ICH GUIDELINES: STRESS DEGRADATION STUDY

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ABSTRACT

The ICH Guidelines were developed by the International Council for Harmonization (ICH) of Capacity of producing of Therapeutics for Human Use. The International Conference on Harmonization (ICH) aims to create uniform technical specifications for pharmaceuticals intended for human health. Various degrading conditions, such as light, oxidation, dry heat, acidic, basic, hydrolysis, and so on, are shown in the ICH guidelines. The forced degradation investigations are represented by ICH Q1A, QIB, and Q2B. degrading conditions, such as light, oxidation, dry heat, acidic, basic, hydrolysis, and so on, are shown in the ICH guidelines. The forced degradation investigations are represented by ICH Q1A, QIB, and Q2B. Stress degradation studies are a method for determining a drug's stability. These forced degradation studies can identify the drug's stability, which impacts the drug's purity, potency, and safety. Studies on forced degradation of drug molecules are very important to develop and validate a stability indicating method also to resolve stability-related problems.

Keyword: Introduction, Regulatory guidelines, degradation condition, Factors affecting stress condition.

INTRODUCTION

Stress degradation is a process in which varied stress conditions are applied to therapeutic compounds, leading to the production of various chemical compounds. Stress analysis or stress degradation studies are some other names for these experiments. The International Conference on Harmonization (ICH) standards make it necessary to perform stress degradation studies, and stress degradation of innovative medicinal products is clearly recommended. The stability of the molecule, various degradative mechanisms, and implementation of the proposed stability methods are examined utilizing forced decomposition experiments, according to the International Committee for Harmonization (ICH) recommendations. Stress testing, stress studies, stress decomposition studies, and forced decomposition studies are all terms are called as stress deterioration study. [1]

Stress Degradation studies are important in following aspects;

- Methods for determining stability are being developed.
- To investigate molecular physicochemical properties.

- To find out how drug substances and drug products degrade.

- To make formulations that are more stable.

- To determine the drug substance and drug product's degradation processes, such as hydrolysis, oxidation, thermolysis, or photolysis. [1, 2]

Stability testing is used to establish a re-test period for a drug substance or a shelf life for a drug product, as well as recommended storage conditions, and to provide evidence on how the quality of a drug substance or drug product varies over time under the influence of a variety of environmental factors such as temperature, humidity, and light. [3]

1.1 REGULATORY GUIDELINES: STRESS DEGRADATION STUDY

The Different international guidelines represent stress degradation studies. The ICH guidelines that are applicable to stress degradation studies are as follow;

1. ICH Q1A:- New Drug Substances and Products Stability Testing,

2. ICH Q1B:- Photo stability Testing of New Drug Substances and Products,

3. ICH Q2B:- Validation of Analytical Procedures: Methodology. [2, 4]

ICH Q1A:-

These guidelines are used to determine a drug's intrinsic stability**.** These guidelines will assist in the development of techniques for assessing medication stability. Degradation, according to Q1A, is dependent on the drug molecules and the type of the drug products**.** Stress testing of drug material can assist identify the most likely byproducts, which can then be utilized to establish the degradation processes and intrinsic stability of the molecule, as well as confirm the analytical techniques' stability indicating power. The stress testing will be largely dependent on the active ingredients and the regarding drug product involved. Forced degradation studies on drug compounds and drug products should be performed under the appropriate matters. The findings of temperature (above that for atmospheric pressure, i.e. >50 C), humidity (75 percent RH), oxidation, and photolysis should be examined. When evaluating a solution or suspension, a wide pH range should be calculated. Finally, these samples established a method for evaluating stability. [1, 2, 3]

ICH Q1B:-

In the sections on the necessity for forced degradation of medicines and regulatory guidelines, respectively, forced decomposition of drug molecules and their products were discussed. In confirmatory investigations, forced degradation experiments can be used to detect photolytic degradants. Normally in the stage of development, these techniques are employed to evaluate the photo stability of pharmacological compounds. These recommendations explain how to evaluate the photo stability of molecules being studied for stability test. Stress degradation parameters for drug material and drug product are given in Sections II and III, respectively. The exposure amounts in forced degradation experiments are unknown. Photo stability testing can be done on solids or in solution/suspension. These samples are then utilized to build a technique for determining stability testing. [1, 2, 5]

ICH Q2B:-

The ICH Q2B guidelines detail the procedures to be taken for the validation of various analytical methods. In section B 1.2.2 (impurities not accessible), it is suggested that samples from forced degradation experiments be used to show specificity. It adds that the samples should be stressed under a variety of accelerated circumstances, such as humidity and heat, before being utilized to determine specificity. In forced degradation studies, the ICH guidelines provide no recommendations on how much deterioration is necessary. Some degradation routes may not be seen if too little stress is applied, which would not affect the method's capacity to identify and monitor organic compounds during process

validation. When too much pressure is applied, artificial degradation products may appear, and the analysis approach used to identify them may be inappropriate for detecting realistic degradation products generated during stability testing. In Furthermore, these principles are beneficial for quantitative analysis of determining the degradants that are generated. [1, 2, 6]
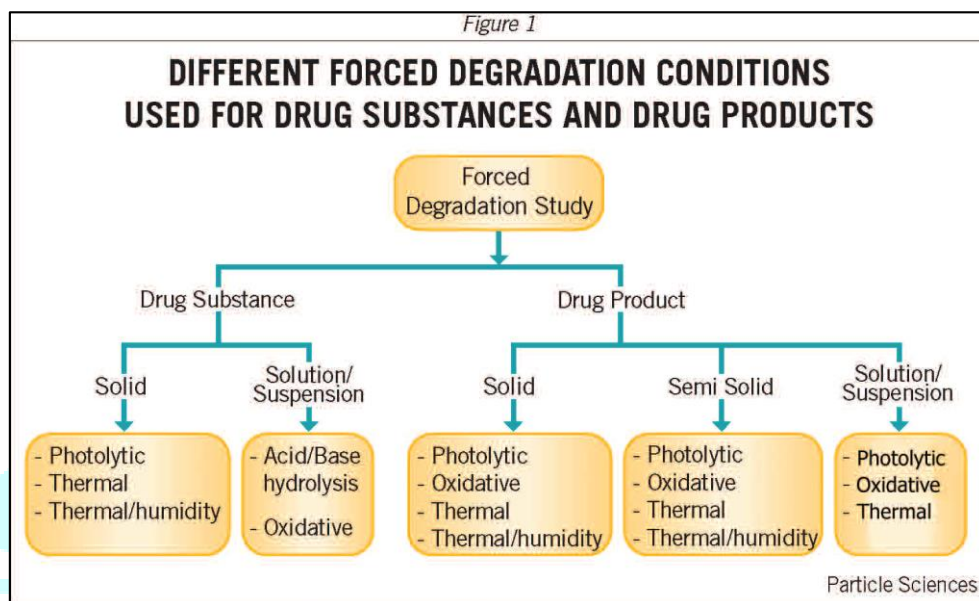
2.1 DEGRADATION CONDITION

Figure no 1 Different degradation condition

Hydrolysis: The breakdown of a Chemical substance by reaction with water is called Hydrolysis. Hydrolysis is a typical breakdown process that occurs when a chemical reacts with water at various pH levels. The medication interacted with water under acidic and basic conditions during forced degradation. The acid or basic concentration is chosen based on the stability of the medicinal ingredient. The class and amounts of acid or base used should be determined based on the stability of the drug ingredient. Hydrochloric acid or sulphuric acids (0.1-1 M) are recommended for acid hydrolysis, whereas sodium hydroxide or potassium hydroxides (0.1-1 M) are recommended for base hydrolysis. Drug compounds and pharmaceutical formulations in solution can be subjected to acid and base hydrolytic stress tests at room temperature or at higher temperatures. The type and concentrations of an acid and a base are determined by the pharmaceutical drug's stability. [2, 4, 8]

Oxidation: Auto oxidizers are present in the majority of pharmacological drugs.

For the oxidation reaction, they need free radical precursors. Free radical initiators include hydrogen peroxide, trace contaminants, and metal ions. The transport of electrons is involved in this form of deterioration. Hydrogen peroxide is often used for oxidative forced degradation. The drug ingredient determines the oxidizing agent to use, as well as its concentration and circumstances. Oxidative degradation can occur in drug substance solutions and solid/liquid drug products. In the oxidative breakdown of a pharmacological substance, an electron transfer process occurs. These tests should be carried out for 1–7 days at 40°C. It should be regarded abnormal if more than 20% of the degradants are generated. [1, 9]

Thermal Condition: Thermal deterioration (ex, dry heat and moist heat) should be performed under more difficult circumstances than those specified in ICH Q1A accelerated evaluation. A number of medicines have been discovered to be thermo labile in nature. The rate of the reaction tends to increase as the temperature rises, resulting

in the formation of degradation products. Dry and moist heat should be applied to samples of solid-state drug compounds and drug products. Dry heat should be applied to liquid medicinal preparations. Studies may be done at greater temperatures for a shorter length of time. These tests should be carried out at a temperature of 40–80°C. Thermal stress experiments generally last 1–2 months and are carried out at 70°C and heavy humidity. [1, 4, 10]

Photolytic Conditions: The pharmacological compounds are subjected to UV or fluorescent conditions in photolytic deterioration investigations. The drug compounds or active pharmaceutical (solid/liquid) are exposed to the light source in accordance with the ICH Q1B procedures in this investigation. The drug substance is not affected by light exposure, therefore photo stability testing is done. By exposing a pharmaceutical ingredient to UV or fluorescent light, photo stability investigations are carried out to create main degradants. The most frequent wavelength range for deterioration investigations is 300–800 nm. Degradation develops under photolytic conditions either to oxidation through an oxidative mechanism. Isomerization, dimerization, and other non-oxidative breakdown processes are involved. Singlet/triplet oxygen states are involved in the oxidative photolytic reaction. [2, 4]

3.1 FACTORS AFFECTING STRESS DEGRADATION

The following are the many factors that induce drug substance degradation. They are as follows:

- **Temperature:** Temperature changes might have a negative impact on the drug's stability. The rate of drug hydrolysis increases significantly as the temperature rises.

- **pH:** The rate of drug degradation through hydrolysis is significantly affected by pH. To overcome this, pharmaceutical formulations are carried out with pH-stable buffer solutions.

- **Light:** Several drugs are photo labile, because they disintegrate when exposed to light. The sensitivity to photolytic degradation can be determined by comparing the stability of the substance in the presence of light to the stability of the substance while stored in the dark.

- **Oxygen:** Oxidation of certain drugs is enhanced when oxygen is present. The Purifying nitrogen or carbon dioxide from the storage container stabilizes drugs that decompose more quickly in the presence of oxygen.

- **Moisture:** Water-soluble compounds may get absorbed in the presence of moisture. As a result, the molecule undergoes physical and chemical modifications. [1]

4.1 CONCLUSION

The stress degradation studies are used to determine the stability of drugs and to identify the degradants that are produced. The degradants produced are normally characterised in accordance with ICH guidelines. ICH Q1A, Q1B, and Q2B are the ICH guidelines that discuss stress degradation studies. ICH guidelines sometimes apply to the marketing applications for new drug substance. The physicochemical stability of drug ingredients and drug products can also be assessed using stress degradation studies. Stress degradation studies are the most common method for developing degradation pathways and identifying active component degradation products.

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