# Pharmacology

Subject : Introduction + Pharmacokinetics

Lec no : 1 + 2

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للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

تجدون في guidance مادة الفارما على موقع النادي :

# GENERAL PHARMACOLOGY

This chapter provides basic knowledge necessary for subsequent study of individual drugs. Important terms & definitions are presented, together with the two basic areas of pharmacology; pharmacodynamics & pharmacokinetics.

## Pharmacology

- It is the science that deals with drugs, their nature, pharmacodynamics, pharmacokinetics, therapeutic uses, adverse effects, preparations and administration.

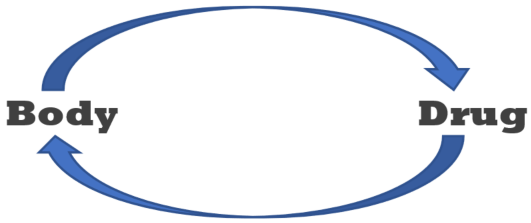
## Drug

- It is a chemical substance that alters body functions and can be used for treatment, prevention or diagnosis of disease.

## Pharmacokinetics

- They are the studies of the **A**bsorption, **D**istribution, **M**etabolism and **E**xcretion of drugs (**ADME**) and their mathematical relationship, i.e. **what body does to drugs.**

**Ph.Kinetics**




**Ph.Dynamics**

## Pharmacodynamics

- They are the studies of the biological and therapeutic effects of drugs and their mechanism of action, i.e. **what drugs do to the body.**

## Pharmacotherapeutics:

- Study the selection & use of the drugs for treatment, prevention or diagnosis of diseases

## Sources of drugs:

1. **Plant:** e.g. atropine from leaves of belladonna / Morphine
2. **Animal:** insulin from the pancreas of pigs (causes allergy)
3. **Mineral:** $MgSO_4$, iodine
4. **Microorganisms:** penicillin from the fungus penicillinum
5. **Synthetic:** in laboratory e.g. aspirin (acetylsalicylic acid)
6. **Biotechnology:** human insulin by genetic engineering

## Drug nomenclature:

1. **Chemical name:** N-acetyl p-aminophen
2. **Generic name:** Acetaminophen (paracetamol)
3. **Trade name:** Panadol- Adol

| Routes of Administration | Advantages | Disadvantages | Dosage form |
|---|---|---|---|
| | | Enteral (GIT) → Mesenteric Artery (provides oxygenated blood & nutrients to GIT) | |
| 1) Oral (by mouth, swallowing) | Most convenient, Safe, Economical , Easy | *Not suitable for: Unconscious, Uncooperative, excessive Vomiting or Diarrhea, Emergencies, Irritant drugs, drugs destroyed by (gastric acidity, enzymes , 1st pass effect) | *Solid: powder, effervescent granules, tablet (simple, sugar-coated, enteric coated, sustained release; SR), capsule (hard, soft, SR)<br>*Liquid: syrup, suspension, solution |
| 2) Rectal (by Anal Canal) | Escape 1st pass effect, useful if oral is unsuitable: not diarrhea | | *Solid: suppository<br>*Liquid: enema |
| 3) Sublingual (without swallowing because it's rich in blood supply) | *Escape 1st pass effect, acidity, enzymes<br>*Rapid absorption | | *Pellet, spray<br>*(buccal route for local effect: lozenge, wash, paint, gargle) |

* 1st pass effect → drug is metabolised before entering circulation

* enteric coated → coated because of irritant drugs or can be destroyed by stomach

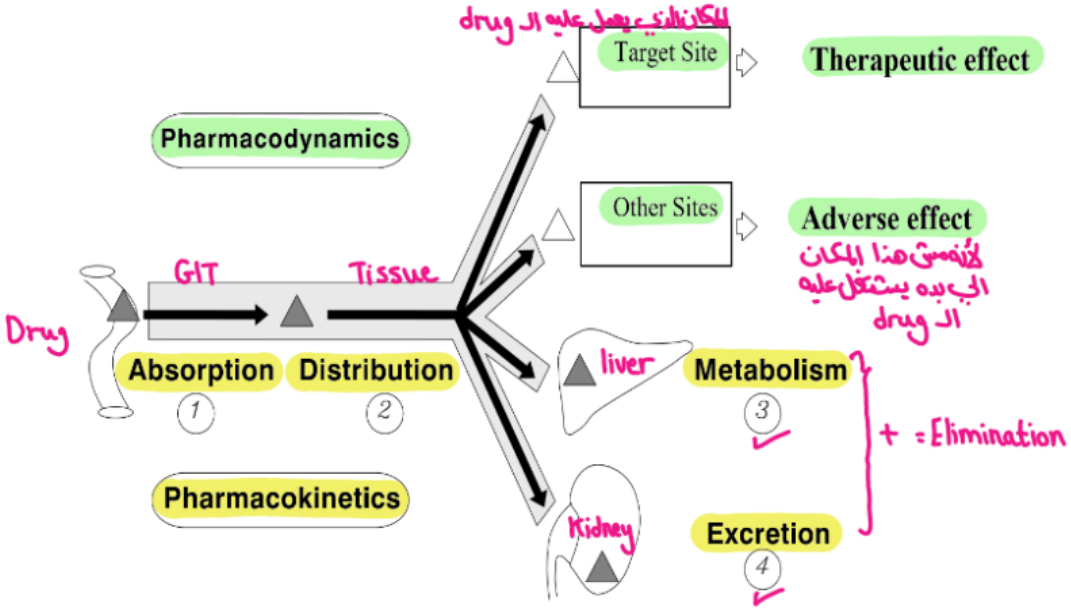
| | | | |
|---|---|---|---|
| | | **Parenteral** (outside GIT) → by injection الحقن (immediate) | |
| **1) Intravenous (IV)** | Rapid onset, 100% bioavailab., suitable for emergency and large volume drugs<br>bioavailab → Absorption | *Most dangerous<br>*transmission of diseases e.g. AIDS Hepatitis/malaria<br>*If allergy…> anaphylactic Shock<br>*Pyrogenic reaction رفع درجة حرارة الجسم<br>*Not suitable for oily preparation, irritant drugs | Ampule (single dose), Vial (multiple doses), bottle |
| **2) Intramuscular (IM)** | Suitable for mild irritant drugs, oily preparation | Unsuitable for large volume, (no space-just 5 cm) | Ampule, vial |
| **3) Subcutaneous (SC)**<br>dermis تحت<br>heparin/insulin مثل (الأنسولين) | | | *Water solution or fine suspension<br>*SC implant: small rods عصيان (هرمونات منظمة الحمل) |
| | | **Others** | |
| **Inhalation**<br>to blood by lungs | Excellent absorption due to rich blood supply and alveoli …>large surface area, porous, thin<br>منها مسامات | الحويصلة الهوائية | Gases, solution (nebulizer), Fine powder(spinhaler), vapours of volatile liquids<br>(بخار السوائل المتطايرة (الكحول/الإيثر / أدوية التخدير الكلي) |
| **Topical** موضعي | | | |
| **1) Local effect**<br>(منتظم المكان) | For skin,<br>nose,<br>eye | | Ointment, cream, lotion, spray, drops → قطرات<br>Drops, ointment → مرهم |
| **2) Transdermal: TDS (Transdermal Delivery System)**<br>(تدخل إلى الدم عن طريق الجلد) | Prolonged effect and avoid 1st pass effect e.g. nitroglycerin, estrogen<br>أدوية لذبحة الصدرية | | Patch, ointment, cream (للاهمكة) |

IV ←
- *Not suitable for oily preparation → because blood majorly is water (plasma) → just Intramuscular
- فإذا حطينا فيه مادة زيتية مارح تذوب وبح تسكر الـ capiliary فهنا يحصل فيه tissue or organ infraction جلطة
- *Irritant drugs: affects the endothelium of the vien which causes infections

*Intradermal injection → between epidermis & dermis e.g: Vaccines

# PHARMACOKINETICS

The term pharmacokinetics denotes the quantitative studying of drug **A**bsorption, **D**istribution, **M**etabolism and **E**xcretion **(ADME)** and their mathematical relationship.




**Fate of the drug in the body** → drug works systemically (على الجسم كله)

*ملاحظة: هذه الأربع عمليات لا تحدث بالترتيب فـ drug ينتقل بالدم (through circulation) وبيذهب إلى عدة أماكن

إذا حققت شروط action دخل action إذا حققت شروط metabolism دخل metabolism وإذا حققت شروط Excretion دخل Excretion هيك.

إذاً العمليات بتتم مع بعض

* لو ما حصلش للدواء passage في وين site of administration يكون الـ Local effect مثل بعض مضادات البكتيريا اللي تؤخذ orally

لكن تعمل فقط على mucous membrane of GIT (locally) في حالات Diarrhea

ومن أدوية تُوضع على skin مثل أدوية الذبحة الصدرية ومنظفات الحمل وتعمل passage لأنه بدخل للدواء systemically

## ABSORPTION OF DRUGS

❖ **Definition:** absorption is the passage of drug from the site of administration to the systemic circulation.

❖ **Methods of transport across cell membranes:** كيف drug بيعبر tissue إلى الدم ويتصير العملية؟

1- **Passive transport:**

a. **Simple (lipid) diffusion:** the **lipid soluble** drugs can easily cross lipid membranes along concentration gradient with no energy. (most common) (from high concentration to low) (cell membrane (phospholipid bilayer))

b. **Aqueous diffusion (filtration):** the **water soluble** drugs can pass only through water filled **pores or channels**.

* أهم طريقة يتم فيها Diffusion هي Simple or lipid diffusion لأن drug الـ water soluble بدقيقة حتى يكون water channel ضروري

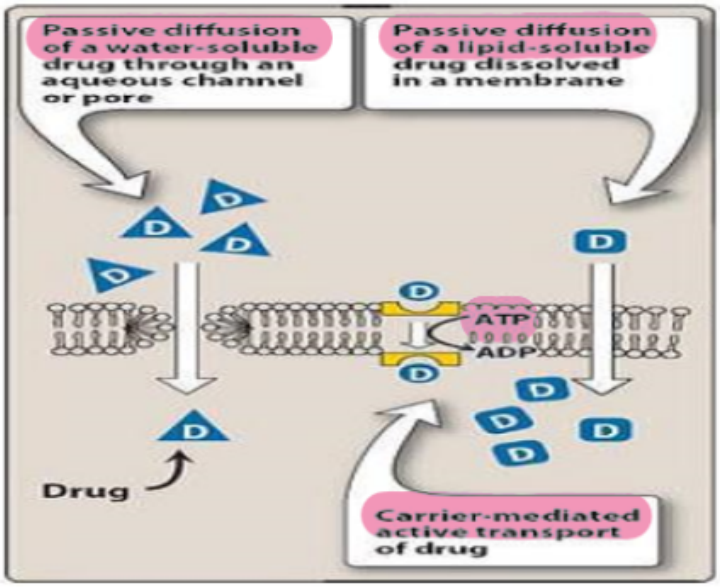
والحجم لازم يكون مناسب حتى يعبرها وهذا الشرط ممكن يتوفر بكل الأدوية فقط $K^+$ / $Na^{+2}$ (صغيرة الحجم) وليس لديه side chain

2- **Carrier-mediated transport:** the drug passes across cell membrane by specialized carrier molecules (which are sites for saturation & competition): with protein structure

   a. **Facilitated diffusion:** as simple diffusion but with aid of carrier. e.g. glucose uptake (without energy / along concentration gradient)

   b. **Active transport:** the drug is carried against concentration gradient by energy. e.g. Na/K pump

3- **Endocytosis (pinocytosis):** it occurs in cases of large molecule by invagination هبدم of part of cell membrane and engulfing the drug molecule. Energy is needed. e.g. absorption of vit.B12 + & intrinsic factor in terminal ileum. الأمعاء الغليظة




* Saturation ← the carrier has a capacity لا يستطيع تخطيها

فلو افترضنا إنه كمية drug من الـ saturation capacity of the carrier فحيتزاحم بالجسم ويسبب toxicity or adverse effect

* Competition ← تنافس

drug مجموعة بوخذ carrier كل لا drug له carrier من كل drug تحتاج Uric acid أو glucose ممكن ينقل

فممكن الـ carrier بينقل جلوكوز نفسه ينقل مجموعة أدوية ويحصل بين هاي molecules تنافس وتسبب adverse effect ← adverse effect

* What is the difference between Phagocytosis & Pinocytosis?

→ Phagocytosis: when the molecule is solid e.g: (when white blood cells engulf bacteria)

→ Pinocytosis: specially for the drug (liquid)

## ❖ Factors affecting drug absorption:

### A. Factors related to drug:

1. **Molecular size:** small molecules are absorbed than large molecules
2. **Pharmaceutical preparations**
   - **Dosage form:** - solutions (completely dissolved) are better absorbed than suspensions (not completely dissolved) (يستخدم مادة لتكون وسيط مثل الصمغ العربي)
   - sustained-release preparations are slow in absorption
   - **Rates of disintegration (التفكك) & dissolution (الذوبان):**

     Rapid with paracetamol and slow with digoxin (يستخدم في علاج Heart failure)

* طفل عنده Pharyngitis & fever وأعطيته خافض للحرارة بصورة solution وبنفس الوقت بصورة antibiotic على صورة suspension
من نفس الوقيت، مين فيهم يشتغل أسرع؟ خافض الحرارة لأنه يعمل absorption أسرع
* Sustained-release ← لما يكون absorption طويلة بتبطأ عملية وصول molecules of drug مجيبوا مجموعة بحيطوها بـ layer معينة وبعاودوا يطلقوا بالدم وجوده داخل الدم
* Disintegration ← تفكك molecules of drug عن tablet
* Dissolution ← ذوبان molecules في media
stomach ← HCl
kidney ← secretion

↑ Rate of Disintegration & Dissolution ↑ Absorption يعتمد على طبيعة الدواء والوسط حوله

3. **Lipid and water solubility:**
   - Drug must be water soluble ~~as well as~~ + lipid soluble
   - ***More lipid solubility → high lipid/water partition coefficient → better absorption***

* نقول أن الدواء completely water soluble رح يعبر cell membrane لكن بحتاج لـ channel رح يعبر فيه عن طريق absorption لكن ببطء
* نقول أن الدواء extremely or highly lipid soluble رح يعبر cell membrane لكن طبيعة cytoplasm أو الدم water compartment فمدري بيقدر يتركك منعبر
* نقول أن الدواء mixed (lipid + water soluble) فكلما كان lipid solubility أعلى رح يعبر phospholipid bilayer of cell membrane ومن نفس الوقت نسبة lipid/water partition coefficient = $\frac{\text{lipid solubility}}{\text{water solubility}}$ بعملوا نسبة فذلك water compartment داخل الموجودة water solubility تسمح له بالترك وكلما كان البسط أكبر (الناتج أكبر من واحد) كلما كان absorption أعلى.

4. **Ionization:** - *Ionized (polar or charged)* forms are poorly absorbed because of repulsion between charges (بدّن cell membrane مستحيل)

- *Unionized (non-polar or non-charged)* forms are more absorbed

e.g. - Quaternary ammonium compounds: always ionized → poor absorption ($NH_4^+$) orally من خلال أخذ الدواء GIT تعمل فقط على locally

- Tertiary amines (physostigmine): always unionized → better absorption ($NH_3$)

❖ Most drugs are either weak acids or weak bases.

❖ Acidic drugs (HA) release an H+ producing a charged anion (A-):

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

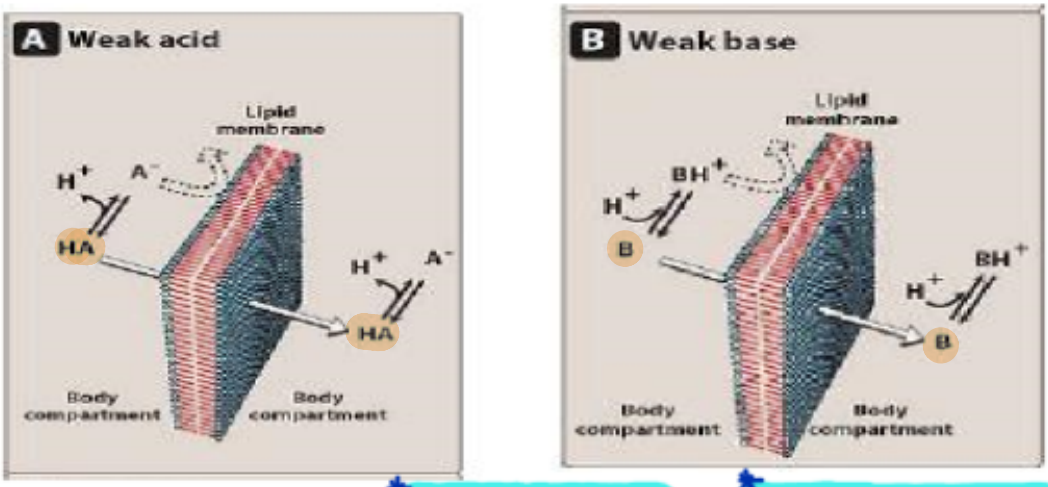
(protonated form) — unionized, to absorption

❖ Weak bases (BH+) can also release an H+ producing the uncharged base (B):

$$BH^+ \rightleftarrows B + H^+$$

(nonprotonated form) — to absorption, why? unionized

→ Weak → can release or accept $H^+$




❖ Ionization depend on pH of the medium and pKa of the drug (pKa is a measure of the strength of the interaction of a compound with a proton). قوة ارتباط الدواء مع $H^+$

❖ **The lower the pKa** of a drug, **the more acidic** is the drug. Conversely, **the higher the pKa, the more basic** is the drug.

(release) (accept)

Acid ⟶ releases $H^+$ $\quad HA \longrightarrow H^+ + A^-$

Base ⟶ accepts $H^+$ $\quad B + H^+ \longrightarrow BH^+$

→ strong المواد هذه حارقة وليست أدوية

pH: (Hydrogen Ion ($H^+$) concentration)

حسب المعادلات

*مثال: Acidic drug حطيناه في stomach اللي هي فيها HCl ف drug رح يميل مرتبط بـ ($H^+$) ويصير absorption

∴ الدواء Acidic إذا حطيته في Acidic media رح يزيد absorption (HA)

أما إذا حطيناه في intestine (Alkaline media) فيها نسبة $H^+$ قليلة فالدواء رح يفعل release ويعطي $H^+$ إلى media

∴ الدواء Acidic و حطيته في Alkaline media رح يكون عنده poor absorption ($A^-$)

إذا الدواء Basic وحطيناه في acidic media مثل stomach فالدواء رح يميل مرتبط بـ ($H^+$) وما رح يصير absorption

∴ الدواء Basic وحطيته في Acidic media رح يكون not absorbed ($BH^+$)

إذا الدواء Basic وحطيته في Alkaline media رح يفعل release $H^+$ إلى media ويحصل absorption (B)

special for

pka ⇝ Drug

pH ⇝ Media

إذا كان دواء و الوسط متشابهين بزيد Absorption

because the most molecules of the drug present in unionized form

أما إذا كانوا مختلفين يقل Absorption

the most molecules of the drug present in ionized form

❖ 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:

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

® If 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.

log 1 = zero

ionized form = unionized form

NOBODY SAID IT WAS EASY.

#النادي_الطبي

#معكم_خطوة_بخطوة