Plasma Half-Life of Drugs

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Overview

Definition

- Plasma half-life ($t_1/_2$) = Time required for the plasma concentration (or amount of drug in the body) to decrease by 50% after reaching its peak level.
- Reflects how quickly the body eliminates a drug.

Types

- α (Alpha) $t_1/_2$ → Distribution Half-Life: Time for drug to distribute between plasma and tissues.
- β (Beta) $t_1/_2$ → Elimination Half-Life: Time for the drug to be removed from the body during the elimination phase.

Formula for Determination

$$t_1/_2 = 0.693 \times Vd / Cl$$

Where:

- Vd = Volume of distribution
- Cl = Total body clearance

🔁 Flow of Events

Drug Administration → Absorption into Blood → Distribution into Tissues → Metabolism (mainly Liver) → Excretion (mainly Kidneys) → Plasma Concentration Falls → Half-life Reached (↓50%)

📊 Factors Affecting Plasma Half-Life

Factor	Effect / Explanation	Examples
Pharmacokinetic Pattern of Elimination	Determines how drug concentration declines over time	First vs. Zero Order Kinetics
Hepatic or Renal Disease	↓ Clearance → ↑ Half-life	Almost all renally/hepatically excreted drugs
Active Metabolites	Metabolite may prolong effect	Aspirin, Fluoxetine, Diazepam

Enterohepatic Circulation	Reabsorption prolongs duration	Rifampicin, Doxycycline
Plasma & Tissue Protein Binding	High binding = slow elimination	Highly protein-bound drugs
Volume of Distribution (Vd)	↑ Vd = ↑ $t_{1/2}$	Chloroquine (stored in tissues)

⚖️ Pharmacokinetic Patterns of Drug Elimination

◈ First-Order Kinetics

- Fixed fraction of drug eliminated per unit time.
- Elimination ∝ Concentration (rate decreases as concentration falls).
- Half-life remains constant.
- Example: *Most drugs.*

Flow:

Drug concentration ↑ → Faster elimination
Drug concentration ↓ → Slower elimination

◈ Zero-Order Kinetics (Saturation Kinetics)

- Fixed amount of drug eliminated per unit time.
- Elimination independent of concentration.
- Half-life increases with higher doses.
- Examples: Phenytoin, Alcohol, Salicylates

Flow:

Low dose → Enzymes unsaturated → First-order
High dose → Enzymes saturated → Zero-order

📉 Comparison Table

Parameter	First-Order	Zero-Order
Elimination pattern	Constant fraction per time	Constant amount per time
$t_1/_2$	Constant	Increases with dose

Example drugs	Most drugs	Phenytoin, Alcohol, Salicylates

🧠 Clinical Significance of Plasma Half-Life

Concept	Explanation / Importance
Rate of Elimination	Indicates how quickly drug leaves body
Duration of Action	Drugs with long $t_1/_2$ act longer
Dosing Interval	Determines how frequently doses are given
Time to Reach Steady State	≈ 4–5 half-lives
Therapeutic Drug Monitoring (TDM)	Adjust dosing in patients with altered clearance
Active Metabolites	May extend clinical effects

⏱️ Time to Steady-State & Elimination

No. of Half-Lives	Drug Remaining (%)	Drug Eliminated (%)
0	100	0
1	50	50
2	25	75
3	12.5	87.5
4	6.25	93.75
5	3.125	96.875

Flow:

1 $t_1/_2$ → 50% eliminated

2 $t_1/_2$ → 75% eliminated

3 $t_1/_2$ → 87.5% eliminated

4–5 $t_1/_2$ → ≈ 95–97% eliminated (≈ steady state)

⏳ Examples of Plasma Half-Life ($t_1/_2$)

Drug	Approximate Half-Life

Esmolol	10 minutes
Aspirin	25 minutes
Acetaminophen	2 hours
Atenolol	6 hours
Clonidine	12 hours
Lithium Carbonate	22 hours
Digoxin	39 hours
Chloroquine	1-2 months

💬 Quick Recap Flow

Dose given → Drug absorbed → Distributed to tissues → Metabolized & excreted → Plasma levels fall → $t_1/_2$ = time for 50% reduction → Guides dose interval, duration, and steady-state time