PHARMACOLOGY

Modified no. 4

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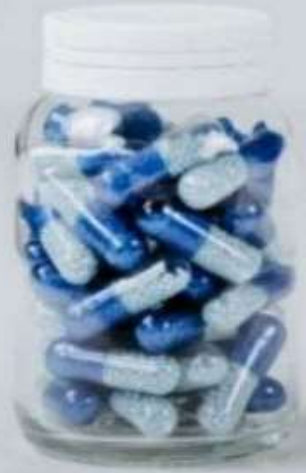


Cont. factors affecting absorption:

NOTE: The lipid solubility is the major factor

- Concentration of drug = dose

NOTE: The more the dose, the more the absorption.

- Surface area of absorption

NOTE: The larger the absorption site's surface area, the more the absorption ;that's why intestine is considered the major site of drug absorption.

- Blood circulation to absorbing area

NOTE: If the blood supply is good to the absorbing surface, the better the absorption.

- Route of administration (I.V the fastest)

NOTE: Example: Absorption isn't the fastest process orally; it takes 30-60 minutes to start its action. However, when you get the drug I.V., the entire dose has 100% bioavailability, so the drug acts within 5-10 minutes maximally.

- Dosage forms

NOTE: Example: the oral route is slower compared to the subcutaneous solution

- Food

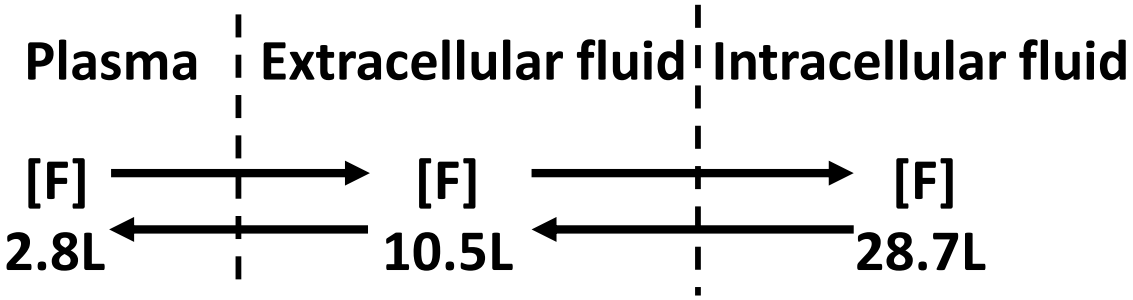
NOTE: Sometimes, taking the drug with food may either slow down or speed up the absorption of the drug.

Side note : the scientists usually make the calculations of pharmacokinetics without food and then see if the food affects on absorption or not.

Drug distribution

Passage of drugs from blood to different tissues (site of action)
Extent of distribution could be measured by a constant known as AVD

70 Kg man 60% H2O ≈ 42 liters



Apparent volume of distribution (AVD):

The total volume in which the free form of a given drug distributes in different body compartments at equilibrium

AVD = Dose (mg)/C_0 (mg/L) ****pay attention to units**

C_0 = Concentration of drug in blood at time zero

NOTE:

**** C0 is determined by I.V administration**

**** The volume of distribution of any drug is determined by (AVD) constant.**

Highly lipid soluble drugs e.g. digoxin, have a very high Vd (500 liters)

Drugs which are lipid insoluble e.g. neuromuscular blockers, remain in the blood, and have a low Vd

Very very high Vd indicates extensive tissue binding

NOTE:

lipid soluble → high VD
lipid insoluble → low VD

NOTE:

AVD=VD

Factors affecting drug distribution:

- **Compartmental selectivity**

- **Organ selectivity**

- **Protein binding (Major factor)**

***ملاحظة مالها علاقة بالمحاضرة: احنا جيل مدلع لأنو الايباد او اللابتوب يفتحو بسرعه**
بس على زمن الدكتور كان يستنى الكمبيوتر ثلاث ساعات ليفتح تخيلوا!☺

- Natural barriers

1) **BBB (Blood Brain Barrier)**

NOTE: "If we need the drug to penetrate the BBB, we must use different administration routes.

2) **Placenta**

3) **Mammary glands**

NOTE:"That's why pregnant or breastfeeding women should be cautious about taking medications that can penetrate these barriers."

A low Vd

Usually denotes that the drug is mainly in the plasma i.e. high plasma concentration and low tissue distribution and binding

A High Vd

Indicates significant distribution or uptake by many tissues

A high Vd is commonly associated with very long half-life to a given drug

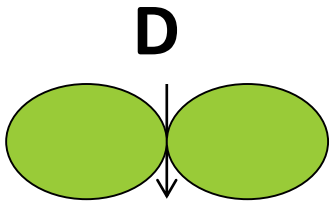
High or extensive plasma protein binding may result in:

- Restricted drug distribution
- Reduced intensity of pharmacological effects
- Predisposes the drug to many interactions
- Increases drug’s duration of action (half-life)
- Decreases drug’s AVD

Mechanisms of drug transfer across membranes:

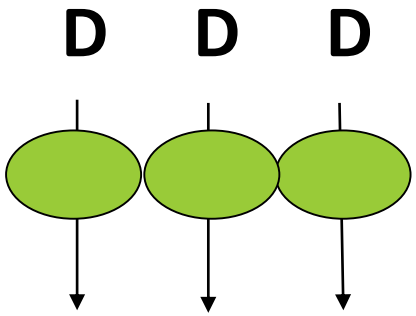
- Simple diffusion

Crossing through water pores of membranes, no energy or carrier required, from high to low concentration, drugs with low M.W (must be lipid soluble and concentration gradient is the driving force)



- Passive diffusion (major mechanism)

Crossing through cells or the lipid bilayer, no energy or carrier required, from high to low concentration



The only requirement for passive diffusion is that the drug should be lipid soluble

- Facilitated diffusion

Requires a carrier, no energy required, from high to low concentration

- Active transport

Requires energy ± carrier, could be from low to high concentration

(Facilitated diffusion and active transport follow saturation kinetics because No. of carriers is limited)

- Endocytosis

1) **Phagocytosis (solid particles)**
2) **Pinocytosis (fluid particles)**

NOTE: "The cell itself engulfs the drug."