Dosage Form Stability

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Drug Stability

- Is the extent to which a product retains within specified limit the same properties and characteristics throughout its shelf life.

Mechanism of Drug Degradation

Hydrolysis

- Also termed Solvolysis in which drug interacts with water and leads to the decomposition of the drug.
- Example: Aspirin acetylsalicylic acid in presence of water breaks down to salicylic acid and acetic acid.

Oxidation

- Occurs under the influence of atmospheric oxygen proceeds slowly at first and then more rapidly.

Methods to Enhance Product Stability affected by Hydrolysis

1. Elimination of water: e,g antibiotics to be reconstituted with water at time of dispensing.
2. Use of buffering agents to maintain a certain pH.
3. Protection from humidity if drug is moisture sensitive by
   1. Waterproof coating
   2. Use of tightly closed container.
   3. Replacing water with non-aqueous solvent

Methods to Enhance Product Stability affected by Oxidation

1. Antioxidants: ascorbic acid and sodium sulfite.
2. Preparation and storage under oxygen free atmosphere.(vials and ampules).
3. Chelating agents e.g calcium disodium edetate. EDTA
4. Packaging in light resistant or opaque containers.
5. Storage of oxidizable drugs in a cool place.

Stability Concerns

1. Chemical. Important in selecting storage conditions(temperature, light, humidity, container choice (amber)
2. Physical: appearance, palatability, uniformity, dissolution.
3. Microbiologic: sterility and resistant to microbial growth
4. Therapeutic
5. Toxicologic

Shelf Life Estimation "Q_{10} Method"

- Pharmacist can estimate the shelf life of a product that is going to be stored or has been stored under a different set of conditions.
- See example in textbook Physical Pharmacy Capsule 4.19 page 148-149.
- Reasonable estimate can be made using a value of 3 for Q_{10}.

- FDA's Current Good Manufacturing Practice Regulation (GMP) include a section on stability.
- Following FDA product approval and initial marketing, pharmaceutical manufacturers retain product samples for 5 years or longer and continue studies for signs of degradation under various conditions of storage.

Stability Testing

- Before Approval for Marketing product stability must be assessed with regard to

1. Formulation
2. Influence of pharmaceutical ingredients
3. Influence of container and closure
4. Manufacturing and processing condition e.g heat
5. Packaging components
6. Condition of storage and shipping
7. Condition of pharmacy shelf life and patient use.

Accelerated Stability Studies

- Studies designed to increase the rate of chemical degradation or physical change of a drug substance or drug product by using **exaggerated** storage conditions as part of long-term, intermediate and accelerated studies. A refrigerator/ freeze cycle is also studied.

Accelerated Stability Conditions

Study design	Storage condition	Minimum time period covered by study for submission of data
Long term*	25°C±2°C/60% RH±5% or 30°C±2°C/65% RH±5%	12 months (choice-1) or 6 months (choice-2)
Accelerated	40°C±2°C/75% RH±5%	6 months
Intermediate**	30°C±2°C/65% RH±5%	6 months

*= Alternate long term' stability condition based on feasibility, **= Alternate stability study condition (i.e. Intemediate) in case the drug substance/ product fails to meet the specifications at 'Accelerated stability condition, RH= Relative humidity

http://www.archivepp.com/article.asp?issn=2045-080X;year=2015;volume=6;issue=3;spage=48;epage=57;aulast=Khan