CHEMICAL STABILITY OF DRUGS

Abstract

For the process of creating new medications, stability is very essential. Any pharmaceutical product that wants to be approved or accepted must first undergo stability tests, which ensure that the product's quality, safety, and efficacy will not change over its shelf life. By providing comprehensive information about drug stability, the principle of drug degradation, force degradation studies, stability studies and their classification, factors affecting drug stability, the mechanism of drug degradation, stability testing, and various methods to increase drug stability, this article will close the knowledge gap on the most crucial topic for researchers or developers who are developing a formulation. Since the various sources discussed above in this article address issues related to drug stability, they will also influence individuals who are science or research oriented to develop formulations by offering comprehensive knowledge on this particular topic.

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I. INTRODUCTION

The stability of a drug can be defined as its capacity to maintain its chemical, physical, microbiological, therapeutic, and toxicological characteristics within predefined limits throughout its shelf life.

Chemical stability in chemistry refers to a substance's (drug's) thermodynamic stability. The system is in its lowest energy state, or it is in chemical equilibrium with its surroundings, according to thermodynamic stability. The rate of change in a pharmaceutical dose form is used to gauge stability (PDF). In order to protect industrially produced goods from harmful climatic influences like temperature, light, moisture, humidity, pH change, etc., stability is generally required. The stability tests are defined as "a series of tests designed to obtain information on a pharmaceutical product's stability in order to define its life time and utilization period under specified package and storage conditions."

Using amber-colored bottles, drugs can be kept and conserved to preserve their life from exposure to numerous impacting conditions. Storage of the product in cool, dark areas, carton packaging that serves as a physical barrier to light exposure, and polymer film coating on the tablet surfaces that protect against moisture are all recommended.

II. OBJECTIVES OF DRUG STABILITY

"The physical characteristics of the formulation have not changed significantly or adversely during the period from the date of manufacture and packaging until its chemical or biological activity is NLT a predetermined level of labeled potency."

The major objectives of stability testing are as follows

- To select adequate formulations.
- To determine shelf life and storage conditions.
- To determine maximum expiration date/ shelf life.
- To verify that no changes have been introduced in formulation that adversely affects the stability.
- To ascertain the components of the packaging.
- To compile data in order to create a stable product during the pre-formulation phase.

1. **Types of Drug Stabilities:** The safety and efficacy of a drug product are greatly impacted by its stability. Degrading contaminants have the potential to cause negative effects as well as a decrease in efficacy. Thus, it is crucial to attain both chemical and physical stability in drugs to guarantee their quality and safety.

   Stability of drugs may be classified as follows:

   - **Physical Stability:** This category of stability encompasses physical characteristics such as visual appearance, color, dissolution, and palatability.

   - **Chemical Stability:** Chemical stability refers to the drug's ability to resist undergoing chemical changes. In the context of materials science, a chemical substance is

considered stable when it exhibits low reactivity when exposed to the environment or during typical usage, maintaining its beneficial properties throughout its shelf life.

- **Microbiological Stability:** Microbiological stability, or the ability to resist microbial growth, is maintained in accordance with specific criteria, and any antimicrobial agents present continue to remain effective within defined limits.

- **Therapeutic Stability:** Drug stability pertains to the degree to which a drug substance or product maintains, within defined parameters, the same attributes and qualities it possessed when initially manufactured, throughout its storage and utilization period.

- **Toxicological Stability:** In toxicology, stability is defined as the state of being unchanging, and when this broad concept is applied to pharmaceutical formulations, it means that the product should not exhibit alterations in its characteristics and properties from the time of its manufacturing.

2. **Chemical stability of drugs:** Chemical stability refers to the absence of any breakdown in the chemical component that is integrated into the formulation, such as the drug itself, preservatives, or other additives. This breakdown can have an impact on both the physical and chemical stability of the drug.

   The stability of a drug is critical for ensuring the safety and effectiveness of the drug product. Degradation impurities have the potential to cause negative effects as well as reduce efficacy.. Hence, it is imperative to attain both chemical and physical stability in pharmaceuticals to guarantee their quality and safety.

   Chemical stability denotes the ability to resist chemical changes or reactions. In materials science, a chemical substance is deemed stable when it does not display significant reactivity in its environment or under normal usage conditions, and it retains its useful properties throughout its anticipated lifespan.

   - **Chemical stability and expiration date:** The expiration dates of drugs indicate the duration within which the product is expected to maintain its stability, ensuring that it preserves its potency, quality, and purity when stored as directed on the label.

     In the course of a stability study, substances are stored under different temperature and humidity conditions. At specified intervals, samples are withdrawn and subjected to a series of examinations. These assessments may encompass an identification test, assay, physical examinations, microbiological assessments, and tests for preservative effectiveness, among others.

3. **Factors influencing the stability of drugs:** Temperature, light, humidity, radiation, air exposure, particle size, solvents, pH levels, storage conditions, and the presence of additional compounds that may arise from contamination or deliberate mixing of different substances are some of the variables that might affect stability.

- **Effect of temperature:** Extreme temperatures can also have a significant impact on the stability of medications. High temperatures, in particular, can initiate the degradation of medicines, leading to the formation of impurities that can compromise the medication's effectiveness in treating individuals. Furthermore, these impurities may pose potential risks to the individuals who consume the medications.

- **Effect of pH:** In the field of pharmacy practice, pH is a crucial factor, and having a fundamental grasp of its principles and measurement is of paramount significance. It is imperative to have a thorough comprehension of pH and its impact on the solubility, stability, and absorption of drugs.

  The pH range for optimal stability usually lies between 2.5 and 7. This is attributed to the superior nucleophilic nature of the hydroxyl ion when it attacks a carbonyl carbon (in the case of an ester or amide) compared to water attacking a protonated carbonyl.
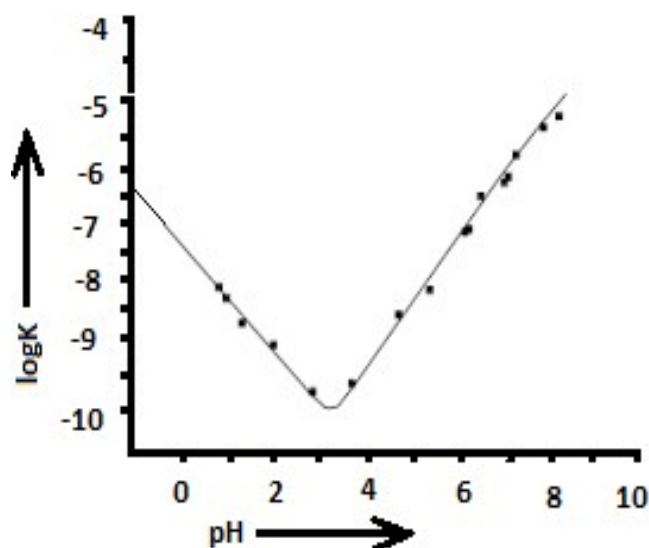
- **Effect of Moisture:** Chemical reactions including oxidation, hydrolysis, and reduction are all catalyzed by water. Water promotes microbial growth.

  The following dosage forms are impacted by moisture: solid dosage forms: dissolving rate, chemical stability, crystal structure, powder flow, compaction lubricity, and permeability of polymer films; semi-solid dose forms: microbial growth and thixotropy change.

  Furthermore, it is evident that the quantity and quality of water available affects unit operations.

  As a result, moisture affects the characteristics of specific excipients and active substances, therefore it is crucial to describe how moisture affects these specific parts.

- **Effect of light:** The medication molecules are significantly degraded when exposed to light. When molecules are exposed to electromagnetic radiation, they absorb particular wavelength photons of light, which increases their energy and can:

  ➢ Cause decomposition.
  ➢ Retained or transferred.
  ➢ Be converted to heat.
  ➢ cause the emission of light at a new wavelength. (fluorescence, phosphorescence).

  The wavelength range of natural sunlight is 290-780 nm, with only the higher energy (UV) region (290-320 nm) responsible for medication photodegradation.

4. **Reasons behind Stability Study**

- The active drug may undergo chemical degradation, resulting in a significant reduction in the quantity of the therapeutic agent present in the dosage form.
- Chemical degradation of the active drug may occur without extensive decomposition, potentially leading to the formation of toxic byproducts.
- Drug product instability can result in a reduction in its bioavailability, rather than the loss of the drug or the formation of toxic degradation products.
- Substantial alterations in the physical appearance of the dosage form may occur.
- Excipients such emulsifying agents, suspending agents, solubilizers, and antimicrobial preservatives may break down and compromise the integrity of the product, even though the medicinal material itself might remain potent.

5. **Advantages of Stability Studies**

- Stability studies are crucial for the well-being of patients suffering from the targeted disease.
- These studies ensure the integrity, potency, and purity of both individual ingredients and the final formulated products.
- Accelerated stability studies are conducted to determine the rate of product degradation when stored for an extended period under specific conditions.
- Forced degradation studies are undertaken to assess the impact of external stressors on the drug product.
- The primary purpose of a stability study is to provide substantiated evidence for establishing the drug's shelf life and recommending suitable storage conditions.
- Stability studies serve the purpose of identifying potential degradation pathways, including physical, chemical, or microbiological factors.

6. **Expiry Date or Shelf Life of Drug Product**

- Definition: The medication cannot be used beyond this date since its concentration has dropped below the therapeutic range. Furthermore, some drug breakdown products are poisonous and dangerous to patients.
- Shelf life, as defined by the International Conference on Harmonization (ICH) of Technical Requirements for the Registration of Pharmaceuticals for Human Use guidance document Q1A(R2) (ICH Q1A), is "the time period during which a drug

product is expected to remain within the approved shelf-life specification, provided that it is stored under the conditions defined on the container label."

- The expiration date, conventionally expressed as the last day of the month, signifies the date beyond which the product should not be used.
- The expiration date must be visible on both the immediate container and the outer retail packaging.
- When single-dose vials are sealed in separate cartons, the expiration date could be printed on the separate carton instead than the product container itself.
- Both the dry combination and the reconstituted product have expiration dates when a dry product needs to be reconstituted at the time of dispensing.
- Tamper-resistant packaging is utilized when applicable.
- Shelf life is typically indicated in months, such as 24 months or 36 months, with a maximum limit of 60 months.
- The terms "shelf life" and "expiry date" are often used interchangeably in the industry, as they both convey the concept of a finite period during which a product remains stable and safe for use, based on comprehensive stability research.
- Shelf life and expiration dates indicate how long a product will continue to work safely and effectively.
- This is why "shelf-life testing" is synonymous with "stability testing."
- The duration a product can maintain stability under specific environmental conditions defines its shelf life.
- Once a drug container is opened, the expiry date may be shorter due to factors like reduced drug concentration during use and the influence of external elements.
- Shelf life is also defined as the time required for the reactant's concentration to decrease to 90% of its initial concentration, denoted as t90 and measured in units of time/concentration.
- Shelf life encompasses the duration from the formulation's manufacturing and packaging date until its chemical or therapeutic activity remains at a predetermined level of labeled potency, with minimal to no noticeable alteration in its physical characteristics.

III. PROTECTION

Use of amber-colored bottles as protection. In addition to keeping the goods in a dark place, carton packaging serves as a physical obstruction to light. tablet coating with polymer films.