stable under long-term conditions with minimal changes in drug content and dissolution profile. However, the accelerated conditions revealed the formation of a degradation product that necessitated reformulation to improve stability.

Case Study 2 : Stability Testing of Ophthalmic Solutions[49]

Context	Approach	Findings
Ophthalmic solutions are sterile products that require	A study on a preservative-free ophthalmic solution involved testing under various storage conditions, including freeze-thaw cycles, to evaluate physical and chemical	The solution maintained sterility and chemical stability under refrigerated conditions (2-8°C) for up to 12 months.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1258-1269 www.ijprajournal.com ISSN: 2456-4494

rigorous stability testing to ensure sterility and efficacy.	stability, sterility, and pH changes.	Freeze-thaw cycles caused some physical changes but did not affect the overall efficacy. However, storage at higher temperatures led to a decrease in pH and drug potency.

Case Study 3 : Stability Testing of Biologics[50]

Context	Approach	Findings
Biologics, such as monoclonal antibodies, are complex molecules that require stringent stability testing due to their sensitivity to environmental conditions.	A study conducted on a monoclonal antibody product involved accelerated stability testing under various temperature and humidity conditions. The testing included assays for potency, aggregation, and degradation products.	The results indicated that the biologic product was stable at 2-8°C for up to 24 months but showed significant degradation at 25°C and 60% relative humidity (RH) after 6 months. The study underscored the necessity of cold chain logistics for such products.

Case Study 4 : Stability Testing of Liposomal Formulations[51]

Context	Approach	Findings
Liposomal formulations present unique stability challenges due to their structure and potential for drug leakage or degradation.	A stability study on a liposomal formulation containing a chemotherapeutic agent involved testing at different temperatures (4°C, 25°C, 37°C) and humidity conditions. Parameters such as particle size, encapsulation efficiency, and drug leakage were monitored.	A stability study on a liposomal formulation containing a chemotherapeutic agent involved testing at different temperatures (4°C, 25°C, 37°C) and humidity conditions. Parameters such as particle size, encapsulation efficiency, and drug leakage were monitored.

Case Study 5: Stability Testing of Sustained-Release Metformin Tablets[52,53,54]

OBJECTIVE

The goal was to evaluate the stability of a newly developed sustained-release metformin tablet to ensure it maintains its efficacy, safety, and quality over its intended shelf life.

BACKGROUND

Metformin is a widely used antidiabetic medication. Sustained-release formulations are designed to release the drug slowly over time to improve patient compliance and maintain steady blood glucose levels.

METHODOLOGY

1. Formulation Development:

The sustained-release metformin tablets were formulated using a hydrophilic matrix system. Excipients included HPMC as a release-controlling polymer, along with other common excipients.

2. Stability Testing Conditions:

Accelerated Stability Testing: 40°C ± 2°C/75% ± 5% RH for 6 months.
Long-term Stability Testing: 25°C ± 2°C/60% ± 5% RH for 12 months.
Intermediate Stability Testing: 30°C ± 2°C/65% ± 5% RH for 12 months.

3. Parameters Tested:

- Physical Attributes: Appearance, tablet hardness, and dissolution profile.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 1258-1269 www.ijprajournal.com ISSN: 2456-4494

- Chemical Attributes: Assay of metformin, degradation products.
- Microbiological Attributes: Microbial limits testing.

II. RESULTS

Physical Attributes:

- Appearance: No significant changes in color, shape, or texture.
- Hardness: Slight variation within acceptable limits, ensuring tablet integrity.
- Dissolution Profile: Consistent release profile maintained within USP specifications.

Chemical Attributes:

- Assay of Metformin: Remained within 95-105% of the labeled claim throughout the study.
- Degradation Products: No significant increase in degradation products. All were within ICH acceptable limits.

Microbiological Attributes:

No significant microbial growth detected, meeting the required specifications.

III. DISCUSSION

- Accelerated Conditions:

Some minor changes were noted, such as a slight increase in hardness and a minimal change in the dissolution rate. However, the product remained within acceptable limits.

- Long-term Conditions:

The metformin tablets showed excellent stability with no significant changes in physical, chemical, or microbiological attributes.

- Intermediate Conditions:

Results were consistent with long-term stability data, confirming the robustness of the formulation

IV. CONCLUSION

Stability testing is now essential method for developing new drugs and formulations in the pharmaceutical sector.The review study determined that, stability tests ensure drug is safe and effective under approved storage and shelf life settings.To ensure accuracy, the stability test should follow scientific methodologies as well as consider the climate zone, current guidelines, and other factors.

The sustained-release metformin tablets demonstrated robust stability under both long-term and accelerated conditions. The product met all regulatory requirements, confirming a shelf life of 24 months under recommended storage conditions (25°C/60% RH).

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