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Stability study "Kinetic study"

- Measuring [drug] at given intervals under a specific set of conditions, (Temp, pH, ionic strength, light intensity).
- The measurement of [drug] at the various times reveals the stability or instability.
- Each of the original conditions may be varied to determine the influence of such changes on the drug's stability.
- The findings may be presented graphically, by plotting [drug] vs time. From the experimental data, the reaction rate may be determined and a rate constant and half-life calculated.

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Accelerated Stability Studies

- Provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors, such as:
  - Temperature,
  - Humidity,
  - Oxidation,
  - Light
  - Microbial exposure.
- Establish the shelf life for a drug product and recommended storage conditions.

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Forced degradation studies

- Dry heat exposure
- UV radiation exposure
- Influence of pH
- Influence of temperature
- Influence of ionic strength

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- ***Expiration date:*** The date placed on the container label of a drug product designating the time prior to which a batch of the product is expected to remain within the approved shelf life specification, if stored under defined conditions, and after which it **must not be** used.
- ***Shelf life*** *(also referred to as* ***expiration dating period****):* 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.

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Arrhenius Equation

- Arrhenius equation is used for studying the effect of temperature on solution at controlled conditions.
- The fractions of remaining drugs are assayed using UV, HPLC (the best?).
- After determination of the rate constant at 25°C, the shelf life can be calculated using the equation: $t_{10\%} = 0.105/K_{25}$
- Depending on the results, we can decide if, the drug can prepared in soluble, stable and effective form or not.

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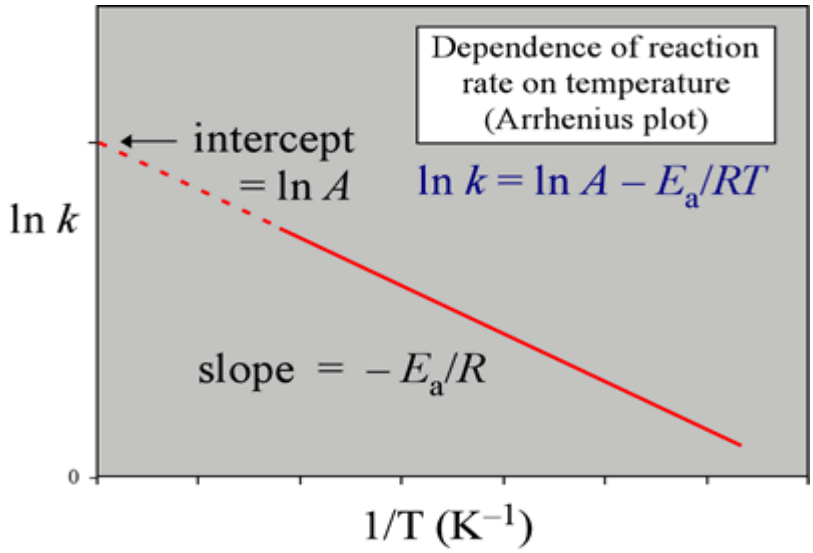

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Steps of stress testing

- Step 1: Calculate **K** value at different temperature

Graph **Log Concentration** vs **Time**

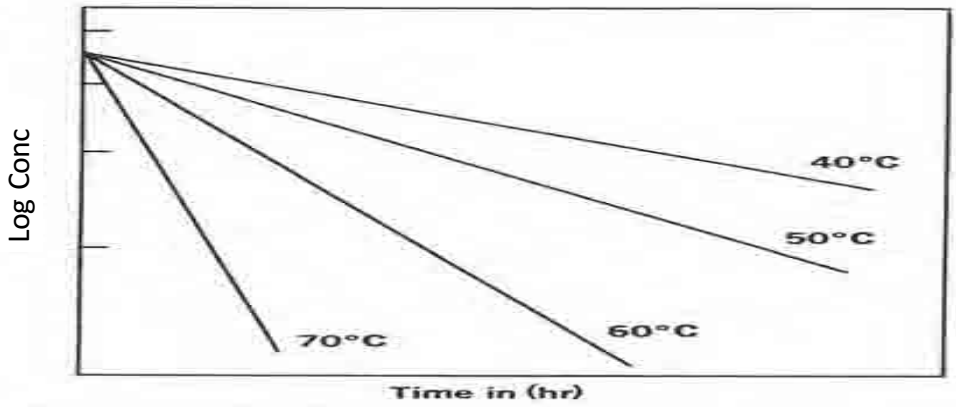

Fig. 14–19. Accelerated breakdown of a drug in aqueous solution at elevated temperature.

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Steps of stress testing

- Step 2: Calculate K_{25} from:

Graph **Log K** vs **1/Abs Temp**

- Step 3: Calculate $t_{90\%}$ from equation :

$t_{90\%} = 0.105 / K_{25}$

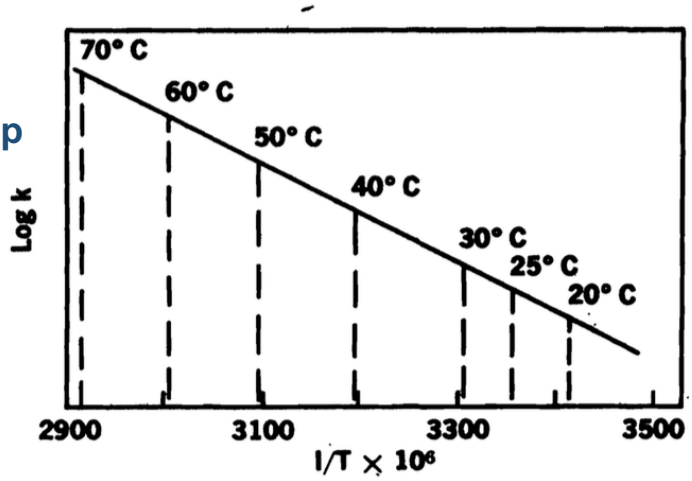

Fig. 12–21. Arrhenius plot for predicting drug stability at room temperatures.

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Q_{10} Method of Shelf life Estimation

- At two temperature the equation will be:

$$\log \frac{k_2}{k_1} = \frac{E_a}{2.303R}\left(\frac{T_2 - T_1}{T_2 T_1}\right)$$

$$t_{90}(T_2) = \frac{t_{90}(T_1)}{Q_{10}^{(\Delta T/10)}}$$

- Q_{10} is : ……

$$Q_{10} = \frac{k_{(T+10)}}{k_T} \qquad Q_{10} = \exp\left[-\frac{E_a}{R}\left(\frac{1}{T+10} - \frac{1}{T}\right)\right]$$

- Ea ranges from 12-24 Kcal/mole so Q_{10} will be 2-4 when Temperature increased from 20° to 30°, How?

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What or Who is ICH?

- **ICH** stands for **I**nternational **C**onference on **H**armonization of Technical Requirements for Registration of Pharmaceuticals for Human use

Objectives of ICH

- Harmonization of registration applications within the three regions of the EU, Japan and the United States.
- ICH is a joint initiative involving both regulators and industry as equal partners in the scientific and technical discussions of the testing procedures which are required to ensure and assess the safety, quality and efficacy of medicines.

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