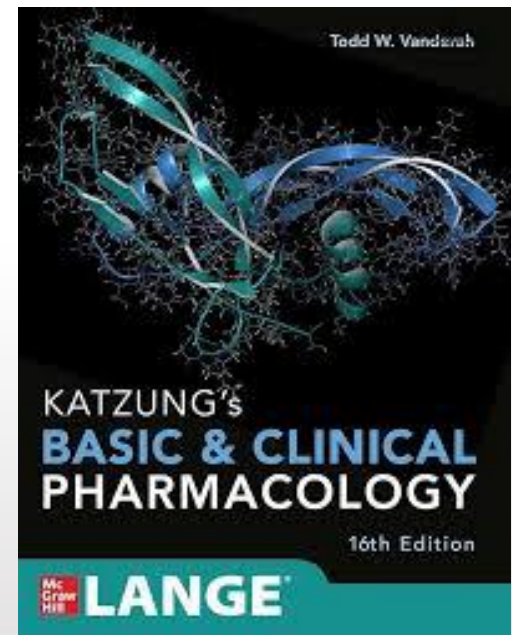


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Principles of Pharmacology-Part II

Department of Pharmacology & Toxicology



Two major fields in Pharmacology

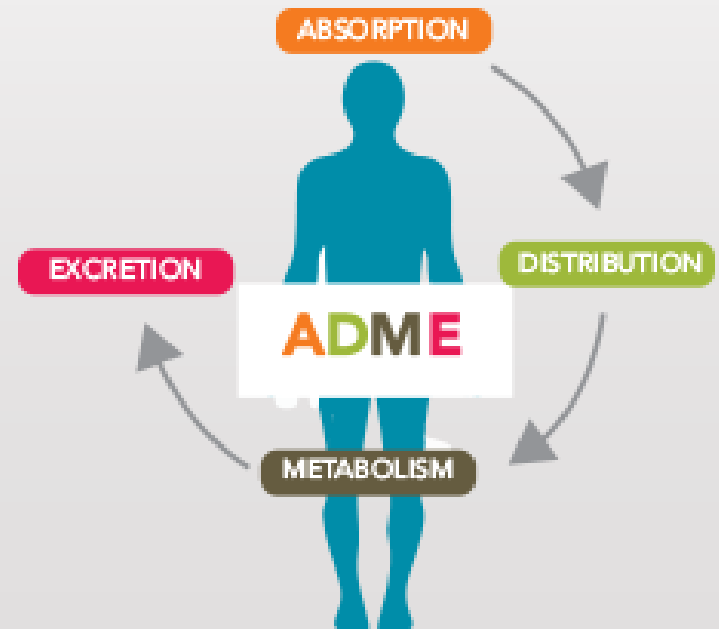
1. Pharmacokinetics
2. Pharmacodynamics



Two major fields in Pharmacology

1. Pharmacokinetics

- ✓ The actions of the body on the drug
 - Absorption
 - Distribution
 - Degradation
 - Excretion



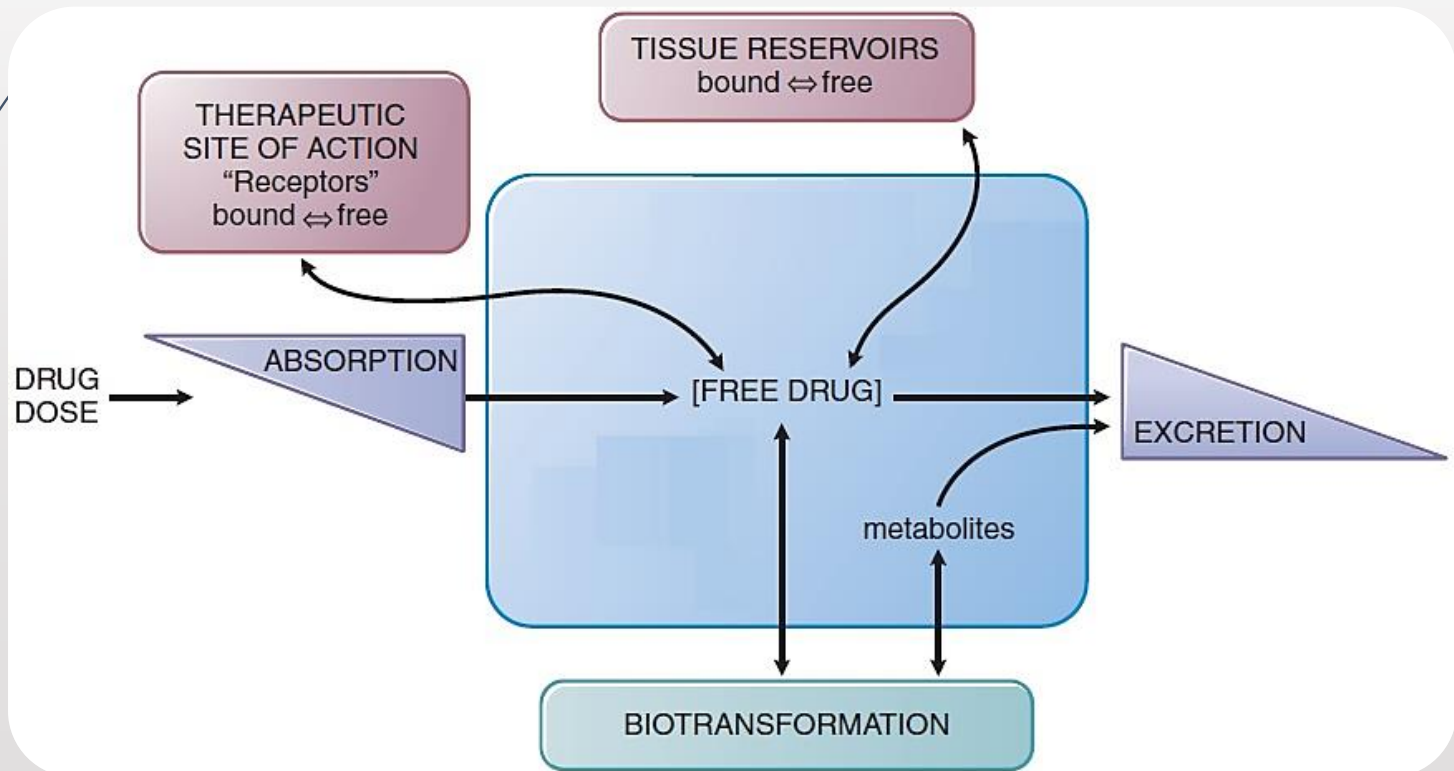
pharmacokinetics

- **The goal of therapeutics is**
 - **to achieve a desired beneficial effect**
 - **minimal adverse effects**
- ✓ the right administration route
- ✓ the right dose or concentration
- ✓ the right time



Pharmacokinetics

- What Happens After Drug Administration?



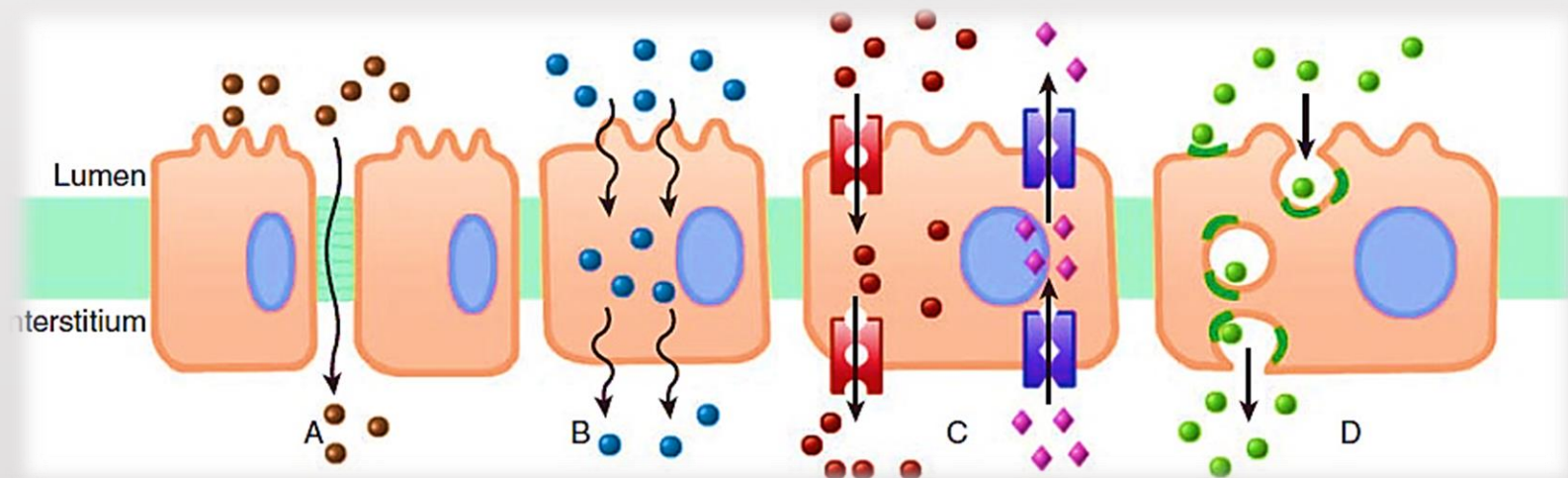


Absorption

- **Movement of a drug from its site of administration into blood circulation**
- **Factors that affect absorption**
 - ✓ Drug concentration
 - ✓ Drug dosage form
 - ✓ Physicochemical properties of drugs (solubility, pKa)
 - ✓ Route of administration
(blood flow, pH, surface area)

Absorption

- **Lipid bilayers are the barrier against absorption**
 - A. Aqueous diffusion**
 - B. Lipid diffusion**
 - C. Special carriers (active transport or facilitated diffusion)**
 - D. Endocytosis and exocytosis**



Pharmacokinetics (cont.)

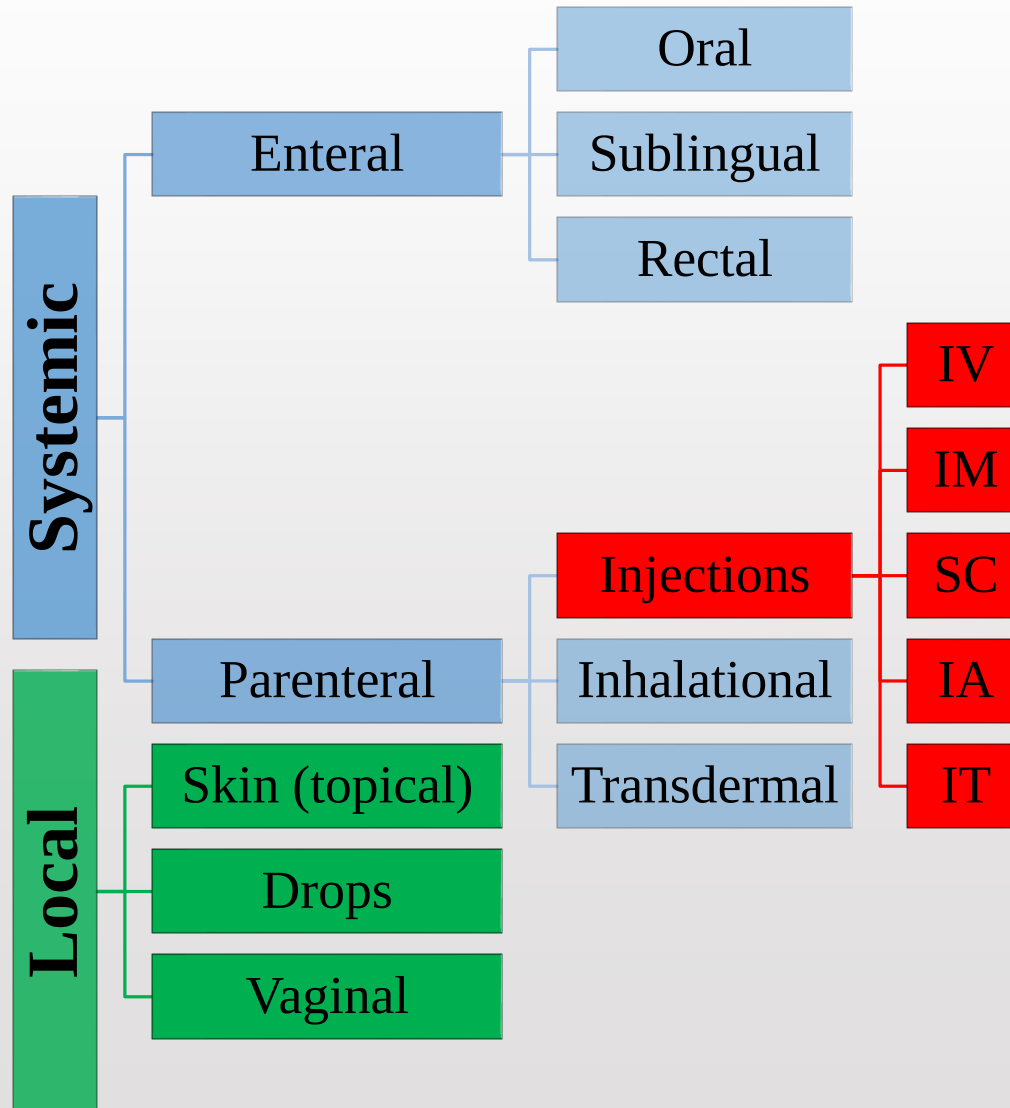
- **Bioavailability**

- ✓ the fraction of unchanged drug reaching the systemic circulation

- **First-Pass Elimination**

- ✓ metabolism of drugs at the liver prior to entry into the systemic circulation in oral way
- ✓ results low Bioavailability of oral drugs

Route of administration

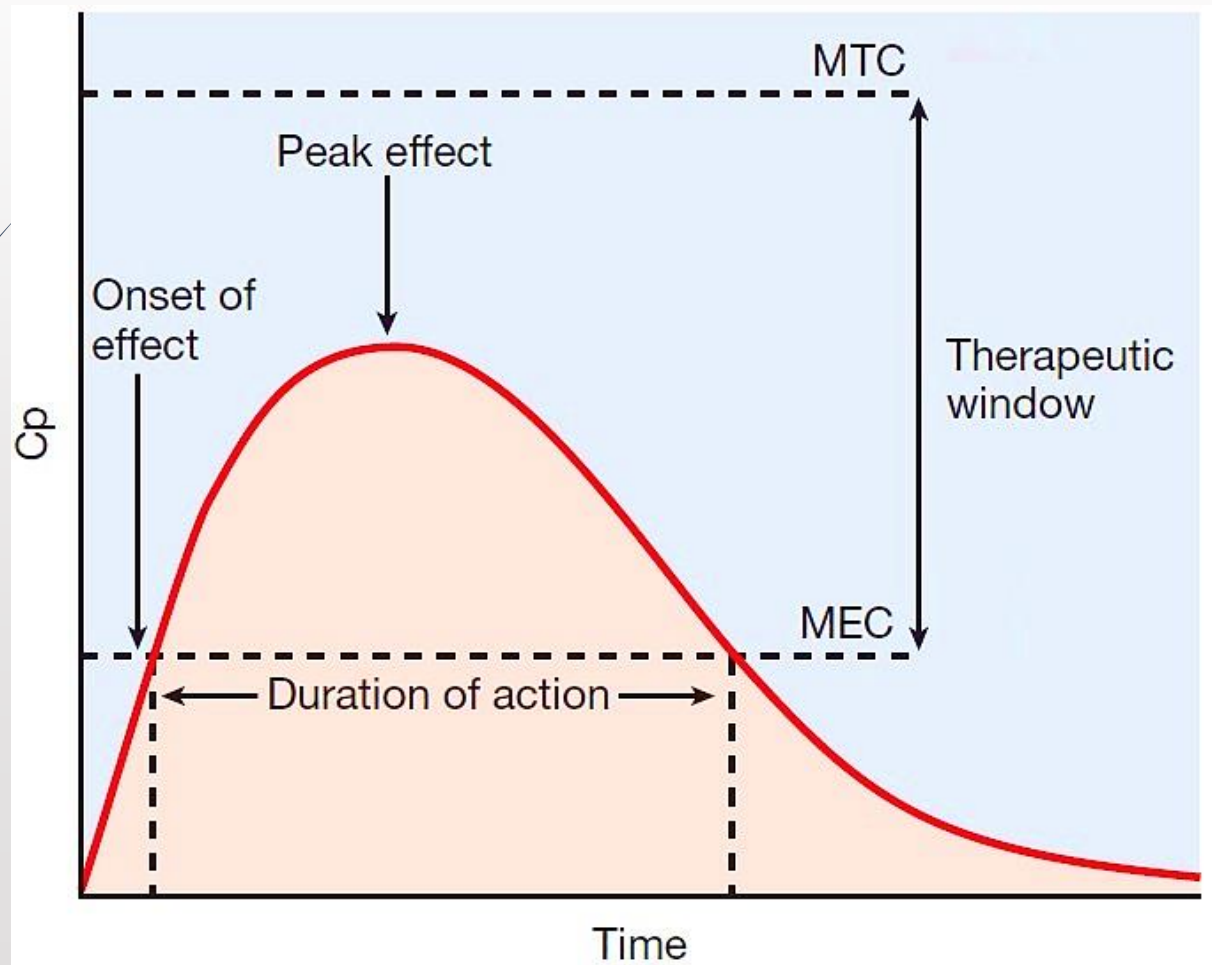




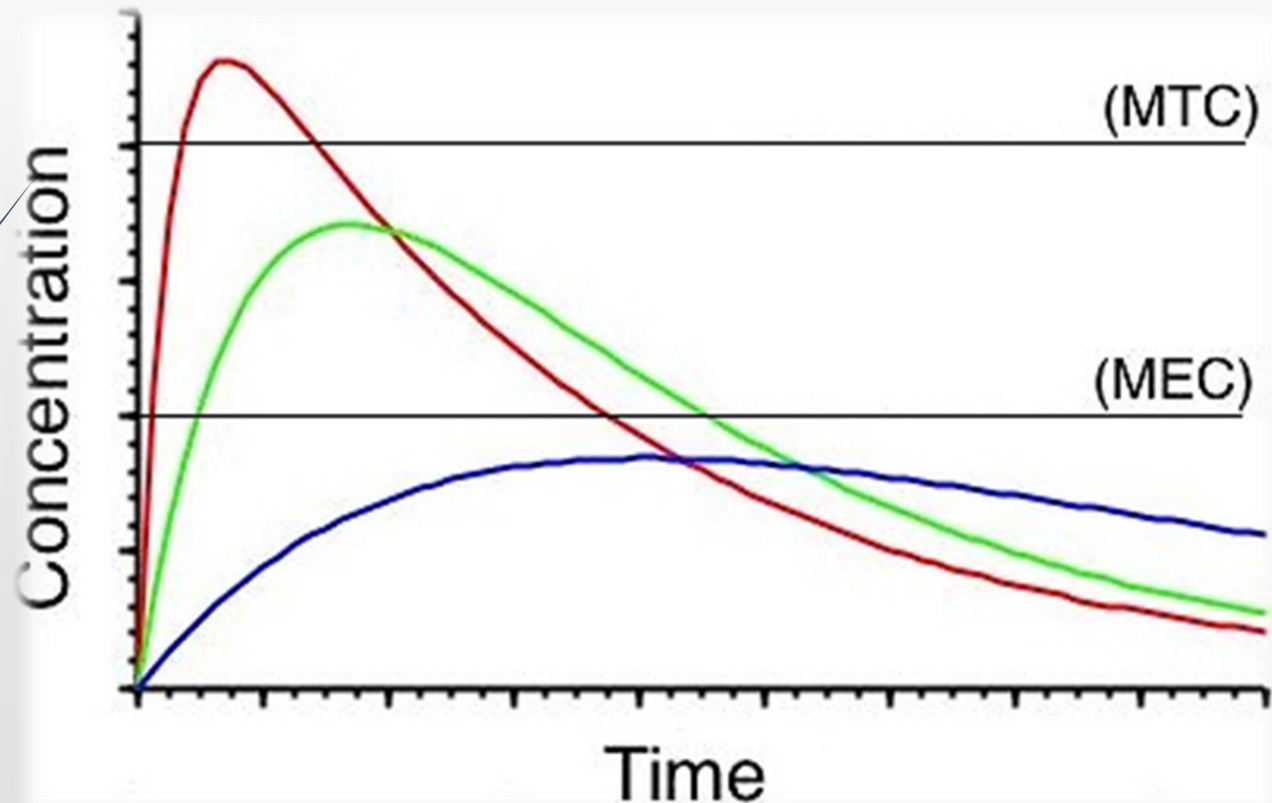
Route of administration

- Rate of Absorption
- Extent of Absorption
 - ✓ Bioavailability
 - ✓ First-Pass Elimination
- Onset of action
- Duration of action
- Side effect risk

Pharmacokinetics curves



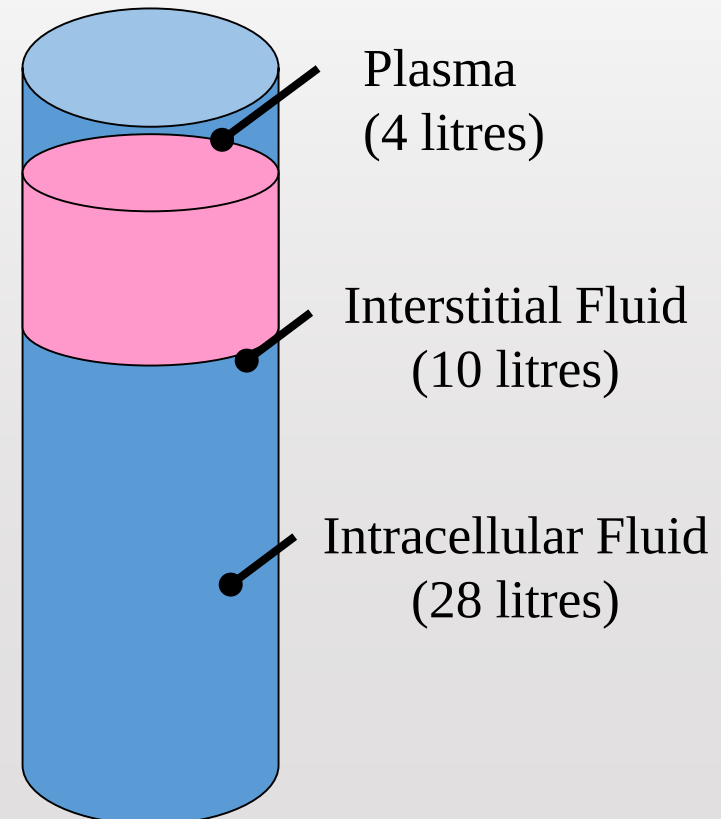
Pharmacokinetics curves



Distribution

- **Transport of a drug in the body by the bloodstream to its site of action.**
- **Drugs distribute into any or all of the following compartments:**

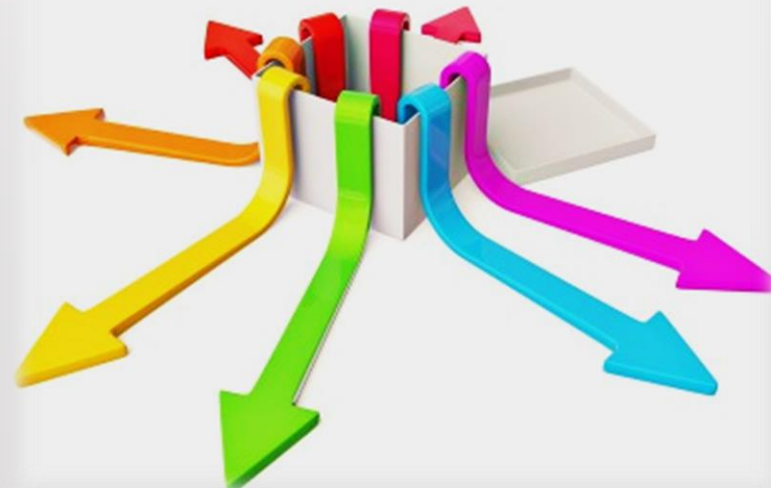
- ✓ Plasma
- ✓ Interstitial Fluid
- ✓ Intracellular Fluid



Distribution

■ Factors that affect distribution

- ✓ Protein binding
- ✓ Drug solubility
- ✓ Blood flow
 - brain, heart, kidney ,liver
 - Fat, bone
- ✓ Capillary permeability
- ✓ Organ size
 - muscle



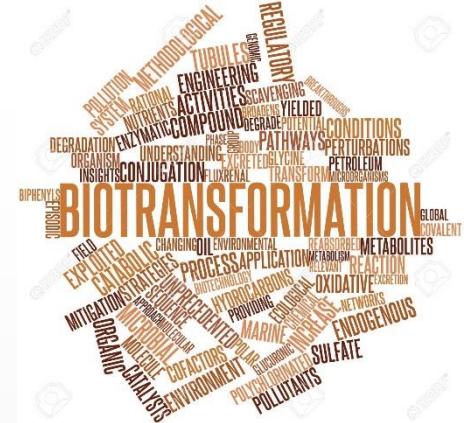
Distribution

- **Apparent volume of distribution (V_d)**

$$V_d = \frac{\text{Dose (mg)}}{C_p}$$

- ✓ Drug solubility affects V_d
- ✓ V_d is important for determining the dose

Metabolism



- **Chemical alteration of the drug in the body**
 - ✓ Convert non-polar lipid soluble compounds to polar water soluble compounds
- **Metabolism is a detoxifying process**
- **Metabolism product (metabolite)**
 - ✓ Inactivation (Elimination)
 - ✓ Activation (prodrug)
- **Metabolism occurs in**
 - ✓ Liver (main organ), kidneys, plasma, intestinal mucosa



Metabolism

- **Factors that affect biotransformation**
 - ✓ Genetic polymorphism
 - ✓ Pollutant exposure from environment or industry
 - ✓ Pathological status
 - ✓ Age
 - ✓ Sex
 - ✓ Concurrent use of drugs and food



Metabolism

- **Enzyme induction & inhibition**
 - ✓ One drug can induce or inhibit metabolism of other if utilizes same enzyme
- **Enzyme inducer:**
 - ✓ phenobarbital, phenytoin, rifampin, cigarette smoke
- **Enzyme inhibitor:**
 - ✓ ketoconazole, grape juice, allopurinol

Excretion (→Elimination?)

- **Transport procedure which the drug or its metabolites are excreted through excretion organ**
- **Hydrophilic compounds can be easily excreted**
- **Free form of drug can be excreted**
- **Excretion organ**
 - ✓ Major organs; kidney, biliary excretion, lung
 - ✓ Minor organs; milk, sweat, saliva



Pharmacokinetics (cont.)

- **Clearance**

- ✓ The volume of plasma from which drug is completely removed in unit time

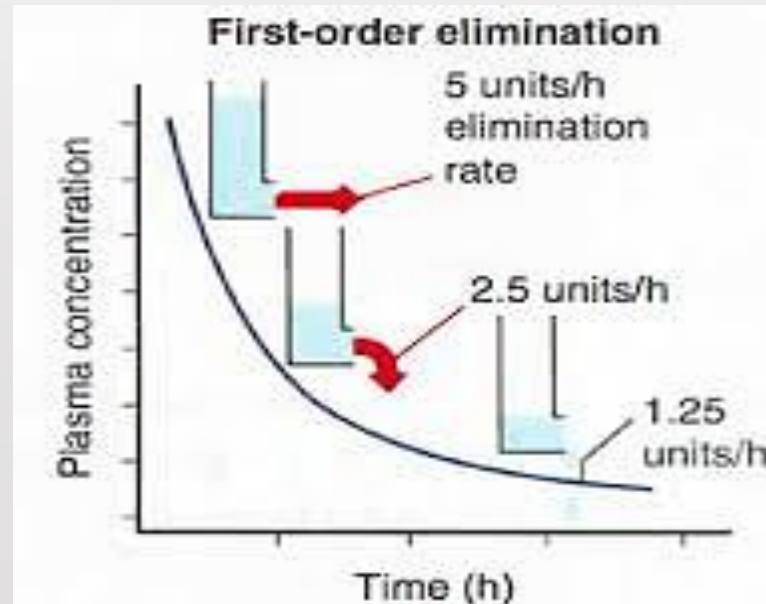
- **Plasma half-life**

- ✓ The time taken for plasma concentration to be reduced to half

Excretion

- **Kinetics of Elimination**

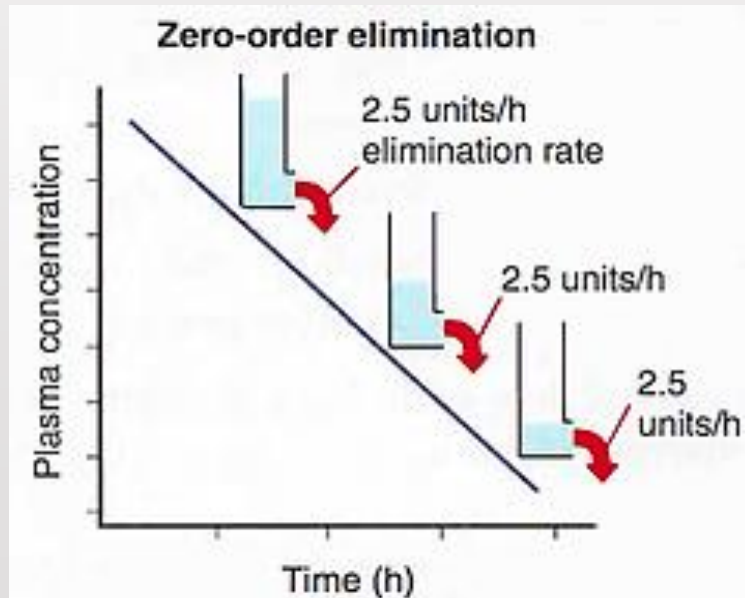
- ✓ **First order kinetics:** Rate of elimination is directly proportional to drug concentration



Excretion

- **Kinetics of Elimination**

- ✓ **Zero order kinetics:** The rate of elimination remains constant irrespective of drug concentration
 - ethanol, theophylline





Any question?