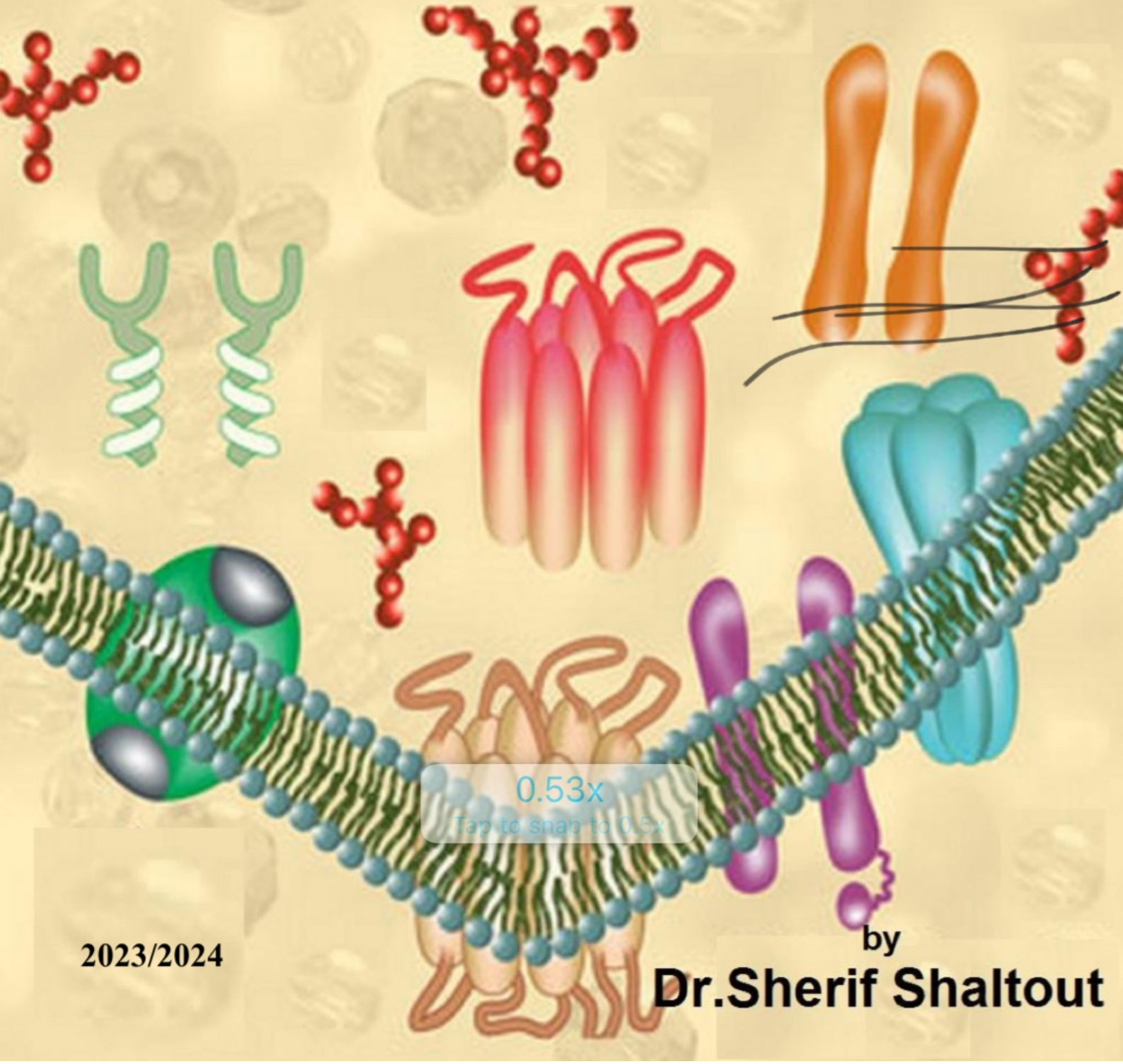

النادي الطبي
Pharmacology
Subject :
Lec no : 3
Done By : Mass
وقل رب زدني علما

General Pharmacolog



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by

Dr.Sherif Shaltout

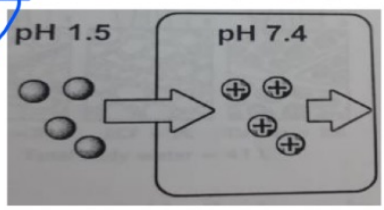
the **ionized** form and 50 % in the **unionized** form.

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".

if we take high dose of aspirin



2. Kidney: treatment of drug toxicity

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

Not useful

To treat toxicity :

1-decrees the drug absorbtion
2- treat the important thing like in case of coma
3-increase the excretion in kidney

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

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

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

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

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

$$100 = \frac{un}{I} = \frac{99}{1}$$

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

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

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

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

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

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

قلب

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

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

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

لانه جزء Alkalinize

٩/٢ تصاعد حقلية

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

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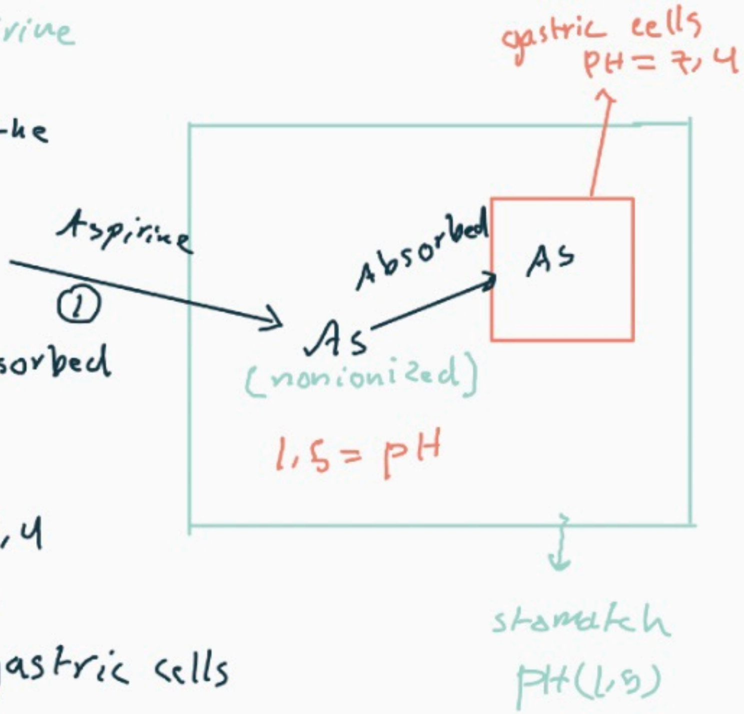
ion trapping of Aspirine



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

2- non ionized form can absorbed to the gastric cells

3. in gastric cells the pH 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

IV is the fastest rout of administration but has No absorption phase (drug is delivered directly to the systemic circulation)

B. Factors related to patient:

route اسرع

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

2. **Absorbing surface:**

مثال على الaspirin هو حمضي فالامتصاص الافضل يكون بالstomach و لكن الكمية الاكبر بال intestine و كمان لانه المساحة اكبر

   a. **Vascularity:** Alveoli > skeletal muscle > subcutaneous

   b. **Surface area:** Intestine > Stomach Because of microvilli

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

يتنقل الدم حتى ينتشر بالجسم

بيحصل edema باخر الا متصاص

3. **Systemic circulation:** Shock & heart failure ↓↓ absorption

4. **Specific factors:** intrinsic factor for vit.B_{12} زي الناس يلي عندهم anemia

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

الفحم النشط

   - Activated charcoal ↓↓ oral absorption of most of drugs

Injection by subcatenous route

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

Vasoconstriction

مكان بالجيم بقدر استخدم فيه ادرينالين زي الأصابع في اليل و القدم

available to affect

❖ Bioavailability (Biological Availability)

بشوف الكميه المتاحه بالدم الي بتعطي ال biological effect

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

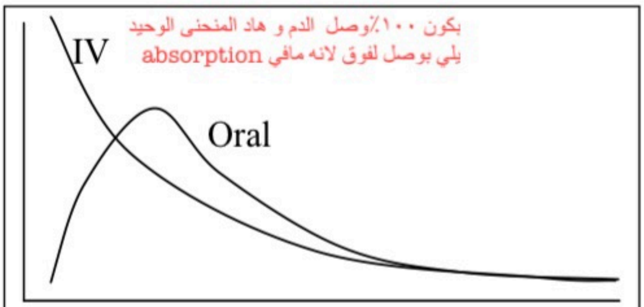
-It is calculated by: $\frac{\textbf{(AUC) after any route of administration}}{\textbf{(AUC) after IVI.}}$ **X 100**

ثابتة

يكون وصل ١٠٠٪ للدم في حاله ال IV

(AUC = the Area Under the blood concentration-time Curve)

نفس الجرعه يلي اعطيتها I'v بعطيها مكان اخر مثل oral و بصير امتصاص و بعدها decrease بنحسب المساحه تحت المنحنى و يلي بتعبر عن الكميه يلي بالدم



Concentration-Time curves after oral & IVI

انعكاس ال absorption هو ال bioavailability بحسبها حسب ال route
1. oral bioavailability
2. rectal bioavailability

Factors Affecting Bioavailability

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

A. Factors related to drug: …….

B. Factors related to patient: ……….+

مع ذلك مش كل الادويه بقدر اعطيهم بال empty stomach فالمسكنات بعد الاكل

4. Presence of food:

و في استثناء زي الفيتامين د يزيد امتصاصه مع الدهون

- 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

الوقت يلي بتحتاجه في انتقال الدواء م الstomach الى ال intestine لو صار تاخير بالانتقال رح يتاخر الامتصاص في ال intestine

7. Gastric emptying:

مضاد للقيء

a. Metoclopramide → accelerates gastric emptying →

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

لو اخذته مع ال metoclopramide هاي النتيجه

Gastric empty يعمل تاخير بل

b. Atropine → slowdowns emptying →the REVERSE effects

Absorption

بيتاخر الامتصاص

parasympathetic system بمنع شغل ال

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

metabolism to بصير قبل وصوله للدم the drug فبتكون ال bioavailability قليله

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

اكثر مكان بصير فيه first past effect

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.

و ممكن تصير بمكان تاني زي ال mucosa و اثناء مرورها و هي رايحه للدم و ممكن حموضة المعده يكون الها اثر بال first past effect

الذبحة القلبية

liver ادويه بتتكسر بال

B. Gut 1ST pass effect:

- Gastric acidity: benzyl penicillin بنوخذه injection بس لانه لو اخذناه oral رح يتكسر بسبب حموضه
- Digestive enzymes: insulin & pituitary hormones الانسلوين عباره عن بروتين و ما بصير ينهضم لهيك ما باخذه oral عشان ما ينهضم
- Mucosal enzyme: L-dopa , alpha-methyldopa لا يؤخذ Oral.

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

موجود بالدخان و بصيرله fast past effects و باثر على lung

How to overcome the First-pass Effect

تجنب

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

غني بال blood supply لانه بصيرله امتصاص على طول