Pharmacology – how drugs behave in the body

0.1.1 Phramacokinetics (PK)

Movement of drugs in the body

0.1.2 Pharmacodynamics (PD)

Body's response to drugs

We will focus more on PK (movement of drugs)

- absorption
- distribution
- elimination or clearance

FDA - Federal Drug Administration Questions:

- Dosage – what is appropriate
- Toxicity
- Side effects!

The upper level is the minimum toxic level (MToL) and the lower level is the minimum effective therapeutic level (MTL). The concentration of the drug within the body must stay within the therapeutic region window ($MTL < conc < MToL$).

Modeling Tool: Compartment Analysis

Let $x(t)$ = the amount of drug in blood at time t.
Multiple compartments (kidneys, liver, etc).

Question: How is drug removed from a compartment?

Elimination, clearance or removal process.

0.2.1 Simple Assumption

First Order Chemical Reaction! ($A^k \rightarrow$ products)
Chemical Kinetics $x(t)$ = amount

$$\frac{dx}{dt} = -kx, \quad x(0) = x_0$$

Example 1 IV drip delivery system - one compartment model

IV infusion $\rightarrow$ blood $\rightarrow$
I = infusion rate, $[I] = MT^{-1}$
ODE: $(x(0) = 0)$

$$\frac{dx}{dt} = \text{input} + \text{output (removal)}$$
$$\frac{dx}{dt} = I - kx$$
$$\left[\frac{dx}{dt}\right] = [I] - [kx]$$
$$MT^{-1} = MT^{-1} - [k]M$$
$$MT^{-1} = [k]M$$
$$T^{-1} = [k]$$
$$[k] = T^{-1}$$
$$\frac{dx}{dt} = I - kx$$
$$\frac{dx}{dt} + kx = I$$
$$I.F. = e^{\int k dt}$$
$$= e^{k\int dt} \qquad = e^{kt}$$
$$e^{kt}x' + ke^{kt}x = Ie^{kt}$$
$$\frac{d}{dt}\left(e^{kt}x\right) = Ie^{kt}$$
$$e^{kt}x = \int Ie^{kt}$$
$$e^{kt}x = \frac{I}{k}e^{kt} + C$$
$$x = \frac{I}{k} + Ce^{-kt}$$
$$0 = \frac{I}{k} + Ce^{-k(0)}$$
$$0 = \frac{I}{k} + Ce^{0}$$
$$0 = \frac{I}{k} + C(1)$$
$$-C = \frac{I}{k}$$
$$C = -\frac{I}{k}$$

$$x = \frac{I}{k} - \frac{I}{k}e^{-kt}$$
$$x = \frac{I}{k}\left(1 - e^{-kt}\right)$$

Pk Metrics

$x(t) =$ amount in plasma $c(t) = \frac{x(t)}{V_{blood}}$ where the average amount of blood (V_{blood}) in a person is $\approx 5L$. This is *incorrect* because it does not match the data.

$$\begin{aligned} V_D &= \text{ apparent volume of distribution.} \\ V_D &= \frac{\text{amount of drug entering the body}}{\text{initial concentration in the plasma}} \\ &= \frac{x(0)}{c(0)} \end{aligned} \tag{1}$$

This data is based off a 70 kilogram man.

Table 1

Drug	$\mathbf{V_D}$
warfarin	8L
theophline	30L
chloroquine	15000L – absorbed in fat

Area Under Curve (AUC)

Measures the total exposure to the drug

$$AUC = \frac{\text{total amount}}{k}$$