

Drug Stability

Drug Stability

Definition

- Drug stability refers to the ability of a pharmaceutical product to maintain its physical, chemical, microbiological, therapeutic, and toxicological specifications throughout its shelf life.
- A drug degrades over time due to:
 - Chemical reactions (e.g., hydrolysis, oxidation, photodegradation)
 - Environmental factors (light, temperature, humidity)
 - Interaction with excipients or container

Types of Stability:

- **Chemical Stability:** Ensures the drug substance retains its chemical integrity and labeled potency.
- **Physical Stability:** Maintains the physical properties (appearance, palatability, dissolution, etc.).
- **Microbiological Stability:** Ensures sterility or resistance to microbial growth.
- **Therapeutic Stability:** Drug continues to exert its intended therapeutic effect.
- **Toxicological Stability:** No increase in toxicity over time.

Factors Affecting Drug Stability:

- **Temperature:** Higher temps can accelerate degradation.
- **pH:** Extreme pH can promote hydrolysis or oxidation.
- **Light:** Some drugs are photosensitive.
- **Oxygen:** Can lead to oxidative degradation.
- **Moisture:** Facilitates hydrolysis.
- **Container and packaging:** Interaction with packaging materials may destabilize the drug.

Stability Testing:

- Stability testing involves subjecting the drug to different environmental conditions to determine its shelf life and proper storage conditions.

Reaction Kinetics and Its Relevance to Drug Stability

- **Reaction kinetics** is the study of rates at which chemical reactions occur.

- In pharmaceuticals, it helps:
 - Predict how long a drug remains stable
 - Design appropriate storage conditions
 - Optimize formulations
 - Set **expiration dates**
- A general rate law expresses how the rate of reaction depends on the concentration of reactants.

General Rate Law:

$$\text{Rate} = -\frac{d[A]}{dt} = k[A]^n$$

- Where:
 - $[A]$ = concentration of drug
 - k = rate constant
 - n = order of reaction (can be 0, 1, 2...)
 - $\frac{d[A]}{dt}$ = rate of disappearance of A over time

Types of Reaction Orders

Zero-Order Reactions

- **Definition:** Rate of degradation is **independent of concentration**.
- **Rate law:**

$$\text{Rate} = -\frac{d[A]}{dt} = k$$

- Separate variables:

$$d[A] = -k dt$$

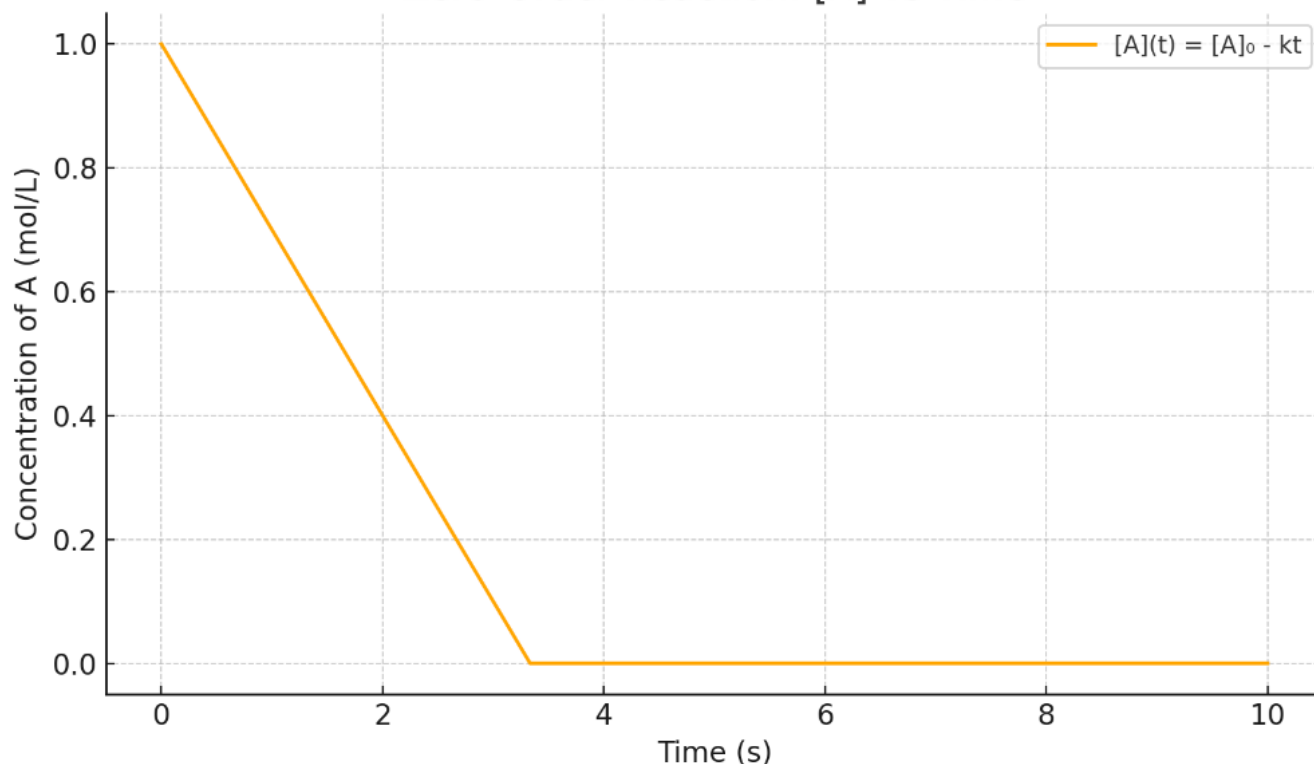
- Integrate both sides:

$$\int_{[A]_0}^{[A]} d[A] = -k \int_0^t dt$$

$$[A] - [A]_0 = -kt$$

- **Graph:** Plot of $[A]$ vs. time = straight line with slope = $-k$

Zero-Order Reaction: [A] vs Time



- **Example:** Decomposition of drug in a suspension (saturated solution), where concentration remains constant.

Features:

- Constant degradation per unit time
- **Half-life depends on initial concentration:**

$$t_{1/2} = \frac{[A]_0}{2k}$$

- **Shelf life (t_{90}):**

$$t_{90} = \frac{0.1[A]_0}{k}$$

Pseudo-Zero Order Reactions

- Not a true kinetic order, but **appears zero-order** due to constant concentration of one or more reactants.
- Occurs when a reactant is in large excess or is replenished (e.g., oxygen or water in excess).
- Often used in formulation studies where degradation appears to follow zero-order despite being inherently higher order.

First-Order Reactions

- **Definition:** Rate of degradation is proportional to the concentration of the drug.



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