Pharmacokinetics

2025-2024

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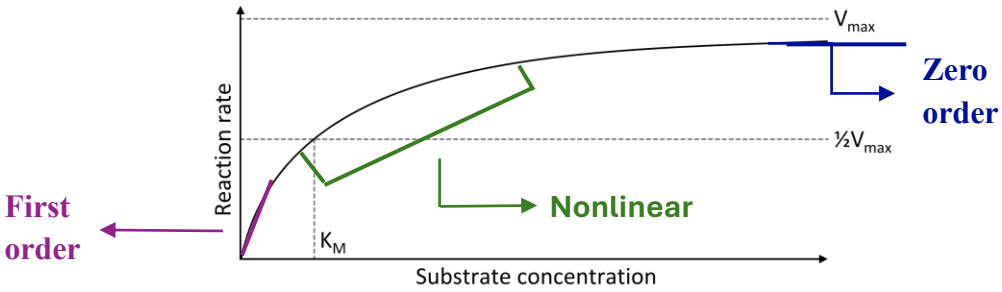
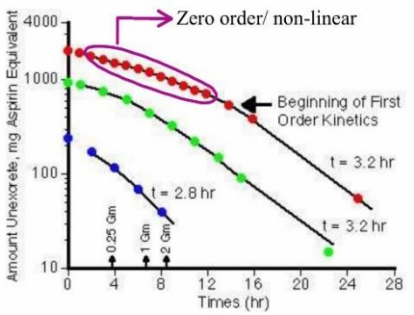
ARKAN ACADEMY

- ***Nonlinear Kinetics:***



- ***So the non-linear pharmacokinetics***
  - Is a combination between first-order and zero-order.
  - If we try to draw *nonlinear pharmacokinetics* on both normal and semi-log papers we would have two areas **linear** area and **curved** area:

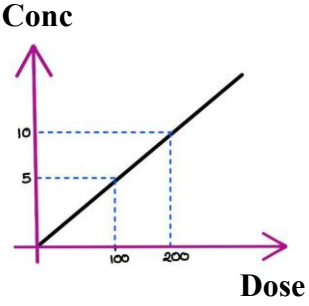
- Here we have nonlinear pharmacokinetics drawn on ***semi log paper*** notice that we have:
  - ***Curved nonlinear area*** at the beginning which represents zero order kinetics.
  - At the end we have ***linear area*** which represents first-order kinetics (all three lines have the same slope).

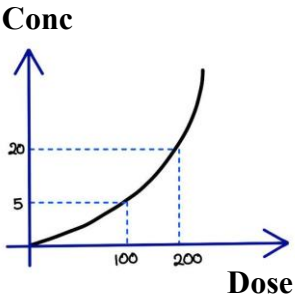


- ***How to know if we have zero order or first order?***
  - Plot it on normal paper:
    - ✓ If you had *linear* relation then it is ***zero order.***
    - ✓ If you didn't have *linear* relation then: plot it on semi log paper, if you had *linear* relation then it is ***first order***.

Linear PK	Nonlinear PK
1-Known as dose-independent or concentraton-independent PK.	1-Known as dose-dependent or concentration-dependent PK.
2-The absorption, distribution and elimination of the drug follow first-order kinetics	2-At least one of the PK processes (absorption, distribution or elimination) is saturable.
3-The pharmacokinetic parameters such as the half-life, total body clearance and volume of distribution are constant and do not depend on the drug conc.	3-The pharmacokinetic parameters such as the half-life, total body clearance and volume of distribution are conc-dependant
4-The change in drug dose results in proportional change in the drug concentration.	4-The change in drug dose results in more than proportional or less than proportional change in the drug conc.

- The relationship between concentration and dose is linear; if I want to double the concentration, I simply double the dose, and everything works as expected!



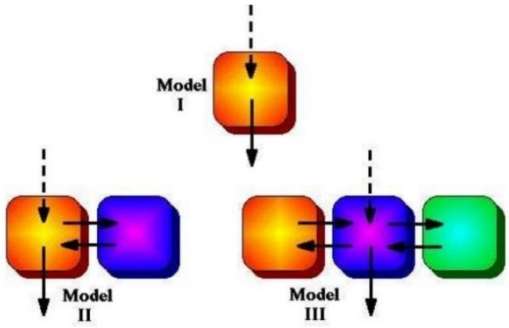


- The relationship between concentration and dose is not linear! If I want to double the concentration, I can't just double the dose. There's no proportionality between dose and conc.

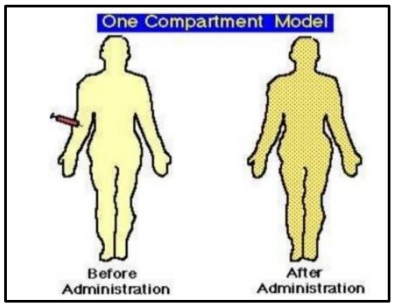
Compartmental PK

- It is common and useful practice to ***divide objects*** of scientific interest into smaller conceptual units until the underlying mechanisms become apparent.
  - For the understanding of pharmacological phenomena a certain class of conceptual unit was developed, the so-called compartments.
  - The organism to which the drug is administered is thought of as a system of interconnected pools, the **compartments**.

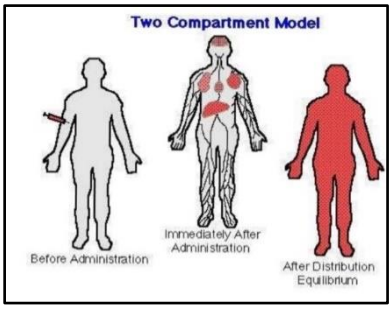
- These compartments are *conceptual* or *hypothetical* and are not related to the anatomy or physiology of the body at all.
  - **For example:** we don't say the heart is compartment or the hands are a compartment. It has nothing to do with anatomy, but rather with *how the drug moves* ***and*** *distributes* in the body.



- If the drug moves freely throughout the entire body without any barriers and has the same affinity for all compartments, we consider the body as a ***single unit*** or ***compartment***.
- In the case of ***two compartments***, the drug divides the body into two distinct parts, with a membrane or barrier between them, affecting how the drug moves between these parts.
- For ***three compartments***, the drug divides the body into three separate parts and moves between them.



- This is **one compartment model** immediately after administration the drug is *distributed* all around the body and *equilibrium* with blood is reached. We are not able to see distribution process because it happens in very short period.



- This is **two compartments model** immediately after administration of drug is *distributed* to certain organs (mostly perfused organs) With time the drug *distributes* to other organs. Then we have equilibrium with the blood (it turns into one compartment model at the end).

- ***Properties of Classical Pharmacokinetic Compartment:***
  - **Kinetic homogeneity**. A compartment contains ***tissues*** that can be grouped according to similar kinetic properties to the drug allowing for rapid distribution between tissues.
  - Although tissues within a compartment are kinetically homogeneous, drug ***concentrations*** within a ***compartment*** may have *different* concentrations of drug depending on the *partitioning* and *binding properties* of the drug.
  - Within each compartment, **distribution is immediate** and **rapidly reversible**.
  - **Compartments** are **interconnected** by first-order rate constants. **Input** rate constants may be ***zero order***.

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