

Exercise walk-through

11.1

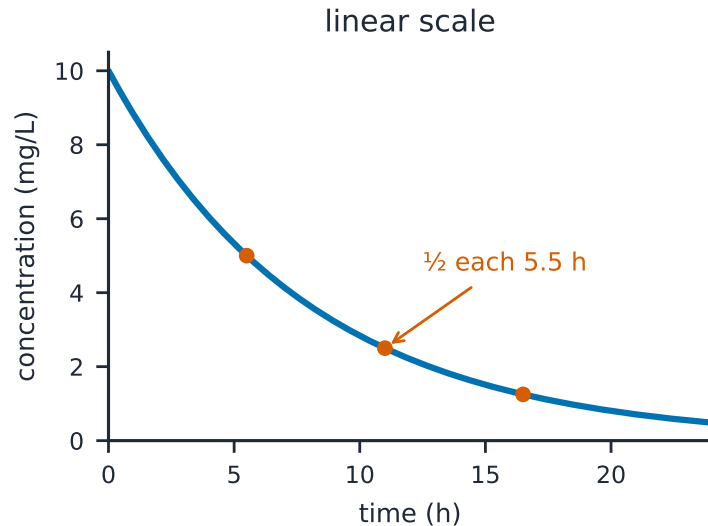
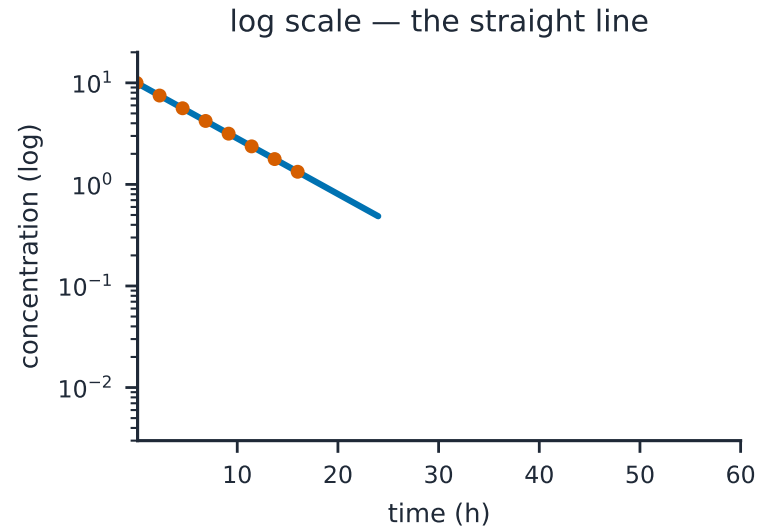
Pharmacokinetics

University Medicine

Pharmacokinetics: three levers

- 1 **Levers** $t_{1/2} = 0.693 \times V_d/CL$ (illustrative V_d 40 L, CL 5 L/h $\rightarrow$ 5.5 h; CL halved $\rightarrow$ 11.1 h).
- 2 **Steady state** $\sim 90\%$ at 3.3 half-lives, $\sim 97\%$ at 5; loading = $C_{target} \times V_d/F$ (10 mg/L $\times$ 40 L = 400 mg illustrative).
- 3 **First pass** F = fraction past the liver: 100 mg oral at F 0.6 delivers 60 mg; liver bypass raises F .

Concentration–time curves



$t_{1/2} = 0.693 \cdot V_d / CL$ · steady state $\approx 90\%$ at $3.3 t_{1/2}$, 97% at 5 · loading = $C_{target} \cdot V_d / F$

Half-life is the log-linear slope; **steady state** after ~ 4 - 5 half-lives.

Exercises 2.1-2.3

2.1 State the half-life formula with all three symbols named. [3]

2.2 What fraction of steady state is reached at 5 half-lives? [3]

2.3 V_d 20 L, CL 4 L/h – compute $t_{1/2}$. [3]

Exercises 2.1-2.3

2.1 State the half-life formula with all three symbols named. [3]

2.1

- $t_{1/2} = 0.693 V_d / CL$: apparent volume, volume cleared per hour ✓.

2.2 What fraction of steady state is reached at 5 half-lives? [3]

2.2

- ~97 % (90 % at 3.3) ✓.

2.3 V_d 20 L, CL 4 L/h – compute $t_{1/2}$. [3]

2.3

- $0.693 \times 20 / 4 = 3.5$ h ✓.

Exercise 3.1

3.1 An illustrative drug: V_d 60 L, CL 3 L/h, oral $F = 0.5$.

Compute $t_{1/2}$ ($0.693 \times 60 / 3 = 13.9$ h); time to ~97 % steady state on a fixed schedule ($5 \times 13.9 \approx 69$ h); and a loading dose for a target of 8 mg/L ($8 \times 60 = 480$ mg, illustrative) ✓. State how each answer changes if CL falls by half ✓. [8]

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3.1

- $t_{1/2} = 0.693 \times 60 / 3 = 13.9$ h ✓.
- 97 % at 5 half-lives ≈ 69 h ✓.
- Loading: 8 mg/L $\times$ 60 L = 480 mg (illustrative) ✓.
- CL halved: $t_{1/2}$ doubles to 27.7 h, steady state later, levels higher on the same schedule ✓.

Exercise 3.2

3.2 Two illustrative oral formulations of the same drug: A with $F = 0.9$, B with $F = 0.5$.

Explain what first-pass extraction differs between them, and compute the labelled circulating amount from a 200 mg dose of each (180 mg vs 100 mg) ✓. Predict what happens to B's effective exposure if the first pass is bypassed ✓. [7]

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3.2

- First pass: liver extraction differs – B loses 50 %, A 10 % ✓.
- $200 \text{ mg} \times 0.9 = 180 \text{ mg}$ vs $200 \text{ mg} \times 0.5 = 100 \text{ mg}$ circulating ✓.
- Bypass removes the extraction: B's F rises toward 1.0 and exposure grows on the same tablet ✓.