

PHARMACOKINETICS

1

Prepared by: Heba Ahmed Hassan
Assistant professor of clinical pharmacology
faculty of medicine, mutah university, JORDEN

Pharmacology

The science that deals with drugs.

Drugs

Substances used to prevent and treat diseases.

Drugs

```
graph TD; A[Drugs] --> B[Pharmacokinetics]; A --> C[Pharmacodynamics];
```

Pharmacokinetics

**what the
body does
to the
drug?**

Pharmacodynamics

**what the
drug does
in the
body?**

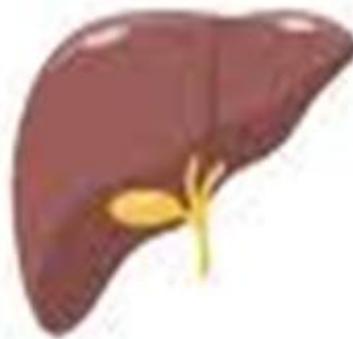
Pharmacokinetics



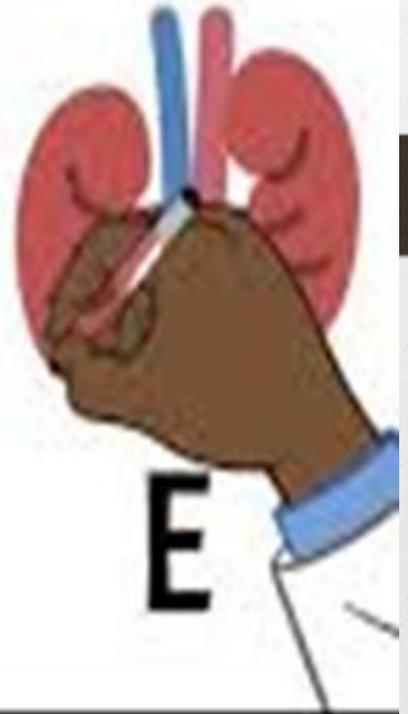
A



D



M



E

Pharmacokinetics

what the body does to the drug?

- Absorption
- Distribution
- Metabolism
- Excretion.

ABSORPTION

**PASSAGE OF DRUG
FROM SITE OF
ADMINISTRATION
TO SYSTEMIC
CIRCULATION**

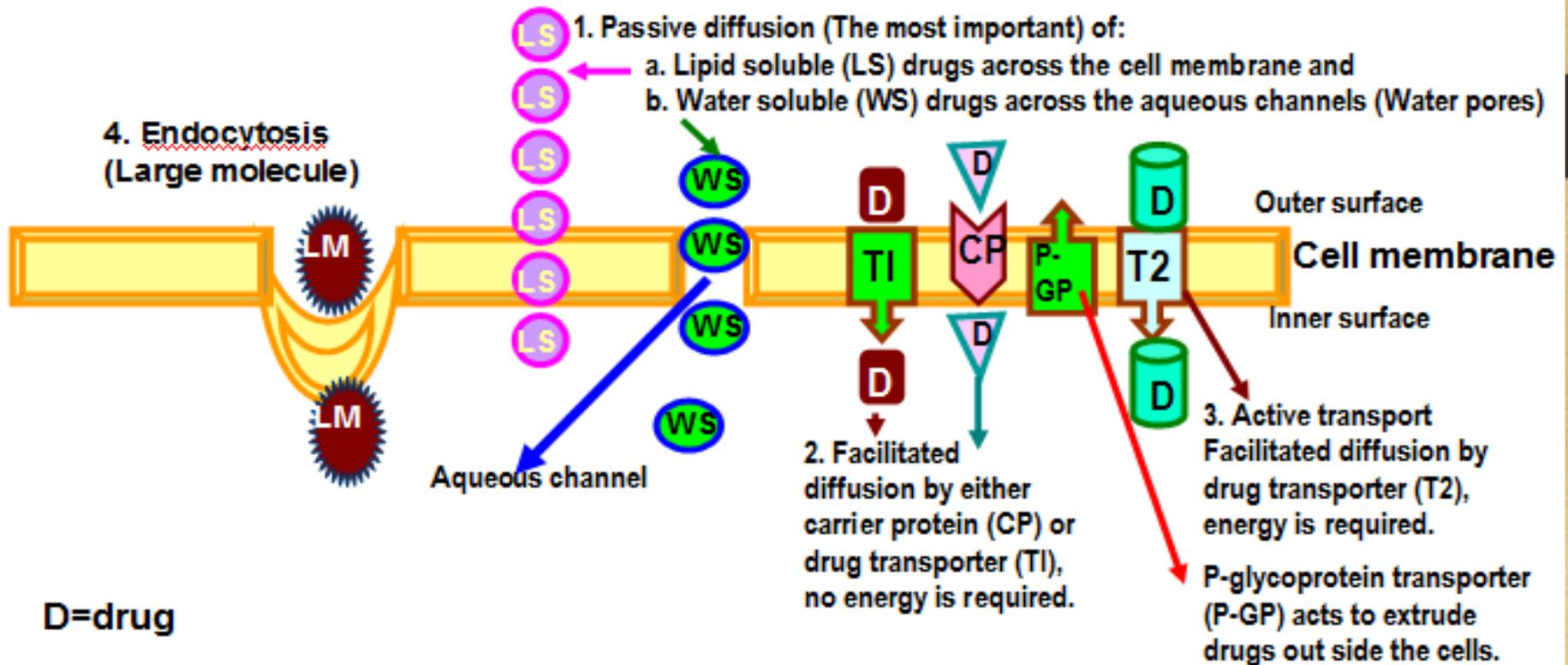
Disintegration → drug breaks down into smaller particles

Dissolution → drug dissolves in body fluids

Passage across membranes →

Mechanisms of drug absorption (how drugs cross biological membranes)

Mechanisms of drug movement across the biological membranes



Please Find Active
Entry"

1. Passive diffusion:

- Rapid movement of **lipid-soluble** drugs across the cell membrane. As aspirin
- Movement of the **water-soluble** drugs across the aqueous channels (water pores) as urea
- No energy is needed, and it occurs along with concentration gradient.

2. Facilitated diffusion

- The drugs are carried into the cell by a **carrier** or **transporter**.
- **No** energy is required, and according to the concentration gradient as glucose

3. Active transport

- The drug movement may be **against** the concentration gradient by drug carrier or transporter. Energy is required
- As L-Dopa

4. Endocytosis

- Drugs of high molecular weight bind to the cell membrane, dip in, and are enveloped by the cell membrane.
- As vitamin B12 and intrinsic factor

Factors affecting absorption:



- Route of **A**dministration
- **A**bsorbing surface
- Co **A**dministration of food or drugs
- **S**ystemic circulation
- **S**pecific factors

Drug RAs into
blood”



- 1- Water & lipid **s**olubility
- 2- Pharmaceutical **p**reparation
- 3- **I**onization of the drugs

A. Factors related to the patient

Route of Administration

I.V. and inhalation > I.M. > S.C. > Oral > Topical

Absorbing surface

- **Vascularity:** (Alveoli > S.C. tissue).
- **Surface area:** (Alveoli > Intestine > Stomach).
- **Pathological conditions:** Diarrhea decrease oral absorption

Systemic *Circulation*

- **Shock** decrease absorption; oral and subcutaneous routes are not suitable.

Specific factors

Intrinsic factor is essential for vitamin B12 absorption.

Co *Administration* of other drugs & food

- ▶ S.C. adrenaline (added to local anesthetics) \longrightarrow V.C. absorption of local anesthetics \longrightarrow longer duration of action of local anesthetics.
- ▶ Ca^{+2} (e.g. in milk) ∇ oral absorption of tetracyclines (antibiotics).

B. Factors related to the drug

What Passes In

1- Water and lipid **S**olubility

- **Completely water-soluble compounds** are not absorbed (e.g. barium chloride).
- **Increasing lipid solubility** leads to increase absorption (lipid/water partition coefficient).

2- Pharmaceutical **p**reparation

- **Dosage form:** Solution > Suspension > tablet.
- **Shape, size of particles and rate** of dissolution of tablets.
- **Excepiant (filler)** containing Ca^{+2} decreases oral absorption of tetracyclines.

3- Ionization of the drug:

No Charge, No
Challenge

- ❑ Ionization decreases lipid solubility and absorption of drugs.
- ❑ Non-ionized (uncharged) \longrightarrow better absorption.
- ❑ Depends on pKa of the drug and pH of the medium .
- ❑ Quaternary ammonium compounds \longrightarrow ionized poor absorption.
- ❑ Streptomycin has high pKa \longrightarrow always ionized not absorbed orally.

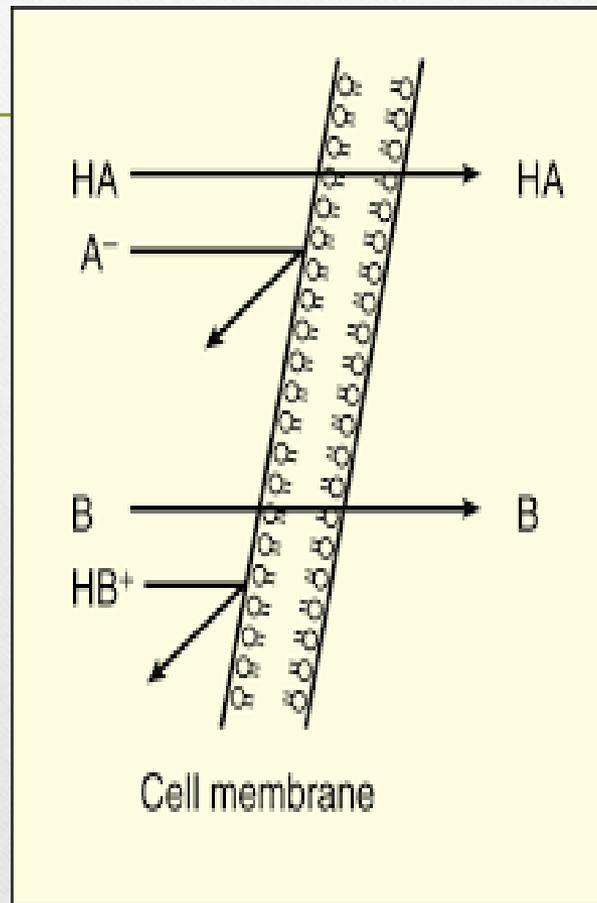
The effect of pH on drug absorption

When drugs bind to hydrogen,

- weak acids become unionized



- Weak bases are ionized



Acids love H^+ → absorb;
Bases hate H^+ → blocked

At low pH weak acids become unionized while the weak bases become ionized.

At high pH weak base drugs become unionized while weak acids become ionized.

- Accordingly, weak acids are more absorbed in acidic media while weak bases are more absorbed in alkaline media.

- The pH at which the concentrations of the ionized and unionized forms of the drug are equal is termed **pKa**.
- Each drug has its own pKa.

Clinical importance of pKa

1- GIT:
Aspirin
(acidic
drug) has
low pKa.

Drug molecules become unionized in the empty stomach (low pH) and can enter gastric mucosal cells. In gastric mucosal cells (high pH) aspirin becomes ionized and trapped in gastric mucosal cell "peptic ulceration"

2- Kidney: In
drug
poisoning,

renal elimination could be enhanced by changing urinary pH to increase ionization of drug and inhibit tubular reabsorption of the drug.

- **Alkalinization** of urine by sodium bicarbonate (to increase urine pH above drug pKa) is useful in acidic drug poisoning e.g. Aspirin and phenobarbital.

- **Acidification** of urine by ascorbic acid (to decrease urine pH below drug pKa) is used in basic drug poisoning e.g. amphetamine.

BIOAVAILABILITY

how much of the drug actually enters the blood

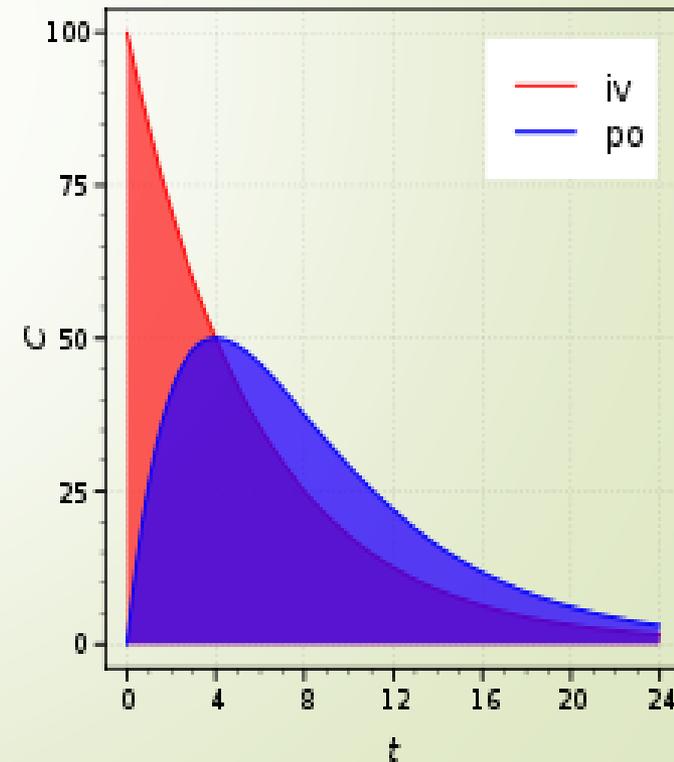
- It is the **percentage** of drug that reaches the **systemic circulation** and becomes available for **biological effect**.

Bioavailability =

Area under the curve (AUC) after oral route

X 100

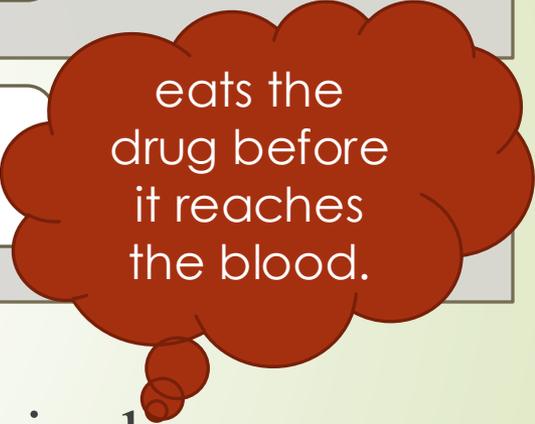
Area under the curve (AUC) after I.V. route



FACTORS AFFECTING BIOAVAILABILITY:

1-The extent of **drug absorption**.

2- 1st pass effect (**1st pass metabolism**):



eats the drug before it reaches the blood.

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

A. Hepatic 1st pass effect:

- Nitroglycerin and propranolol pass from GIT to liver where they are extensively metabolized in their 1st pass through liver before reaching systemic circulation.

B. Intestinal 1st pass effect:

- Estrogens are extensively metabolized in their 1st pass through intestinal wall.

C. Pulmonary metabolism:

- After inhalation, nicotine is partially metabolized in the lung.

A top-down view of a spiral-bound notebook with a white cover and lined pages. The notebook is open to a page with the words "TO BE CONTINUED" written in large, bold, black, sans-serif capital letters. The page is decorated with several crumpled balls of paper in various colors: orange, pink, yellow, and green. A yellow pencil lies diagonally across the bottom right corner of the page. The notebook is set against a light brown, textured background.

**TO BE
CONTINUED**