

* SHEET 7 *

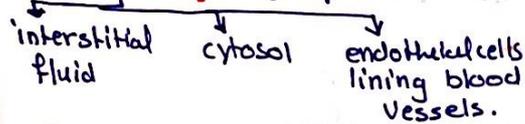
* How the drug moves from the site of administration to the systemic circulation:-

- 1 lipid diffusion
- 2 passive aqueous diffusion
- 3 special carriers
- 4 endocytosis and exocytosis ..

1 Aqueous diffusion:-

- * transport ions and small molecules through aqueous pores within the membrane
- * Facilitated diffusion →
- Ions → electrochemical gradients.
- small molecules → concentration gradient.

* occurs in lung aqueous component



* drugs that are bound to Plasma proteins don't pass through aqueous carriers.

2 Special carriers:-

- * used to transport molecules that are insoluble in lipids but soluble in water and essential for the cell [Glucose, Amino acid and peptides]
- * Selective → each substance has its own carrier
- * passive vs Active
- * e.g.s: ABCs / MDP / SLC

A ABCs + MDP:-

* tumor → cancer cells → growing in petridish → certain drug → initially → cancer cells will be killed

observe that there is resistance against the drug and against a similar drug
 HOW? → by using ATP [against its concentration gradient]

(MDR1)

* they notice that the cancer cells produce P-GLYCOPROTEINS or Multidrug-resistance transp which functions to efflux the drug from the cell before to do any effect inside.

- * beneficial mechanism → getting out of toxins outside the cells.
- * bad mechanism → adaptation of cancer cells against the chemotherapeutics agent and some bacteria to the antibiotics.

3 SLC: solute carriers proteins:-

- * passive facilitated diffusion
- * reuptake for the neurotransmitters from the synaptic cleft to the pre-synaptic neuron.

3 endocytosis and exocytosis

* For large molecules either water soluble or lipid soluble * induced by endocytosis-induced receptors.

* e.g:-

1 Vitamin B12 is complexed with intrinsic factor secreted by stomach cells → flum to be absorbed there

2 transferrin → receptor-induced endocytosis → engulfment into the RBCs → iron inside the cell and the transferrin → degradation by lysosomal enzymes → exit the RBCs and can be reused again.

needs Ca²⁺ ions

e.g.s:

1. placental barrier → separation between the maternal and the fetal circulation
2. testis barrier → preventing the mol to get in
3. blood-brain barriers.

* Barriers against permeation of Drug and transport:-

tight junctions between endothelial cells

the presence of thick basement membrane.

presence of C.T under the basement membrane

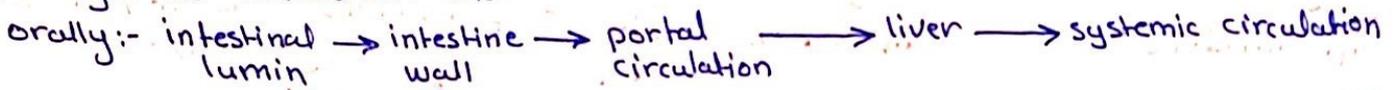
the presence of ABCs and MDP

the presence of intracellular and extracellular enzyme → digestion of the drug.

* Fick law of diffusion *

First-pass effect - (First pass metabolism) - (pre-systemic metabolism):

* **First pass effect:** - the route of the drug from the site of administration to the systemic circulation.



* **organs of metabolism:**

- 1] the LIVER [highest metabolic activity]
- 2] intestine [less efficacy]
- 3] endothelial cells of the portal circulation [less efficacy]
- 4] hair follicles [less efficacy]

* the amount of the drug that will release receive the systemic circulation is decreased due to the first pass effect. (metabolism of the drug) and do not do the therapeutic effect before reaching the systemic circulation. So what is the solutions?

1] increasing the dose with a proportion with first pass effect
e.g: if the FPM = 50% from the drug normal dose = 50 mg so we increase the dose to 100 mg to achieve the therapeutic effect

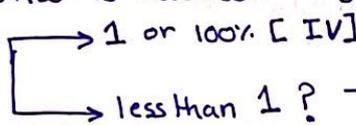
2] change the site of administration to a site where the first pass effect is less
e.g: orally → IV

3] drug with no first pass effect
e.g: patients with liver cherosis they have (shunting blood) - no first pass effect - blood → portal → systemic circulation without metabolism from the liver.
decrease the dose → avoiding toxicity.

* Bioavailability:

* the fraction of the drug that is received to systemic circulation.

* bioavailability might be



- First pass metabolism
- manufacturing
- manufacturing dosage
- hepato Enterhepatic circulation
- distruction by GIT gastric acid or bacteria.
- absorption.

* the drug is very hydrophilic (atenolol) → so it cannot reach the plasma membrane
* the drug is very lipophilic → so it cannot reach or move to reach the plasma membrane (acyclovir)

* **ABCs and MDP:** - P-Glycoprotein which efflux the drug outside the cell before doing its effect.

- 1] absorption phase: - absorption > elimination rate
- 2] peak: absorption = elimination rate

3] + 4] elimination rate > absorption rate.

لازم الجرعة ان تتاخذ تكونه بعينه التاثير ان يدي اياه بدون حاد او سهل toxicity وما تكونه قليلة كثير
مضاد لوالوا يتاخذ على شكل 3 حبات - البوا بكل مرة صبة ال (بعض صبة كل 8 ساعات) - يكون البوا تركيزه قريب من MEC بعد 8 ساعات فياخذ الجرعة الثانية علان يدخل تركيز البوا فعال بدرجة

* Bioavailability can be measured by the area under the curve:

