Biopharmaceutics &
Pharmacokinetics
8th SEM

FACTORS AFFETING DRUG DISTRIBUTION

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INTRODUCTION

- Once a drug enter into a blood stream the drug is subjected to a numbers of processes called as **DISPOSITION PROCESSES** that tend to lower the plasma concentration of drug.

- **DISTRIBUTION** is a process which involves **reversible transfer of a drug** between compartments.

- **ELIMINATION** is a process which involves **irreversible loss of drug** from the body.

FACTORS AFFECTING DISTRIBUTION OF DRUGS

1 Tissue permeability of the drug.

a) Physicochemical properties of drug like Mol. Size, pKa and o/w partition coefficient.

b) Physiological barriers to diffusion of drugs.

2 Organ/Tissue size and Perfusion Rate. 3- Binding

of drugs to tissue components.

a) Binding of drugs to blood components.

b) Binding of drugs to extravascular tissue protein.

4-Miscellaneous

TISSUE PERMEABILITY OF DRUGS

A) PHYSICOCHEMICAL PROPERETIES OF DRUG

1-Molecular size

2 pKa

3 O/W Partition Coefficient

B) PHYSIOLOGICAL BARRIERS TO DIFFUSION OF DRUG

1 Simple capillary endothelial barrier

2 Simple cell membrane barrier

3 Blood brain barrier

4- Blood CSF barrier

5- Blood placental barrier 6- Blood testis barrier

1- MOLECULAR SIZE

- Drugs having molecular weight less than **500 to 600 dalton** easily pass **capillary membrane to ECF.**
- Penetration of drug from ECF to cells is function of **Mol. Size, Ionization constant & lipophilicity of drug**.
- From ECF to cross cell membrane through aqueous filled channels need particle size **less than 50 dalton with hydrophilic property.**
- Larger mol. size restricted or require specialized transport system.

2-DEGREE OF IONIZATION

- The Ph in which half of drug is unionized is called pKa.
- The PH of blood and ECF play important role in ionization & diffusion of drugs into cells.
- The ph of blood plasma, ECF & CSF is 7.4 (constant).Except in systemic acidosis & alkalosis.
- A drug that remains unionised at this Ph values can permeate the cells relatively more rapidly.
- Most of the drugs are either weak acids or weak bases and their degree of ionisation at plasma or ECF Ph depends upon their pKa.

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- All drugs that ionise at plasma Ph (i.e. hydrophilic , Polar drugs) cannot penetrate the lipoidal cell membrane and **tissue permeability is the rate limiting step**) in the distribution of such drugs.

3-O/W PARTITION COEFFICIENT

- Polar and hydrophilic drugs are less likely to cross the cell membrane where Non- polar and hydrophobic drugs are more likely to cross the cell membrane.
- In case of polar drugs where permeability is the rate limiting step in the distribution, the driving force is the effective partition coefficient of drug.
- Effective Ko/w= (Fraction unionized at pH 7.4) x Ko/w of ionized drug

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- Lipoidal drug penetrate the tissue rapidly. Among drugs with same Ko/w but different in ionization of blood Ph.

- One which has less ionization show better distribution.

Ex. Phenobarbitol > Salicylic acid.

- Both drugs having same Ko/w but phenobarbitol is more unionised at blood Ph therefore distributed rapidly.

Thank You