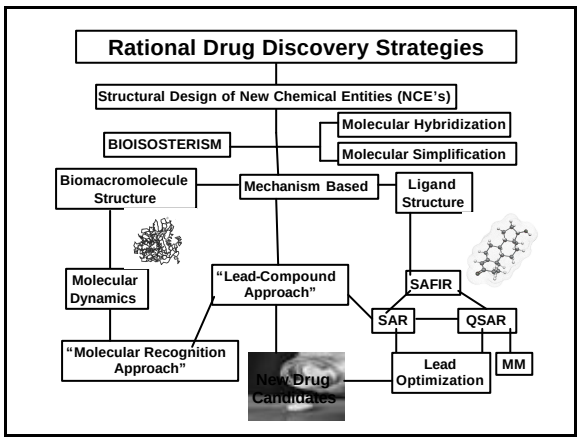
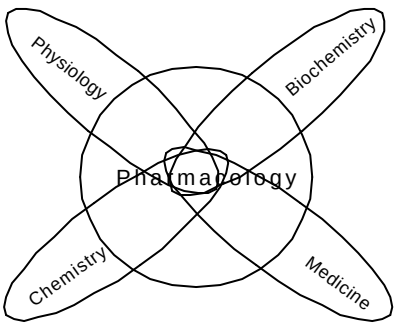


Introduction

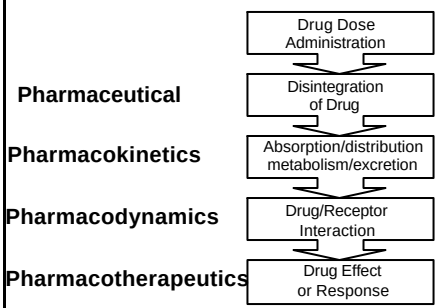
- **Drug**: Any substance that brings about a change in biologic function through its chemical action. Alters state in the body.
- **Pharmacology**: the effect of a drug (chemical) on the body (living system).
- **Toxicology**: undesirable effects of drugs
- **Receptor**: Specific molecule that drug may interact with that plays a regulatory role

A synthesis of several biomedical sciences….



…but unique in its own right

General Concepts

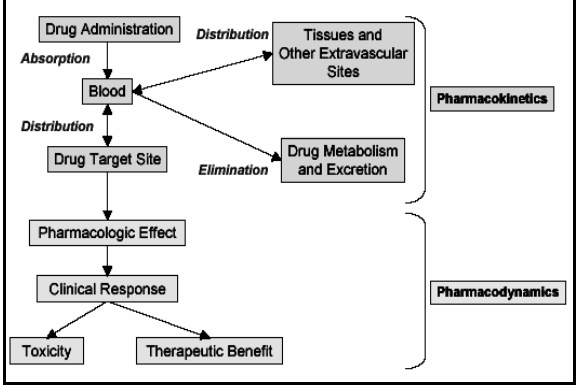


Pharmacology: Its Scope

Two important and interrelated areas:

- **Pharmacokinetics:** study of the absorption, distribution, metabolism and excretion of drugs.
- **Pharmacodynamics**: study of the molecular, biochemical, and physiology effects of drugs on cellular systems and their mechanisms of action.

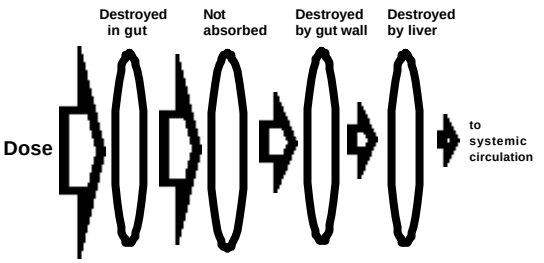
Pharmacokinetics and Pharmacodynamics



Pharmacokinetic Principles

- Bioavailability
- Onset of drug action
- Drug half-life
- Timing of the peak effect
- Duration of drug effects
- Metabolism or biotransformation of the drug
- Site of excretion

Bioavailability



Bioavailability (F)

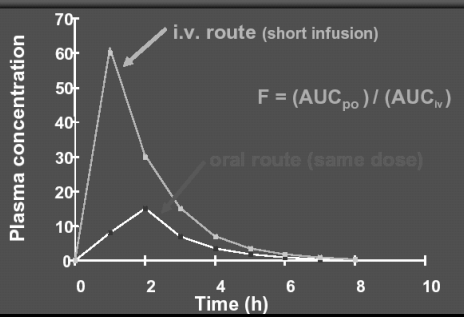
Definition

- the fraction of dose reaching the systemic circulation

$$F = \frac{AUC_{po}}{AUC_{IV}} \times \frac{dose_{IV}}{dose_{po}}$$

- First-pass effect = loss of drug occuring before the drug reaches the systemic circulation

Bioavailability of oral dose



Pharmacokinetic parameters

- Volume of distribution (V)
- Plasma clearance (CL)
- plasma half-life ($T_{1/2}$)

Distribution

- Processes involved in delivery of the drug to the tissues via the arterial blood
- Processes involved in the transfer of the drug from the general circulation to tissues
- defined by the parameter known as the "volume of distribution"

Volume of Distribution (V)

- $V = \frac{\text{amount of drug in the body}}{\text{plasma drug concentration}}$
- determinants :-
  - body mass
  - tissue binding (↑V)
  - drug binding to plasma elements (↓V)

Loading Dose (LD)

Definition

- related to volume of distribution (V)
- first dose of drug treatment, and is required to achieve a target concentration rapidly
- LD (mg) = V (L) x target concentration (mg/L)

- If the V and target concentration are known, then it is possible to workout the loading dose for a drug using this formula

Drug Elimination

Definition

- drug elimination refers to the irreversible removal of the drug from the body
- occurs by two process:
  - drug excretion = loss of drug in bile or urine
  - drug metabolism = conversion of the drug into another chemical species
- defined by the parameter known as clearance

Clearance (CL)

Definition

- Volume of plasma cleared of drug per unit time (L / h)
  - elimination rate (mg/h) = CL (L/h) x conc. (mg/L)
  - $CL_{total\ body} = CL_{renal} + CL_{hepatic} + CL_{other}$
  - CL = dose/AUC

Maintenance Dose Rate (MD)

Definition

- Dose rate to achieve and maintain a target concentration
- At steady state, dose rate in = rate of elimination
  - MD (mg/h) = CL (L/h) x target concentration (mg/L)
- If the CL and target concentration are known, then it is possible to estimate the maintenance dose of a drug using this formula

Half-Life ($T_{1/2}$)

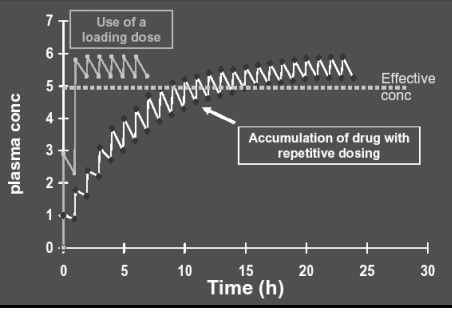
Definition

- Time required for drug concentration to fall by half
- Depends on volume and clearance
- usually constant irrespective of drug concentration
- amount of drug in the body at any time is related to the number of half-lives from drug administration
- If the half-life is known then it is possible to estimate:
  - how much drug is left in the body
  - How long it will take to reach steady-state

Half-life and drug elimination

- after 1 half-life, 50% of the drug will have been eliminated
- after 4 half-lives, > 90% of the drug will have been eliminated from the body
  - applied in the clinic to predict when a therapeutic or toxic drug effect is likely to cease, eg, in overdose

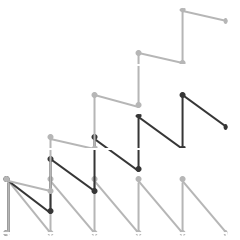
Use of a loading dose gets to target conc/steady state faster



Pharmacokinetics

- Drug molecules interact with target sites to effect the nervous system
  - The drug must be absorbed into the bloodstream and then carried to the target site(s)
- Pharmacokinetics is the study of drug absorption, distribution within body, and drug elimination
  - **Absorption** depends on the route of administration
  - **Drug distribution** depends on how soluble the drug molecule is in fat (to pass through membranes) and on the extent to which the drug binds to blood proteins (albumin)
  - **Drug elimination** is accomplished by excretion into urine and/or by inactivation by enzymes in the liver

Pharmacokinetics



Pharmacokinetic Principles

ADME

A= Absorption

D = Distribution

M = Metabolism

E = Elimination

What Happens After Drug Administration?