MODELLING AND SIMULATION

Lesson 7 - SS 2014 – Michel Kana

What do we do in today's lesson?

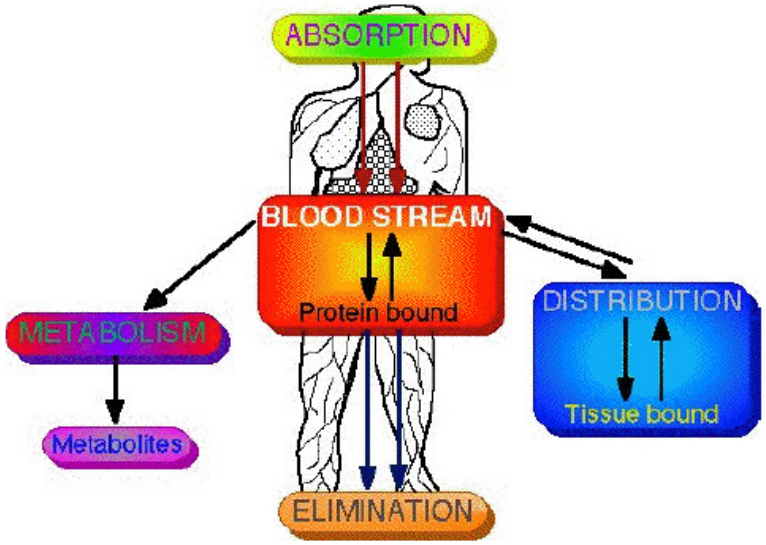
1. **Summary of the previous practice**
2. **Pharmacokinetics**
3. **Projects**
4. **Summary**

Summary of the previous practice

Compartmental models

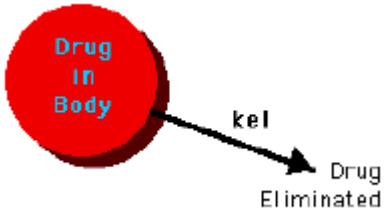
Introduction to pharmacokinetic modeling

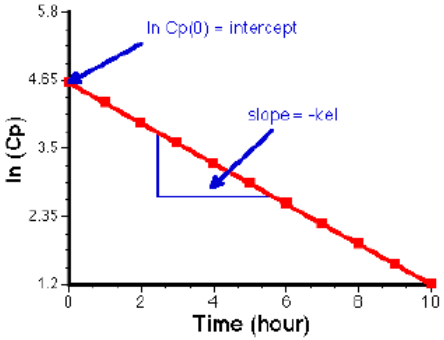
- Pharmacokinetics is the study of how drugs move around the body and how quickly this movement occurs.
- Pharmacodynamics deal with interactions of drug molecules with targets involving receptors, enzymes, ion channels, carriers.
- The four major processes involved in drug transport are: absorption, distribution, metabolism and ends with elimination.
  - Drug absorption can be oral, pulmonary, nasal, injection, transdermal, transmucousal
  - Drug distribution depends on pH, protein binding, fat storage.
  - Drug elimination is performed by the kidneys into urine for polar drugs



One compartment

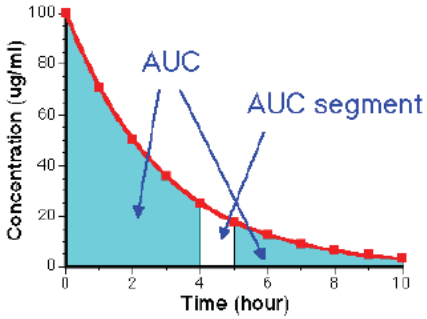
- We assume
  - A rapid intravenous injection
  - Drug in the blood is in rapid equilibrium with drug in the extravascular tissues
  - Drug is mixed instantaneously in blood or plasma within minutes
  - Drug elimination follows first order kinetics.
- kel represents the elimination rate.
  - we can measure kel by determining C_p *versus* time and plotting $\ln C_p$ *versus* time
- V represents the apparent volume of the mixing container, the body. This is not a physiological volume.
  - immediately after the intravenous dose is administered the amount of drug in the body is the intravenous dose, therefore $\mathrm{V} = \frac{Dose}{C_p(0)}$

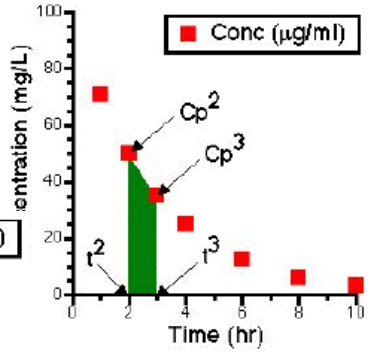


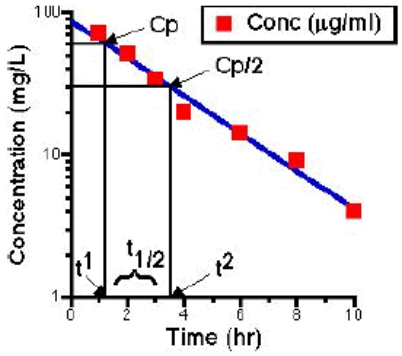


One compartment

- AUC represents the area under the plasma (serum, or blood) concentration *versus* time curve. It can be used as a measure of drug exposure.
  - $AUC = \int_{t=o}^{t=\infty} C_p(t)dt = \int_{t=o}^{t=\infty} C_p(0) \cdot e^{-kel \cdot t} dt = \frac{C_p(0)}{kel}$
  - $AUC_{2-3} = \frac{C_p(2)+C_p(3)}{2} \cdot (t_3 - t_2)$
- Total body clearance CL is defined as the volume of blood or plasma completely cleared of the drug per time.
  - Clearance can be calculated by measuring the amount of drug eliminated during some time interval and the drug concentration at the midpoint of this collection interval.
  - $CL = \frac{\int \frac{dX}{dt} dt}{\int C_p dt} = \frac{Dose}{AUC} = kel \cdot V$
- The half-life $t_{1/2}$ is the time taken for the plasma concentration to fall to half its original value.
  - $t_{1/2} = \frac{0.693}{kel}$







Summary of today's lesson

[Population models]
Pharmacokinetics
Projects

[What is next?]
Identifiability analysis