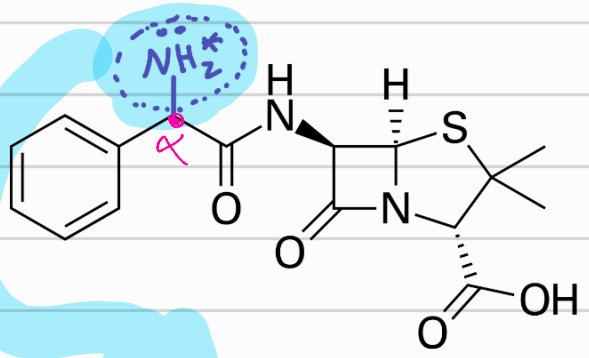
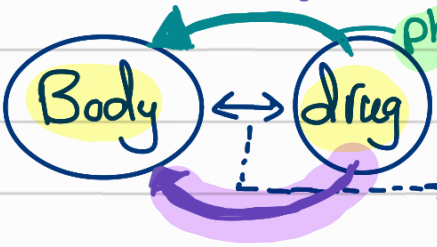
L02 - How Structure affects the Absorption. Week 01



penicillin g → Can't be given orally, its not Absorbed.

⊛ addition of $\ddot{N}H_2$ increase the oral Absorption (amoxicillin).



pharmacokinetics: usually Constant (ADME)

Both affect each other

توافق تضاريسي

Pharmacodynamics - Must have a proper topological match.

- *Kidney failure one of the most serious diseases, bic it's irreversible.
- *Drinking water is essential especially when taking drugs.

How Chemical Structure effects the Absorption ?

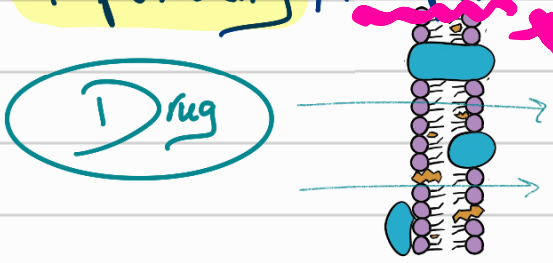
كيف تؤثر التركيب الكيميائي على الامتصاص

* most Common route: oral, easy, Controllable allergic rxns, ↑ paitent Complaince, Self-administered, most favourable route.

التزام . يأخذ الوصفة . أفضل طريقة

* Absorption of most of the drugs happen in duodenum.

* All membranes are phospholipid bilayer, but they differ in porousity, less porous is BBB, highly porous is glomerulous.



Lovely

Absorption

① Must be in solution, so it must contain hydrophilic functional groups

② To cross the membrane it must contain hydrophobic group.

⟹ There must be a hydrophilic-hydrophobic Balance.

☆ Oral Absorption Mechanisims (from GI):

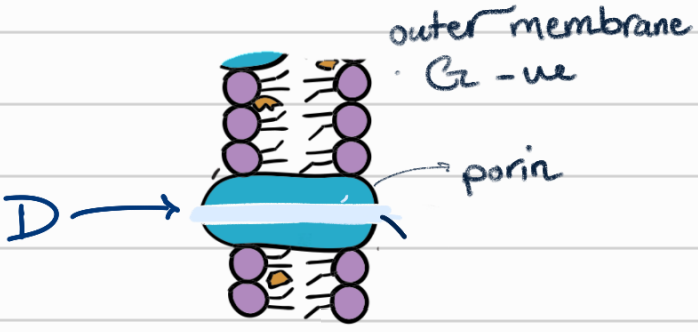
انتشار - توزع - نفاذية

[1] Permeation by partitioning (Diffusion) (depends on concentration gradient. it must partition between the membrane & fluid in order to penetrate the membrane.

[2] Water Channel (only drug absorbed through it's (Li^+) ion) b/c molecule must be smaller than (4 Å), all drugs are much bigger than 4 Å.*

$Å = 10^{-10}$ → angstrom*

* Gram -ve bacteria have an outer membrane, & it contains water channels called "porins" → which they're relatively larger than our GI water channels

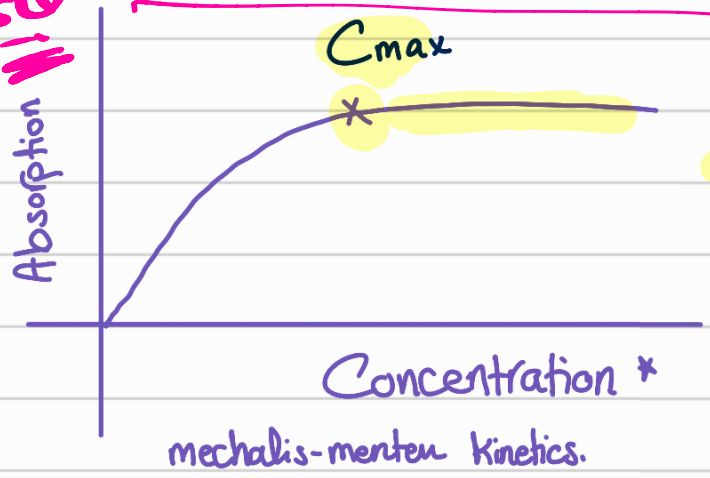


* the more hydrophilic the Drug, the more it penetrates to the Bacterial cell. ↑ effect

But !! → high hydrophilicity can cause poor penetration → this will ↓ oral Absorption, this problem can be overcomed by giving the Drug parentrally esp. for wide-spectrum antibiotics.

→ if the Drug is absorbed by carrier-mediated mechanism, the Drug will get Absorbed even if its extremely hydrophilic.

3) Carrier Mediated Absorption:



mechalis-menten kinetics.

☆ Carrier-mediated absorption is Conc. Dependent But to a certin point (C_{max}) when all Carriers are saturated (it becomes a Conc. independent mechanism).

* it's stereo-selective
* Could be facilitated diffusion or active transport
* There may be an individual variation in carrier types & no.

* Amoxicillin & Metformin Abs. is Carrier Mediated, same dose Could Differ accourding to variations, so dose adjustment is needed.

→ Since our drug contains Various functional groups, & pH range in GI is wide, it can get ionized in different regions accourding to its pka & Handerson Hasselbalch eqn.

pH-partitioning hypothesis:
for a drug to get partitioned & Absorbed, the drug must be unionized.

- Drugs
  - acidic (H+ Doner) -vely charged when ionized
  - Basic (H+ Acceptor) +vely charged when ionized

- Acidity
  - strong pka < 2
  - moderate 2 < pka < 10
  - weak pka > 10

مفيد

Basicity
- strong: pka > 10
- moderate: 2 < pka < 10
- weak: pka < 2

* Drug gets ionized relative to pH & Drug's pka.

e.g: Acidic drug pka = 5 pH = 3 ⇒ most of my drug is Unionized

* Strong Acidic Drugs :-

- pka < 2
  - usually 1.5
- pH range 2~3 → up to pH = 8 in stomach

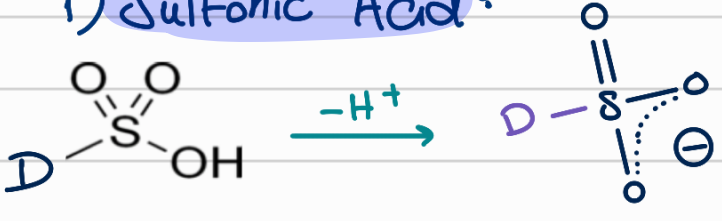
* never get Absorbed → needed for local effect on GI

e.g: Saccarin. ↳ b/c they're ionized throughout GI

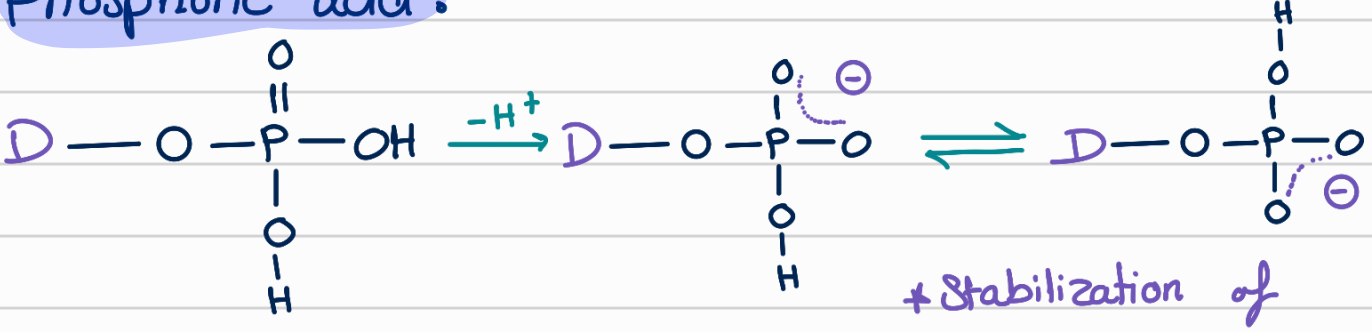
{ ↑ Conj. Base stability = ↑ Acid Strength }

→ There are Specific functional groups, When it exist in any drug, They become strong acidic drugs & never gets Absorbed:

1) Sulfonic Acid:



2) Phosphoric acid:



* Stabilization of Conj base by resonance