Chapter 5:
Biopharmaceutical and Pharmacokinetic considerations

Biopharmaceutic:

Is the science that study **relation of physicochemical properties of drug, dosage form, & route of administration** on **rate and extent** of drug absorption.

Pharmacokinetic:

- It is the study of the **kinetics** of **absorption, distribution, metabolism, and excretion (ADME)** of drugs and their **pharmacologic, therapeutic, or toxic effects** in animals and man.
- Drugs given **IV** go **directly into blood**.
- **Elimination** refers to both **metabolism and excretion**.

- **Drug in blood exists in equilibrium with drug in tissues**.
- In equilibrium **concentration of the drug in blood** different (greater or lesser) than the **concentration of the drug in tissues**. This is due to the **physicochemical properties** of the drug.

- The rate of transfer of a drug **from one compartment to another is proportional to concentration of the drug** in the compartment from which it exits; **the greater the concentration, the greater is the amount of drug transfer**.

- During metabolism a drug substance may be biotransformed into:

1. Pharmacologically active,
2. Inactive metabolites,
3. or both.

For example, anticonvulsant drug carbamazepine (Tegretol) is metabolized in the liver to **active epoxide metabolite.**

 Metabolism of drug to **inactive products** is **irreversible process**.

 In some instances, a **pharmacologically inactive drug** (termed a **prodrug**) administered for known effects of **its active metabolites**.

 (**kel**): **elimination rate constant** for drug describes its rate of elimination from body.

Principles of drug absorption:

1. Passive Diffusion:

1. **From high to low concentration**
2. Depends on the **molecule's lipid solubility**, **particle size**, **degree of ionization**, and **area of absorptive surface**.
3. **Primary mechanism for most drugs**
4. **No need for energy or carrier**.

 Fick's law of Absorbtion, **drug molecules diffuse from a region of high drug concentration to a region of low drug concentration**.

$$\frac{dQ}{dt} = \frac{DAK}{h}(C_{GI} - C_p)$$

Where:

dQ/dt = **rate of diffusion**, **D** = **diffusion coefficient**,

K = **(lipid / water) partition coefficient**

A = **surface area of membrane;**

h = **membrane thickness, and**

CGI – Cp = **difference between the concentrations of drug in the gastrointestinal tract and in the plasma.**

Because **D, A, K**, and **h** are c**onstants** under usual conditions for absorption, a combined constant **P** or **permeability coefficient** may be defined.

$$P = \frac{DAK}{h} \qquad (13.2)$$

□ drug concentration in plasma, C_p, is extremely small compared to the drug concentration in the gastrointestinal tract, C_{GI}. If C_p is negligible and P is substituted

$$\frac{dQ}{dt} = P(C_{GI}) \qquad (13.3)$$

2. Facilitated passive diffusion:

1. From **high to low** concentration

2. Need **carrier** in the membrane combines reversibly with the substrate molecule outside the cell membrane

3. No need for energy.

4. Specific molecular configuration

5. Limited number of carrier

3. Active transport:

1. Against concentration gradient.

2. Selective,

3. Requires energy

4. Limited to drugs structurally similar to endogenous substances (ions, vitamins**,** sugars, amino acids**).**

5. These drugs are usually **absorbed from specific sites** in the small intestine.

Many body nutrients, such as sugars and amino acids, are transported across the membranes of the gastrointestinal tract by **carrier processes**.

Certain vitamins, such as thiamine, niacin, riboflavin, and pyridoxine, and drug substances, such as methyldopa and 5-fluorouracil, require active transport mechanisms for their absorption.