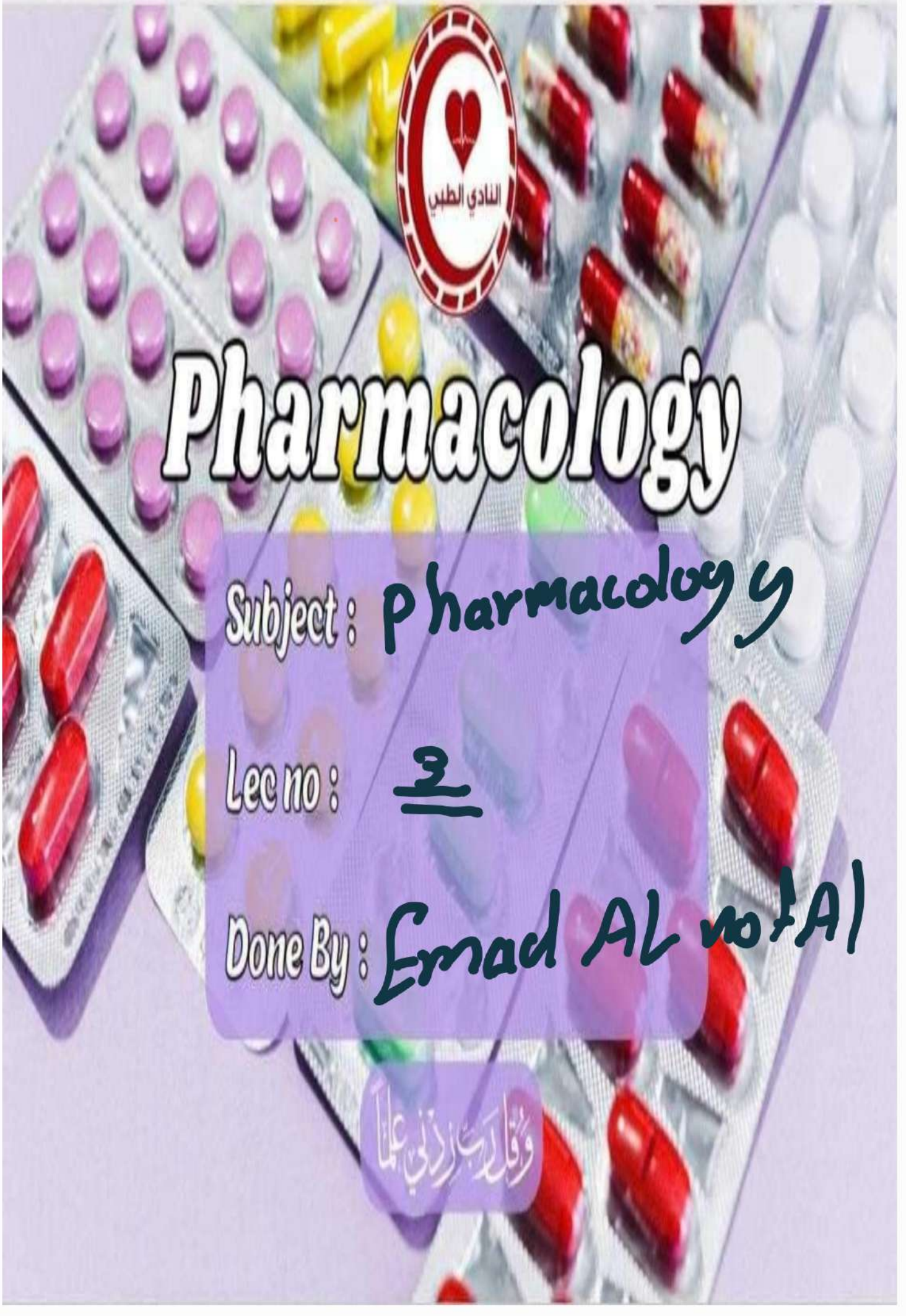
النادي الطبي
Pharmacology
Subject : Pharmacology
Lec no : 3
Done By : Emad AL wotAl
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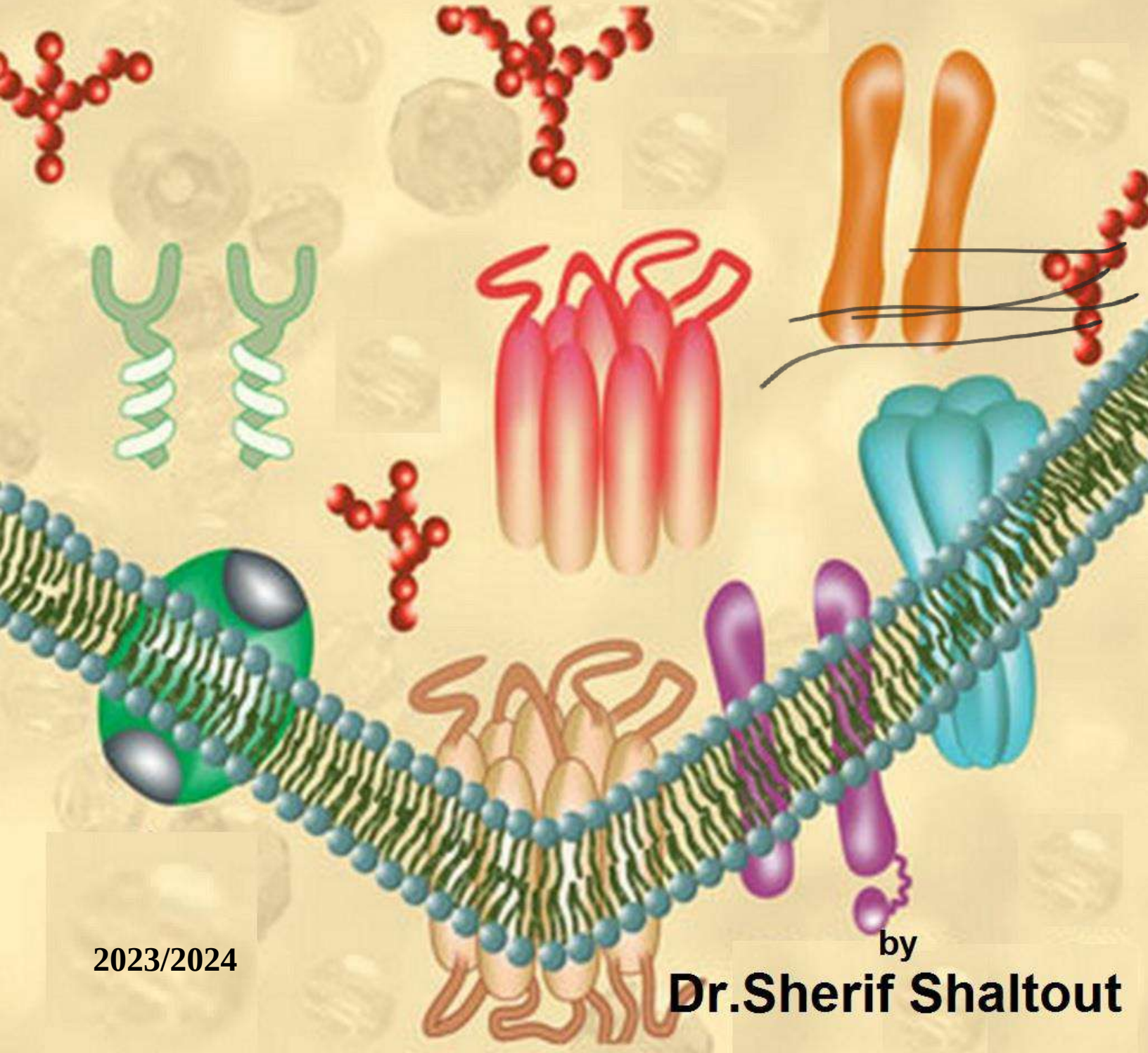
General Pharmacolog



2023/2024

by
Dr.Sherif Shaltout

❖ Relation between pH of the medium and pKa of the drug is presented by **(Henderson-Hasselbach equation):**

$$pka = pH + \log \frac{\text{concentration of protonated}}{\text{concentration of nonprotonated}}$$

® If the drug is weak **A**cid :

$$pka = pH + \log \frac{\text{concentration of Unionized acid}}{\text{concentration of ionized acid}}$$

® lf the drug is weak base:

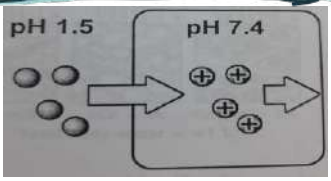
$$pKa = pH + \log \frac{\text{concentration of the ionizd base}}{\text{concentration of unionized base}}$$

- **pKa of a drug:** is the **pH** at which **50%** of the drug molecules exist in the **ionized** form and **50%** in the **unionized** form.

Clinical Significance of pK_a

1. GIT: knowing site of drug absorption:

- Acidic drugs (e.g. Aspirin) become mostly unionized in acidic pH
- Basic drugs (e.g.Amphetamine) become mostly unionized in alkaline pH
- Streptomycin has a very high pKa→ always ionized→ very poor oral absorption
- **Ion trapping of aspirin**: Aspirin (pKa = 3.5) in the empty stomach (pH = 1.5) → more unionized → more absorbable into gastric cells, but once entered the cells (pH = 7.4) becomes more ionized → trapped inside these cells (aspirin trap) → death of the cells inducing "peptic ulceration".



2. Kidney: treatment of drug toxicity

- In drug poisoning, changing urinary pH → increases drug ionization and inhibits tubular reabsorption:
- Alkalinization of urine is useful in acidic drug poisoning e.g. aspirin.
- Acidification of urine is used in basic drug poisoning, e.g. amphetamine.

Aspirin pka = 3,5 stomatch pH = 1,5

$$pKa = PH + \log \frac{\text{unionized}}{\text{ionized}}$$

$$3,5 = 1,5 + \log \frac{\text{unionized}}{\text{ionized}}$$

$$2 = \log \frac{un}{I}$$

$$\log(100) = \log \frac{un}{I}$$

$$100 = \frac{un}{I} = \frac{100}{1}$$

so the ratio between the nonionized and the ionized Aspirin in the stomatch is $\frac{100 \rightarrow \text{nonionized}}{1 \rightarrow \text{ionized}}$

And we know that the absorbed drug is the ionized this proved that the acidic drug most absorbed in the acidic media

---

now If we put aspirin in media which pka = 5,5

$$3,5 = 5,5 + \log \frac{NI}{I}$$

$$2- = \log \frac{NI}{I}$$

$2- = \log \frac{NI}{I}$ قلبي

$2+ = \log \frac{I}{NI}$

$\log 100 = \log \frac{I}{NI}$

$\frac{100}{1} = \frac{I}{NI}$

So the ratio between the I drug and NI drug is $\frac{100}{1}$ and the lonized drug is hard to absorbe * that proved if the acidic drug not absorbed in basic media

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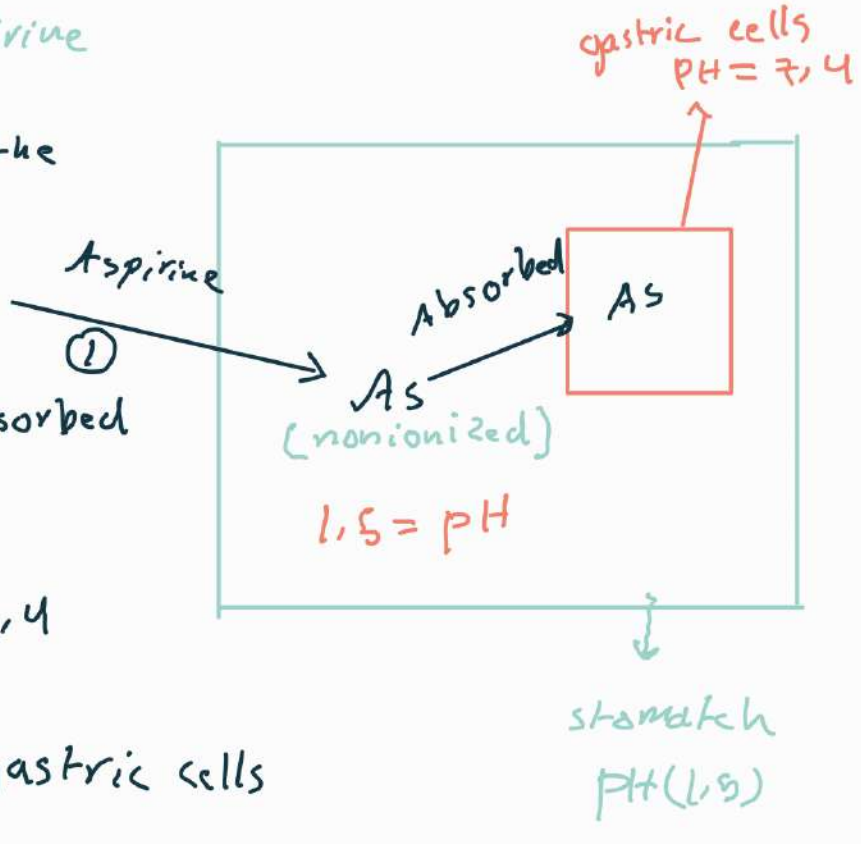
ion trapping of Aspirine

1- when aspirine inter to the stomatch in become in nonionized form

2- nonionized form can absorbed to the gastric cells

3. in gastric cells the plt 7,4 which is Alkalaine media so it can't absorbed in gastric cells



4- by the time the metabolic reaction in the gastric cells will change the pH and gastric cells will be Acidic then aspirin absorbed

Aspirine rate absorbtion in stomatch because of Acidity, but the total absorbtion in intestine is higher because the high surface area

B. Factors related to patient:

1. Route of administration: IV > Inhalation > IM > SC > Oral > Skin

2. Absorbing surface:

a. Vascularity: Alveoli > skeletal muscle > subcutaneous

b. Surface area: Intestine > Stomach → because of microvilli

c. State of health: Diarrhea & malabsorption ↓↓ oral absorption

+ edema

3. Systemic circulation: Shock & heart failure ↓↓ absorption because of low blood pumping

4. Specific factors: intrinsic factor for vit.B_{12}

5. Presence of other drugs: - vit.C ↑ absorption of iron

For treatment the toxicity of drugs ← Activated charcoal ↓↓ oral absorption of most of drugs

- Adrenaline SC → VC → ↓↓ absorption of local anesthetics → longer duration of action

some places of the body we can't use adrenaline (end artrial like fingers or toes)

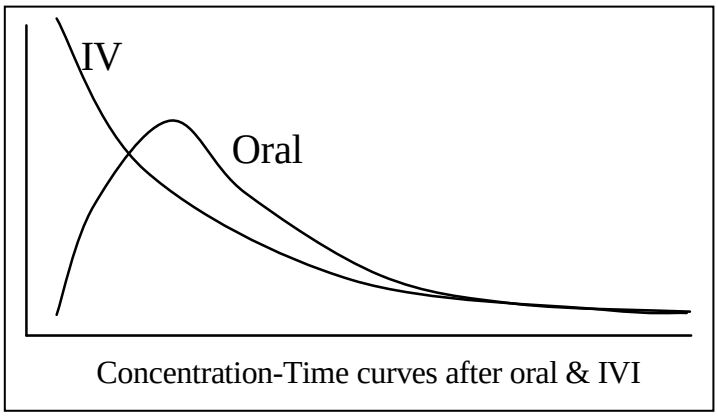
❖ **Bioavailability (Biological Availability)**

-It is the percentage of unchanged drug reaching the systemic circulation after any route and becomes available for biological effect.

Avilable to effect

-It is calculated by: **(AUC) after any route of administration X 100**
(AUC) after IVI.

(AUC = the **A**rea **U**nder the blood concentration-time **C**urve**)**



Concentration-Time curves after oral & IVI

Factors Affecting Bioavailability

I. Factors Affecting Drug Absorption from GIT (oral absorption)

A. Factors related to drug: …….

B. Factors related to patient: …….+

4. Presence of food:

- Empty stomach → ↑absorption (BUT it is bad if irritant drug e.g. Aspirin)
- Milk (calcium) ↓↓ oral absorption of tetracyclines

5. pH: - gastric acidity ↑ absorption of aspirin and barbiturates

- intestinal alkalinity ↑ absorption of amphetamine and ephedrine

6. Gut motility: marked alterations e.g. diarrhea ↓ absorption

7. Gastric emptying:

a. Metocloperamide → accelerates gastric emptying →

- ↑ absorption of paracetamol (rapid rate of disintegration & dissolution)

b. Atropine → slowdowns emptying →the REVERSE effects

II. First-Pass Effect (First-Pass Metabolism; Presystemic Elimination)

- It is the metabolism of some drugs in a single passage through the liver, gut wall or the lungs before reaching the systemic circulation.

A. Hepatic 1ST pass effect: drugs absorbed from the GIT are carried first in the portal circulation to the liver. Some drugs are extensively metabolized in their first-pass e.g. nitroglycerin & propranolol.

B. Gut 1ST pass effect:

- Gastric acidity: benzyl penicillin
- Digestive enzymes: insulin & pituitary hormones
- Mucosal enzyme: L-dopa , alpha-methyldopa

C. Pulmonary metabolism: after aerosol inhalation (nicotine).

How to overcome the First-pass Effect

1. **Increase oral dose**
2. **Other routes: Sublingual - Parenteral - Rectal (to some extent)**