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A Review: Stability Studies of Pharmaceutical Substances and Products.

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ABSTRACT:-

Stability studies are an important aspect of medicine. Stability analysis and shelf life prediction are often important to pharmaceutical scientists in the development of any dosage form. It is also important for the development of small pharmaceutical products, especially considering the importance of the physical properties of the drug in determining the stability properties of the drug. Stability testing is used in product design to estimate shelf life, determine appropriate storage, and recommend written instructions.[1'2]It ensure that product quality, safety and performance are maintained throughout shelf life are considered a prerequisite for certification, information and approval of medicinal products. These studies must be carried out in accordance with the guidelines of ICH, WHO and/or other organizations.[3]The main purpose of drug stability research is to determine the shelf life of drugs during storage. Chemical stability is defined as "the ability of a given formulation to maintain its physical, chemical, microbiological, therapeutic and toxicological properties throughout its shelf life in a given container/closure system." As stated in the International Conference on Harmonization (ICH) guideline Q1A (R2), security research is generally a function of the main approach and agreement to management. There are many types of security surveys, and various methods can be used to determine security, such as instantaneous security assessment, rapid security assessment, storage security assessment model, and thermometer. pH and temperature are important factors affecting chemical stability. The pH value curve (log(k) vs. pH) is the pH dependence of a given rate constant for the degradation of a compound. Forced degradation involves the degradation of new drugs and products under conditions more severe than emergency and demonstrates the accuracy of safety reporting methods. Different conditions used during forced degradation include hydrolysis, oxidation, photolysis and thermal stress. Methods used to measure stability studies are LC-MS/MS, HPLC-DAD, HPLC-MS, HPLC-UV, HPTLC, TLC, LC-NMR etc.[4]

Keywords:- Stability, Stability Studies, and stability Testing [1'2], Types of stability studies, Stability guidelines.

Introduction:-

Stability of pharmaceutical products can be defined as the ability to preserve physical, chemical, microbiological, toxicological, protective and special information of a special design in a special container/closed system.[15]²Safety evaluation of pharmaceutical products is a complex process that requires significant cost, time and expertise to determine the quality, effectiveness and safety of pharmaceutical products. The scientific and commercial success of drugs can only be achieved by understanding the drug development process and the various tasks and activities important to the development plan. The most important steps in the development phase include chemical analysis and safety studies to determine and ensure the identity, potency and purity of the product as well as the ingredients.[15]¹The product retains its properties and characteristics within limits when packaged and used throughout the storage period. Therefore, safety assessment evaluates the impact of the environment on the quality of drugs or products, is used to estimate shelf life, determine appropriate storage and identify good writing tips. Additionally, the information generated during safety testing is important for regulatory approval of the drug or formula.[15]³Many factors affect the stability of pharmaceutical products; Due to their involvement security measures are considered a complex process. These factors are generally related to the stability of the active ingredients; Interactions between active ingredients and excipients, dosage form and manufacturing process, container/closure system used for packaging, humidity during heating, shipping, storage and handling.[16]¹Shelf life of pharmaceutical products is determined as the main objective of safety research. Stability refers to the allowable storage period before the product deteriorates in quantities sufficient to pose a risk to the patient. Determine the shelf life or expiration date of the product according to this period.[16]²

Objectives of Stability Testing:-

The purpose of stability testing is to provide information on how the quality of the drug changes under various environmental conditions such as temperature, humidity, light. Choose suitable models and closed boxes for safety to evaluate storage conditions and shelf life. Prove shelf life claims. Verify that there have been no changes in design or manufacturing that would affect the safety of the drug. The main purpose of safety research is to establish a safety profile in order to predict the shelf life of a medicinal product before it is placed on the market.

Why should products be tested for durability?

The physical, chemical and microbiological properties of medicinal products may vary as expected. For this reason; the shelf life of the product is examined during stability testing. The pharmaceutical industry performs this test to develop new products and determine the shelf life of products. Therefore, safety research is important for the pharmaceutical industry.

Determines Life: The quality of chemical products changes over time according to temperature, humidity and light intensity. Security investigations; how long the product can be stored in its original form and quickly without damage. This research helps determine the shelf life of the product. According to research, the shelf life of the product is fixed.

Storage Recommendations: Different products require different storage. Changes to storage and features are recorded in the security lab. Storage is recommended for certain products based on safety studies.

Removal of impurities: In safety testing, each product is analyzed according to various environmental factors. In this way, foreign substances that may occur during the shelf life of the product can be easily detected and eliminated.

Product Development: Safety testing is a reliable method to examine the effectiveness of new products. This test helps evaluate the physical, chemical and therapeutic stability of the product. Based on research, R&D experts redesign existing products and create new ones.

Quality assurance: Quality assurance is an important part of the pharmaceutical industry. The material is subjected to stress and the rate of decomposition is observed. Rigorous testing ensures ingredient purity and quality of the final product. Safety warnings ensure that pharmaceutical products are fit for human consumption. This gives the company the confidence to create new products in the market. The possibility of product returns may be reduced.

Selection of packaging materials: During stability testing, chemical products are exposed to moisture and temperature. Select the packaging material according to the effect of working water and the temperature of the product. The ideal container should be able to withstand pressure. Packaging must protect the quality of the product during transportation and storage.

Regulatory approval: Regulatory approval requires safety assessment of the medicinal product. If the product does not meet the quality standards set by ICH and WHO, the product will not be approved for marketing.[8]

How to do safety testing?

7 Safety testing below is the formula used to test the safety of cosmetics:

Step 1: Formulation of major substances: Production volume is calculated based on the number of samples used for testing. International Conference on Harmonization (ICH) guidelines say that three batches of a small part should be stable; This batch should represent the quality of products produced on a production scale.

Step 2: Packaged products: The product should be packaged in the appropriate environment and final packaging as per best practice is to check the box and final packaging during the security check. To accurately test products for ultimate stability, samples must represent a variety of batch sizes and shades, fragrances and formulations. The closure system must be the same as the packaging approved for storage and delivery.

Step 3: Pretest (zero time point). Once the prototype is completed, all products should be tested for further evaluation. The exact test depends on the specific product but minimum appearance, colour , pH, viscosity value and aroma need to be recorded. For aerosol products, spray patterns should be tested.

Step 4: Storage. Stability measurements require different temperatures. Some temperature ranges include: 40°C / 75% RH; 30 °C / 65% relative humidity; 25°C / 60% relative humidity; and 5 °C / relative humidity.

Step 5: Product Evaluation. For long-term studies, the frequency of evaluation should be sufficient to determine the stability of the sample. The testing frequency under long-term storage conditions is generally three months in the first year; every six months in the second year; and during the approved retest period each year thereafter. As rapid storage, it is recommended that at least three scores be obtained in a six-month study, including the starting point and end point (i.e., 0, 3, and 6 months). If it is thought that the data obtained from the rapid survey may lead to a significant change, the experiment should be increased by adding samples for the last time or by incorporating them into the design for the fourth time. When testing under intermediate storage conditions, there should be at least four time points starting from 12, including initial and final time periods (e.g. 0, 6, 9 and 12 months), as there is a large change in rapid storage conditions. months is recommended for training. one month.

Step 6: Make a firm decision. After the stability study period, it should be ensured that the structure is solid. If testing is unsatisfactory or unsatisfactory, further testing should be done. Since there will be some changes in almost all products, it will be up to the manufacturer to decide whether the product is finished or not.

Step 7: Final Instructions: Once the test is completed, a safety report must be prepared that includes: Identity of the laboratory performing the test (if a third-party operator was used); Product identification;Samples of packaging materials used in tests; Definition used to determine the process, operating conditions and operating results for the minimum durability of the product; Signature of the person conducting the study.[9]

Importance of Stability studies:

✓ The unstable yield of the active drug may be lower due to distortion of the dosage form.

✓ Toxic substances may be formed during the decomposition of chemicals or products.

✓ During transportation from one sales point to another, drugs mix and change their physical properties.

✓ Instability can be caused by physical changes in kinetics, there is a difference between kinetic and stability studies to estimate the stability of the drug.[5][4]

Guidelines for stability Testing:-

Regulatory authorities in many countries have established safety information provided by manufacturers to ensure that the most stable molecules and products are produced, distributed and made available to the public. First published in the 1980s, this guide covers basic security issues, secure application profiles, and steps for using them. The main goal is to ensure uniformity in testing among manufacturers. These are then harmonized (harmonised) at the International Council for Harmonization (ICH) with the aim of registering products in other countries and reducing trade barriers. Founded in 1991, ICH is a collaboration of industry and regulatory bodies in the European Commission, the United States and Japan that establish distinct standards for the quality, safety and efficiency of APIs and products. These guidelines are called quality, safety, efficiency, and multidisciplinary (also known as Q, S, E, and M) guidelines. The ICH guidelines do not address the extreme weather conditions observed in many countries, so the World Health Organization (WHO) updated these guidelines this year. 1996 and includes only new medicines and products, excluding countries where WHO produces specific products. advert. . In June 1997, the United States Food and Drug Administration (USFDA) also issued an advisory titled "Exclusion Date for Metal-Containing Oral Products." The ICH guidelines were later extended to veterinary products. The Association of Pharmaceutical Manufacturers of India also has a guide on the safety of drugs and products available in India. Information on active medicinal substances, medicinal products or preparations and supplements contains different conditions and regulations. The codes and topics covered by the ICH Guides are shown in Tables 1 and 2. The Committee on Clinical Practice (CPMP) of the European Agency for Medicines Evaluation (EMEA) has also introduced guidance on safety measures to support those seeking marketing authorization for medicines in the EU, as noted in the comments.[16]

ICH Codes	Guideline titles
Q1A	Stability testing of new drug substances and products.
Q1B	Photostability testing of new drug substances and products.
Q1C	Stability testing of new dosage forms.
Q1D	Bracketing and matrixing designs for stability testing of drug substances and products.
Q1E	Evaluation of stability data.
Q1F	Stability data package for registration applications in climatic zones 3 and 4.
Q5C	Stability testing of biotechnological/biological products.

Table 1.1:-Codes and titles used in ICH guidelines.[17]

CPMP Code	Guideline title
CPMP/QWP/576/96 Rev.1	Guideline on stability testing for applications for variations to a marketing authorization.
CPMP/QWP/6142/03	Guideline on stability testing for active substances and medicinal products manufactured in climatic zones III and IV to be marketed in the EU.
CPMP/QWP/609/96 Rev.1	Note for guidance on declaration of storage conditions for medicinal products particulars and active substances.
CPMP/QWP/122/02 Rev.1	Note for guidance on stability testing existing active substances and related finished products.
CPMP/QWP/072/96	Note for guidance on start of shelf life of the finished dosage form.
CPMP/QWP/2934/99	Note for guidance for In-use stability testing of Human medicinal products.
CPMP/QWP/576/96	Note for guidance on a stability testing for a Type 2 variation to a marketing authorisation.
CPMP/QWP/159/96	Note for guidance on maximum shelf-life for sterile products after first opening or following Reconstitution.

Table1.2:-CPMP guidelines on stability studies

Types of stability studies on drug substances.[5][4,5]

The Unified Pharmacopial Protocol (USP) has established standards for the recognition of physical, chemical, microbiological, medical research and toxicological stability.

Physical stability:-The stable body retains the same characteristics of the body, such as appearance, color, resolution, flavor and suspension. Physical stability can affect consistency and release rate and is therefore important for product efficiency and safety. Chemical stability is the effect of chemical resistance on weather conditions, temperature, etc. It refers to the tendency to change or decomposition due to influences. Microbiological Stability The

microbiological stability of a drug refers to its tendency to be sterile and microbial proliferation. Antimicrobial agents used in the formulation continue to work well.

Chemical stability :- It is the effect of chemical resistance on weather conditions, temperature, etc. It refers to the tendency to change or decomposition due to influences.

Microbiological Stability:- Microbiological stability of the drug refers to its tendency to be sterile and microbial proliferation. The antibiotics used in the preparation are still valid to a limited extent. This microbial instability can damage sterile pharmaceutical products.

Therapeutic stability:-The therapeutic effect (drug effect) remains unchanged.

Toxicological stability:-Toxicological stability has no significant increase in the toxicity occurs.[5]

Types of stability studies:-

Stability studies are used for testing the drug product for longer periods under varying conditions of temperature and Relative Humidity (RH). If the drug is to be distributed in different geographical regions and if shipping is required for transportation, in that case long term stability studies are of prime importance. Long term stability studies are performed by testing the sample at specific time intervals and conditions of external parameters are changed accordingly. Main objective of this study is to determine shelf-life of the drug product. There are four types of sustainability research such as long-term sustainability, medium sustainability, rapid sustainability and use of sustainability research. Types of research firms listed in Table 1 and their expectations regarding working hours.[7]

Type of stability studies	Storage conditions	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

Table1.3:-Types of Stability Testing.[7]

Stability Testing:- Stability testing is a routine procedure on medicines and products and is used at every stage of production. Based on the purpose and steps to be followed, the security assessment process is divided into the following three types:

1. long-term security stability.

2. Intermediate stability.

3.Accelerated stability.

Long-Term stability: - Immediate stability tests are usually performed in long-term tests to allow significant degradation of the product under approved storage conditions. Examine the run at 25°C / 60% RH or 30°C / 65% RH. Ideally, 12 months of data will be produced, but 6 months of data will be accepted to be sent to the registry, continuing until the end of its shelf life. To ensure parenteral stability of the drug, it should be stored in the refrigerator at 2-8°C. The test should be performed at 20°C.

Intermediate Stability Tests: - Interim studies are performed at 30°C / 65% RH and are designed to measure the degradation or physical change of the prepared drug over time. It can be stored at 25°C for a long time. In general, these studies are carried out. When it comes out: Fast runs are unacceptable under normal conditions (40°C / 75% RH). At best, 6 months of information should be created.

Accelerated stability Test: - In accelerated stability test, the product is subjected to stress at several high temperatures (higher than ambient temperature) and electrical equipment is required to disregard the goods. Recommended storage conditions for all products are 400C and 75% relative humidity in four zones for APIs and pharmaceuticals. This study lasts 6 months. Rapid storage conditions must be at least 150°C higher than the required storage temperature and have appropriate relative humidity.[6]

A method of exposing the product to high temperatures to simulate what would happen over a longer shelf life. The concept of velocity stability measurement is based on the Arrhenius equation.

$$\log k=\log A-Ea\div 2.303RT$$

Where, K= degradation rate/s,

A= frequency factor/s,

Ea = activation energy (kJ/mol),

R = universal gas constant (0.00831 kJ/mol),

T = absolute temperature.(K)

Depending on the parameters and estimated shelf life of specific pharmaceutical products, various stability studies are used to obtain analytical data to help companies convey product safety and conduct testing business for consumption.[6]

Safety Evaluation Procedures:-

To ensure the effectiveness of molecules and products manufactured, distributed, and administered to patients, regulatory authorities in some countries require departmental companies to provide safety information in their drug policies. Its main purpose is to increase competition between manufacturers. This process includes security-related issues, security requirements for data applications, and steps to implement them. These guidelines were first published in the 1980s. These were agreed upon at the International Conference on Harmonization (ICH) with the aim of overcoming market bottlenecks and registering products in other countries. ICH is an organization made up of regulators and industry officials from the European Commission, Japan and the USA. The World Health Organization (WHO) revised the guidelines in 1996 because the ICH guidelines did not address climate issues in many countries and only covered new drugs and products, and no products were produced under the WHO umbrella. In June 1997, the US FDA also issued a guidance document called "Expiration Dates for Oral Products." In 2004, the World Health Organization also published an international study on environmental sustainability guidelines.[1][4]The ICH guidelines were later extended to veterinary products. The Association of Pharmaceutical Manufacturers of India has also published a guideline on the safety of drugs and products available in India[1]''[2]

Climatic Zones for Stability Testing:-

For the purpose of stability testing, the world is divided into four zones (I-IV) based on the environmental conditions that the drug must meet during expiration. These factors are based on average annual temperature and relative humidity data for these regions. Based on this information, long-term or immediate stability test conditions and rapid stability test conditions were derived. [18]

.**Intended label storage condition**	**Stability studies**	**Storage condition**	**Submission requirements**
Room temperature	Long term Intermediate Accelerated	25°C/60%RH 30°C/65%RH 40°C/75%RH	12 months 6 months 6 months
Refrigerator	Long term Accelerated	5°C/Ambient 25°C/60%RH	12 months 6 months
Freezer	Long term	-20°C/Ambient	12 months

*Test only if there is significant change at 40°C/75%RH

Table1.4:-Climatic zones for stability Testing

Climate zones and stability study conditions:-

It defined in ICH Guidelines Climatic conditions change as you move around the world, meaning that climatic conditions are different in different parts of the world. The safety of pharmaceutical products is affected by security. Therefore, the safety of medical products must be investigated by taking into account the climatic conditions of the country. According to the ICH Stability Study Guidelines, the global climate is divided into four zones (Regions I, II, III, IV). Region IV is divided into Region IV A and Region IV B.[18]

Climatic zones	Climate defination	Major countries/Region	MAT/mean annual partial water vapour pressure	Long term testing conditions
I	Temperature	United kingdom,Northern,Europe,Russia,United states	<15°C/11hPa	21°C/45%RH
II	Subtropical and mediterranean	Japan,Southern,Europe	>15-22°C/>11-18hPa	25°C/60%RH
III	Hot and dry	Iraq,india	>22°C/11hPa	30°C/35%RH
IV a	Hot and humid	Iran,Egypt	>22°C/15-27hPa	30°C/65%RH
IV b	Hot and very humid	Brazil,Singapore	>22°C/27hPa	30°C/75%RH

*MAT-Mean annual temperature measured in open air.

Table1.5:-Climatic zones and long term stability conditions.

Stability studies:-

The purpose of stability testing is to provide evidence of the quality of the API or preparation change over time under the influence of various environmental factors such as temperature, humidity and light and to determine the high turnaround time for the API or planning. Shelf life and recommended storage of drugs or drug products. Due to different climatic conditions in different countries, there is a need for security studies to be carried out in many health centers "against weather conditions" in conditions similar to their own "region". There are also ICH safety assessment procedures that must be followed for general acceptance of the study. You can see them here.[11]

ICH Stability Zones

Zone	Type of climate
Zone I	Temperature zone
Zone II	Mediterranean/Subtropical zone
Zone III	Hot Dry zone
Zone IV a	Hot Humid/Tropical zone
Zone IV b	ASEAN Testing Conditions hot/higher humidity

Table1.6:-ICH Stability Zones.

Long Term Testing Conditions

Climatic zone	Temperature	Humidity	Minimum Duration
Zone I	21°C ±2°C	45%RH±5%RH	12 Months
Zone II	25°C ±2°C	60%RH±5%RH	12 Months
Zone III	30°C ±2°C	35%RH±5%RH	12 Months
Zone IV a	30°C ±2°C	65%RH±5%RH	12 Months
Zone IV b	30°C ±2°C	75%RH±5%RH	12 Months
Refrigerator	5°C ±3°C	No Humidity	12 Months
Frozen	-15°C ±5°C	No Humidity	12 Months

Table1.7:-Long Term testing conditions.

Accelerated and Intermediate Stability Conditions

Climatic zone	Temperature	Humidity	Minimum Duration
Accelerated Ambient	40°C ±2°C	75%RH±5%RH	6 Months
Accelerated Refrigerator	25°C ±2°C	60%RH±5%RH	6 Months
Accelerated Frozen	5°C ±3°C	No Humidity	6 Months
Intermediate	30°C ±2°C	65%RH±5%RH	6 Months

Table1.8:-Accelerated and intermediate stability conditions.

Stability studies conducted determined the shelf life of the medicinal product, the drug retest period and appropriate storage conditions. Robust research is needed to ensure patients receive safe and effective medications.

Stability Study Protocol: -

Stability study is one of the drug development processes. Data security obtained from security studies is used to determine the storage and packaging information of products planned in large quantities. Stability studies are used to determine the shelf life of products.

This security process is a prerequisite for security research and requires a written document containing a description of security management and quality control. Each prescription has a different type of packaging, so the process also depends on the type of medication. The process may also depend on drugs and new preparations available on the market.[14]

The process should reflect the areas identified by ICH. A proper safety study should include the following information:

1. Number of Batch.
2. Containers and Seals.
3. Container storage direction.
4. Sampling time point .
5. Test storage conditions.
6. Test parameters.

1. Batch Number :-

Stability tests are performed in batches since it is difficult to examine the stability in a single step and therefore they are divided into groups. Group safety studies are carried out for products that are stable and do not show any side effects. When new drugs are licensed, safety studies are conducted in three groups when the products are unstable or unstable. When the product is not stable, the relevant six products are checked for stability and if stability does not re-establish, all products produced must be discarded as unmanageable. Initial data are not for all products, the first three groups need to be done after approval, they are long-term studies using the same rules as in the approved drug application. Data collected from the laboratory is not considered preliminary safety data. Batch selection facilitates random sampling of samples from the population of a pilot or production batch.

2. Containers and seals:-

The selection of containers and seals is very important and the safety of containers and seals is little investigated when goods are to be packed in suitable box. Packaging materials include aluminum tape packaging, bubble wrap, aluminum foil packaging, HDFE bottles, etc. takes place. This also includes secondary packaging, but does not include the supplier. All packaging has been checked for safety as incorrect packaging can cause physical harm. Containers are allowed for bulk containers. When the packaging is completed, place the prepared medicine in the appropriate container, because the containers will be contaminated and the shelf life of the medicine will be shorter than it actually is.

3. Container storage condition:-

solutions for samples and semi-finished products used for safety research should be placed upright, ensuring that the product comes into contact with the container. This will help understand the chemical changes the drug makes when it comes into contact with the container, leading to its degradation.

4. Sample time points:-

Evaluation of specific times is crucial for determining the stability properties of new drugs. Products with a shelf life of a few months in the first year, 6 months in the second year, and an estimated shelf life of each year thereafter. In case of vetting there are at least three time points such as 0, 3 and 6 months. In this case, the same product comes in different strengths, sizes, etc. when tested. Security tests with small details can be used. Mitigation schemes are based on cluster and matrix statistical designs. Bracketed design is only possible if some design elements of the model, such as power and ball size, are tested with all models at three time points. Factors that can form matrices may include usage, batch size, batch size, and average time points. Examples of environment, time and selected climatic zones [3,16] are shown in below Table.

Environment	**Sampling time points(months)**	**Methods and climatic zones**
25°C/60%RH	3,6,9,12,18,24,36	Long term for zones I and IV
30°C/35%RH	3,6,9,12,18,24,36	Long term for zones III
30°C/65%RH	3,6,9,12,18,24,36	Long term for zones IVa Or Intermediate conditions for zone I and II
30°C/75%RH	3,6,9,12,18,24,36	Long term for zones IVa Or Intermediate conditions for zone I and II
40°C/75%RH	3,6,9,12,18,24,36	Accelerated condition for all zones

Table1.9:-Test schedule of testing stability for new products

5. Test storage conditions:- Select storage conditions according to the climatic zone in which the product will be sold. ICH, CPMP and WHO have provided general guidelines for storage. Storage of medicinal products for ICH and WHO safety studies is shown in below Tables .

Intended Storage Condition	**Type of Stability Studies**	**Storage Conditions for**					
		ICH			**WHO**		
		Temperature (°C)	**RH (%)**	**Time (Months)**	**Temperature (°C)**	**RH (%)**	**Time (Months)**
Room Temperature	Long Term	25±2°C	60±2°C	12	25±2°C	60±2°C	12
		30±2°C	65±2°C				
	Intermediate	30±2°C	65±2°C	6	--	--	--
	Accelerated	40±2°C	75±2°C	6	--	--	--
Refrigerator	Long Term	5±2°C	---	12	5±3°C	--	
	Accelerated	25±2°C	60±2°C	6			
Freezer	Long Term	-20±2°C	---	12	-20±2°C		

*Relative Humidity(RH)

Table2.0:-Stability study storage condition for drug products.

6.Test Parameters:- Test parameters used in security studies should be evaluated according to security standards. Testing of the sample usually depends on the weather conditions for quality, purity, performance, properties, etc. Contains. Therefore, symptoms, laboratory tests, degradation products, microbiological tests including sterile and antibiotic tests, etc. Safety measures should be based on indicators such as heavy metals, electronic products and residual solvents.[14]

Security research tools:- Tools used for security testing are called security laboratories. They are special environments that simulate storage conditions and enable stable products to be analyzed in terms of instant, rapid and long-term processes. They come in both walk-in and walk-in styles. Smaller rooms

are better for faster testing because the storage period for these products is shorter, while walk-in rooms are better for long-term testing. Such chambers or chambers are designed and necessary to ensure uniformity of the problem for all models in the room. Since they need to be used continuously for many years, these units must be reliable and durable. It is equipped with the necessary information, security and alarm. Additionally, light-stabilized chambers are available and can be used with or without temperature control. Light stabilized rooms generally use two types of lighting; one is a combination of cold light and near-UV fluorescent light, the second is artificial sunlight such as xenon or metal halide. It must have a total exposure of 1.2 million lux hours. Use a lux meter to estimate visible light. Calculate how many hours of exposure are required.[18]1''2Shelf life Estimated shelf life is determined based on data obtained from long-term storage studies. The data were first linearized and goodness-of-fit testing was used. The linearized data is then analyzed to determine the slope and intercept. The differences between the time profile examples for the three groups are shown in below Table. The data is compiled and used to estimate slopes.[1] Statistical tests such as tests should be used to determine the significance of the difference in slope or intercept.

Slope	**Intercept**	**Variation Factor**	**Pooling**
Identical	Identical	Nil	Yes
Identical	Different	Batch,for example unequal initial drug concentrations	No
Different	Identical	Storage,for example difference in the rate of drug loss	No
Different	Different	Interactive forces-both batch and storage factor	No

Table2.1:-Pattern of concentration :Time data and pooling decision.

Evaluation of Safety Studies:-

A method should be adopted to evaluate safety studies, which will include the results of physical, chemical, biological and microbiological tests and even the dosage form of the drug. These tests help understand product degradation by analyzing the data obtained during testing. If the analysis shows little variability from batch to batch, it may be better to combine all data into a single estimate. By analyzing data as an object begins to deteriorate, it is apparently possible to predict its shell life.

Current Trends in Stability Studies:-

The current trend in stability studies of multinational pharmaceutical companies is to determine the requirements of stability tests for the world business. For this reason, companies have updated their regulations regarding processes covering the environment. Specific changes to the international test include increasing the rapid assessment period from 6 months to 12 months and an additional 3 months of assessment at 50°C / 75% relative humidity. The idea behind this change is to avoid competition between security tests in other areas and to use resources efficiently and effectively, since all tests are performed in a single laboratory. It is also reported that experiments conducted with a combination of three environmental conditions (temperature, humidity and light) cause more damage to drugs, chemicals and products than temperature and humidity alone one.[18]1''2'3'4'5'6

Conclusion:-

Safety assessment is an important part of the development of new drugs and new drug applications, as well as an important part of the drug development process. Safety evaluation of pharmaceutical products is an important part of the involvement of new drugs and new developments. Stability studies can distinguish useful chemicals from degradation products produced as expected. It is best to begin degradation studies as early as possible in the drug development process to allow sufficient time to obtain more information about the stability of the molecule. This information helps improve the formulation manufacturing process and determine storage conditions. At the same time, regulations are becoming stricter to achieve the above objectives, such as with more knowledge and attention, all the possibilities that products will meet during their shelf life. Therefore, safety assessment should be based on a good understanding of scientific standards and existing regulations and the climate.[10]Product safety studies are an important process in new drugs and innovations. Any differences in security design will affect its quality, security and performance. To ensure the drug is safe and effective throughout its shelf life, safety tests are performed to recommend storage and shelf life on the label. For this reason, security assessment must be based on correct research methods and made according to current legislation and climate.[c]

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