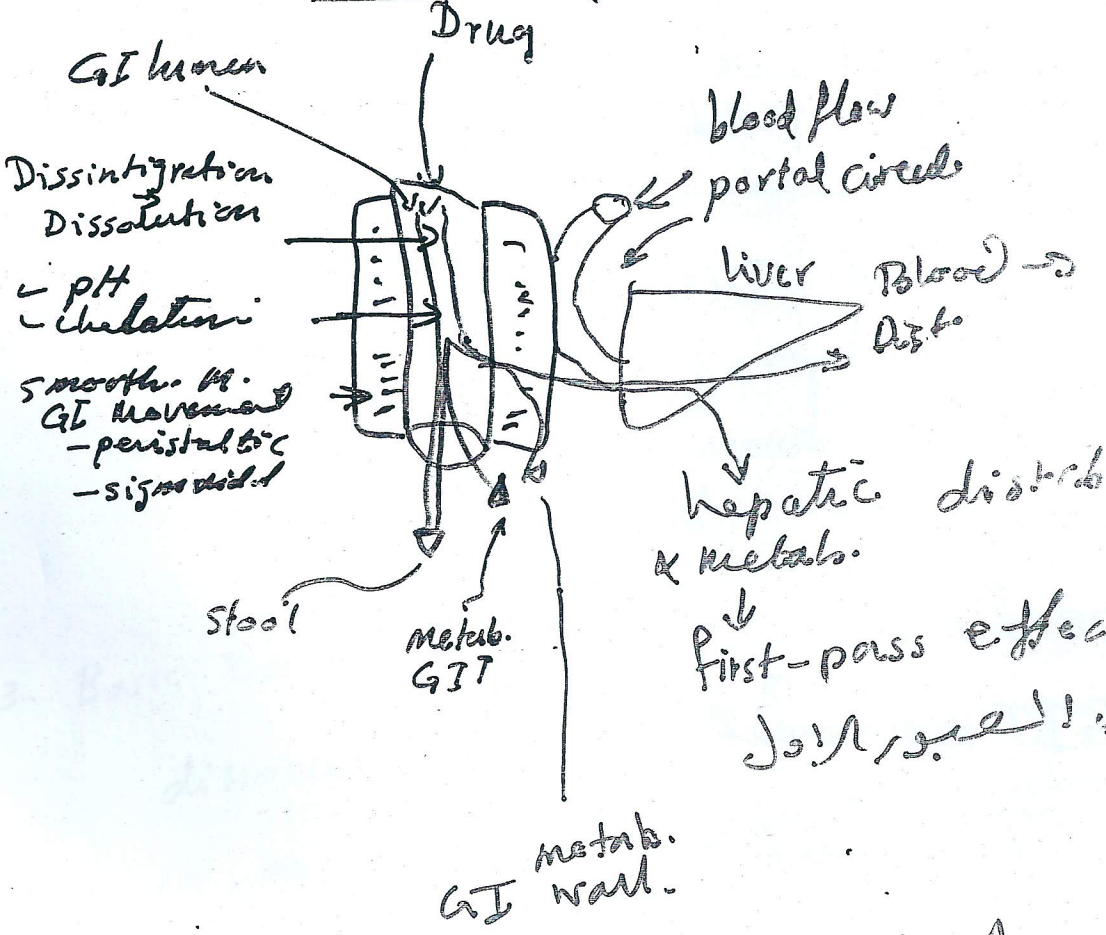
Drug Absorption

Definition: Transportation of Drug from site of adminis. to site of meas. bl.



Drug absorption → Distribution
Blood — central

Drug Transport from GIT → Portal circulation

I - Passive Diffusion

II - Carrier - mediated

Passive Diffusion
الانتقال المنفعل

- Degree of Dissolution
- Degree of lipid solubility
- Ionization & pH
- perfusion الأوعية
- GIT movement
- GIT Surface area
- food

Effect of pH on drug absorption

1- most drugs are:

- weak acids
- weak basis

2- Acidic drugs (HA).

dissociate into $H^+ + A^-$

$$HA \rightleftharpoons H^+ + A^-$$

ie:- Acidic drugs As a result of releasis the proton H^+ resulted in charged mollecule A^-.

3- Basic Drugs BH^+.

dissociate into $H^+ + B$

ie. as a result of dissociation uncharged mollecule B and proton.

$$BH^+ \rightleftharpoons B + H^+$$

4- Only uncharged drugs can pass lipid membrane

i.e. :- . weak acids uncharged HA → can permeate easily (Not A^-)

. weak bases uncharged B → can pass easily. (Not BH^+)

5- The percentage of unionized & ionized drug concentration at the sides of lipid cellular membrane determins the degree of passage of drugs.

- more ionized drug - more water soluble
- unionized form is more lipid membrane permeable.

- sustained release formulations: release the drug slowly to prolong drug action and reduce the frequency of administration.

3- <u>GI motility</u> : - Stasis → slow oral absorption
→ diarrhea = may allow insufficient time for complete absorption.

4- <u>Interaction with other drugs & substances in GI</u>

- food ↓ absorption (generally)
- e.g. tetracycline - Ca^{++} milk cheese
  insoluble complex
  (chelation)

The concentration of charges [illegible]
depend on two main factors:

a- pH of the media

b- the strength of the weak acid & weak base

pKa = pH of the media where 50% of drug is unionized. ie interaction of a compound with a proton.

a- The lower the pK of drug the stronger the acid

b- the higher the pKa the stronger the base.

7- Henderson-Hasselbalch equation:

- relation betwee pKa of drug & pH of the media.
- determin how much of the acid or base present as unionized or ionized form.

$$pH = pKa + \log \frac{[\text{Nonprotonated species}]}{[\text{protonated species}]}$$

For acids = $pH = pKa + \log \frac{[A^-]}{[HA]}$

For base = $pH = pKa + \log \frac{[B]}{[BH^+]}$

[B] non protonated = unionized

$[BH^+]$ protonated ionized.

Henderson - Hasselbalch equation.

Determination of how much drug will be found on either side of a lipid membrane:-

depending on = pH of the medium
pKa of the drug

pH of the media =

- stomach = 1.0 – 1.5
- small intestine → Jejunum - ilium upto 8.0
- blood plasma → 7.4
- urine → 4.8 – 8 varies
  acidic – basic

when pH = pKa

for acids - $HA \rightleftharpoons A^-$
unionized conc. — ionized conc.

for base $BH^+ \rightleftharpoons B$
ionized conc. — unionized conc.

possibilities

A- when pH is less than pKa :- $pH < pKa$

the protonated forms of drugs are predominant

for Acid = HA = unionized form predominant

for Base = BH^+ = ionized form predominant.

ie : in acidic media acids are predominantly unionized & easily absorbed

Bases are predominantly ionized & cann't be absorbed.

B- when pH is greater than pKa :- $pH > pKa$

the deprotonated form are predominant

for acids = A^- = ionized form predominant

for bases = B = unionized form predominant

ie in basic Media

- acids are predominante ionized & cann't be absorbed
- Bases are predominante unionized and easily absorbed.

Factors controlling oral absorption

1 - lipid solubility and ionization:

- intestine = villi, microvilli } main absorption area

- weak acids : less ionized in stomach.
  mostly absorbed in the more alkaline intestin

Note = • rate of absorption → more from acidic media in stomach

• Extent of absorption from intestine → more surface area

2 - Drug formulation:

Rate & extent of drug absorption depends on the pharmaceutical formulation.

tablet
↓
disintegration
(small particles)
↓
disolve
insalution

- only soluble drugs can absorbed