

School of medical and Allied Sciences

Course Code :BP604T

Course Name: BIOPHARMACEUTICS AND
PHARMACOKINTICS

The logo of Galgotias University is a stylized 'G' composed of three curved, overlapping bands in red, yellow, and blue. The text 'TOPIC: DISTRIBUTION' is centered over the logo.

TOPIC: DISTRIBUTION

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BARRIERS

Physiological barriers

3) Blood brain barrier

Capillary in brain is highly specialized & much less permeable to water soluble drugs

ENDOTHELIAL CELLS ; - **Tightly bonded** with each other by **intracellular junctions**

ASTROCYTES :- present @ the base of endothelial tissue and act as **supporting materials**

& it **Form Envelop** around the capillary thus intercellular passage get blocked.

BBB is lipoidal barrier, thus drugs with **high o/w partition coefficient** diffuse **passively** others (**moderately lipid soluble** and **partially ionized** molecules passes slowly.

B. PHYSIOLOGICAL BARRIERS

4) Cerebral Spinal Fluid Barrier;-

Capillary endothelial cells;- have **open junction** or gaps so....

Drugs can **flow freely b/w capillary wall & choroidal cells.**

Choroids plexus;- major components of CSF barriers is choroidal cells which are joined with each other by **tight junctions forming the blood-CSF barrier** (similar permeability to BBB)

Highly lipid soluble drugs can easily cross the blood-CSF Barrier but moderately soluble & ionize drugs permeate slowly.

Mechanism of drug transport is **similar to CNS & CSF** but the Degree of uptake may vary significantly.

B. PHYSIOLOGICAL

BARRIERS

- 5)
- Placenta barriers :-
- It's the barrier b/w **Maternal** & **Fetal** blood vessels
- Both are **separated** by **fetal trofoblast** basement membrane & endothelium .
- Thickness 25μ @ *early pregnancy* later reduce up to 2μ (even its effectiveness remain unchanged)
- Mol wt **<1000** Dalton & moderate to high lipid solubility drugs like.....
(Sulfonamides, Barbiturets, Steroids, Narcotic some Antibiotics) cross the barrier by **Simple Diffusion rapidly**
- Essential Nutrients for fetal growth transported by **carrier-mediated processes**.
- **Immunoglobulines** are transported by **endocytosis**.
- Drugs dangerous to fetus at **Two stages**
- Its advisable to avoid drugs during **1st trimester**
(fetal organ development) some drugs produce **teratogenic effect**
ex. Phenytoin, methotrexate
- later stage pregnancy affect physiological functions like **respiratory depression** ex. morphine
- Better to restrict all drugs during pregnancy.

BINDING OF DRUG TO TISSUE COMPONENTS

Highly lipophilic drugs can cross **most selective barrier** like BBB, ex. thiopental, Highly permeable capillary wall permits passage of almost all drugs (**except those bound to plasma protein**).

Highly perfused tissues **Lungs, Kidneys, Liver, Heart, Brain** are rapidly equilibrated with **lipid soluble drugs**

Drug is distributed in a particular tissue or organ **depends** upon the **size of tissue** (Volume) & **Tissue/blood** partition coefficient
Ex. Thiopental i.v (lipophilic drug) & high tissue/blood partition coefficient towards brain & adipose tissue

But brain is **highly perfused organ** so drug is distributed **fast** and shows **rapid onset of action** than poorly perfused adipose tissue.

3) Binding of drug to blood and other tissue components

- Binding of drugs to blood components
 - Blood cells
 - Plasma proteins
- Binding of drugs to extra vascular tissues

BINDING OF DRUGS TO BLOOD

CELLS

The major component of blood is RBC

The RBC comprises of **3** components each of which can bind to drugs:

- Hemoglobin
- Carbonic Anhydrase
- Cell Membrane

3). BINDING OF DRUG TO TISSUE

COMPONENTS

B. Extra Vascular Tissue proteins

40% of total body weight comprise of **vascular tissues**

Tissue-drug binding result in localization of drug at specific site in body and serve as **reservoir**

As binding **increases** it also **increase** bio-logical half life.

Irreversible binding leads to drug **toxicity**. (carbamazepin-autoinduction)

liver>kidney>lungs>muscle>skin>eye>bone>Hair, nail

4). Miscellaneous Factors

Age:

- a) Total body water
- b) Fat content
- c) Skeletal muscles
- d) Organ composition
- e) Plasma protein content

- Pregnancy
- Obesity
- Diet
- Disease states

REFERRENCER:-

ENCES

- Applied Biopharmaceutics and Pharmacokinetics by *Leon Shargel*
- Clinical biopharmaceutics and pharmacokinetics by *Gibaldi*
- Biopharmaceutics and Pharmacokinetics by *Brahmankar*