Pharmacokinetics 1

By
Dr. Lamiaa Meghawery

Associate professor of pharmacology
Faculty of Dentistry
Mutah university

ILOS

- Recognize the clinical importance of factors affecting drug absorption
- Rationalize importance of pKa
- Identify factors affecting drug absorption

1- Introduction

Pharmacokinetics

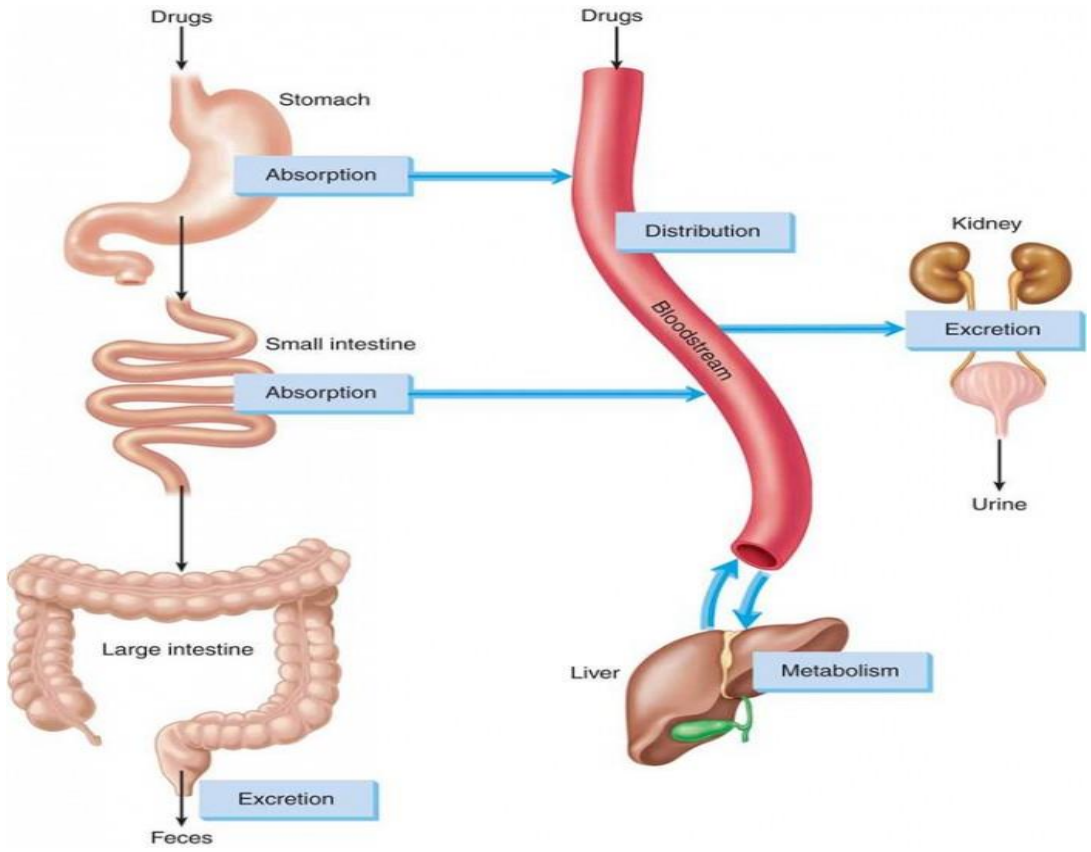
What the body does to the drug

1. Absorption
2. Distribution
3. Metabolism
4. Excretion

Pharmacodynamics

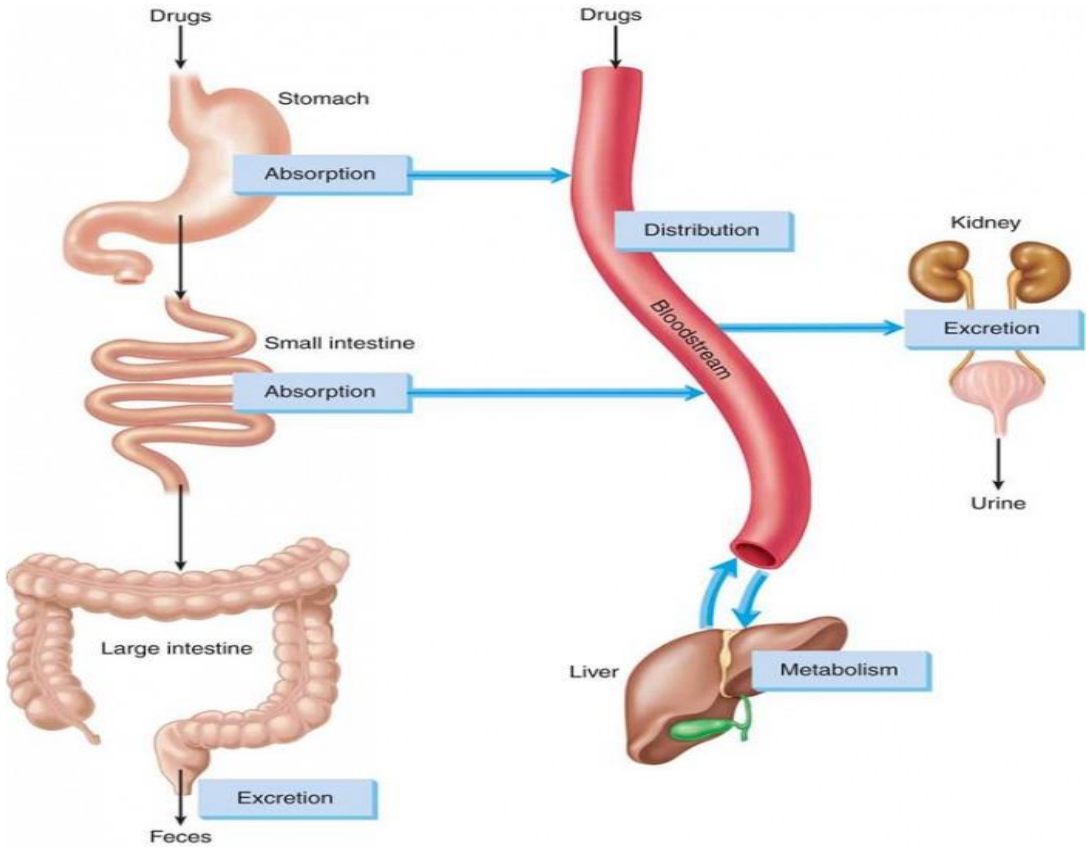
What the drug does to the body

1. Mechanism of action
2. Pharmacological actions



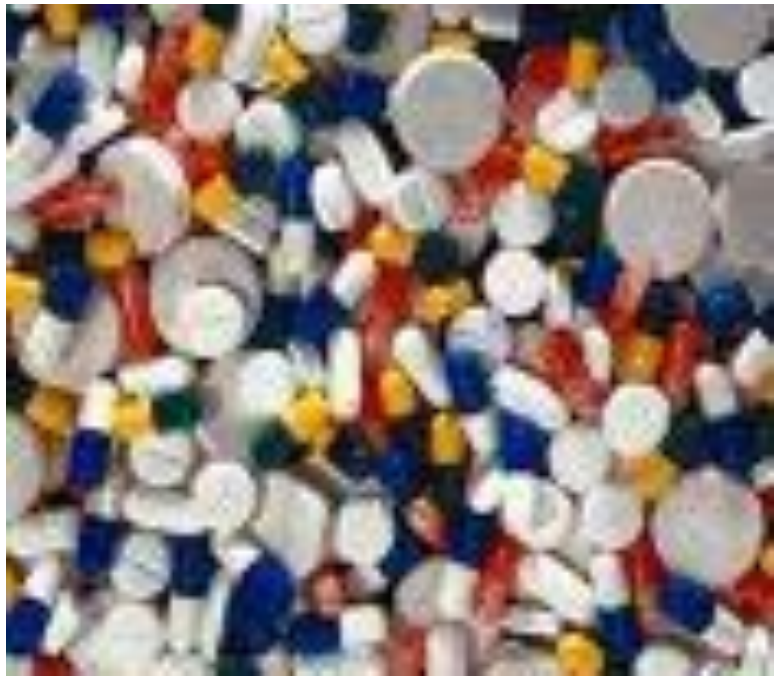
1- Absorption

It is the process of ***entry of drug*** **from** ***site of administration*** **into** ***systemic circulation***.



Factors influencing absorption

A- Factors related to drug



B- Factors related to patient

Factors affecting oral absorption

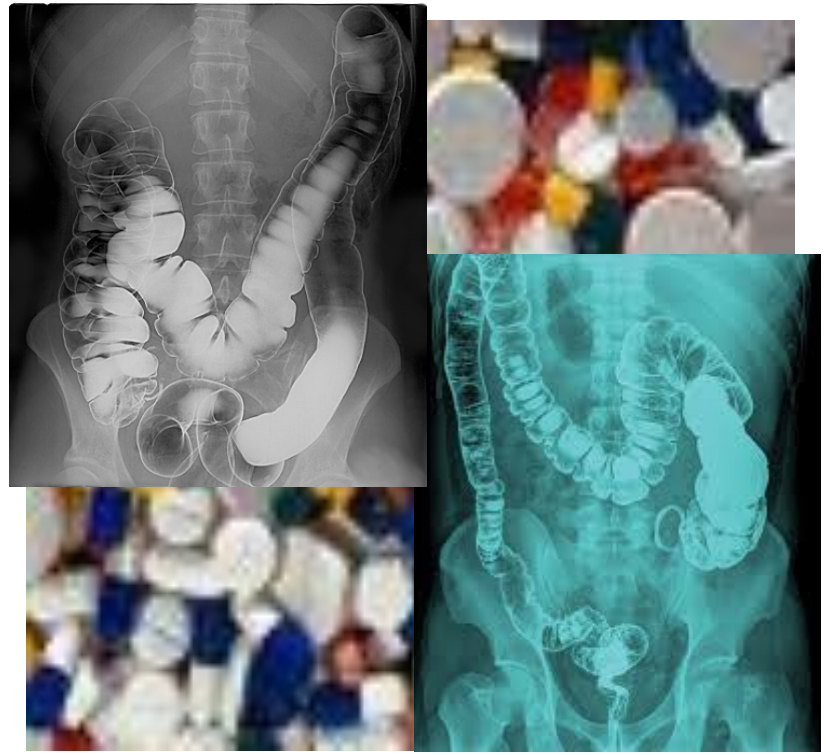
A) Factors Related to the Drug:

1- *Water and lipid solubility*:

a- Drugs must be **completely dissolved in water** to be absorbed.

(Drugs insoluble in water e.g. Barium chloride ($BaCl_2$) are NOT absorbed).

b- **More lipid solubility** → high Lipid/Water partition coefficient → better absorption.



Ba → ينم استخدام هذا الدواء للتشخيص وليس للعلاج

وذلك لأنه لا يتم امتصاصه إذا بقي في الـ (GIT)

إذا تم اعطائه للمريض كشراب ثم تتتبعه بالأشعة

$BaSO_4$ أفضل ويستخدم أكثر للتشخيص

Factors affecting oral absorption

A) Factors Related to the Drug:

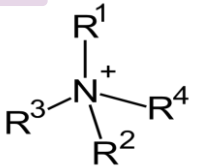
2- Ionization:

a- **Non-ionized** → More lipid soluble → Better absorption

b- Depends on pKa of the drug & pH of the medium.

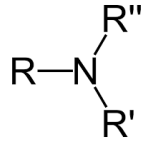
c- **Quaternary ammonium** compounds "Neostigmine" → Ionized → Poor absorption

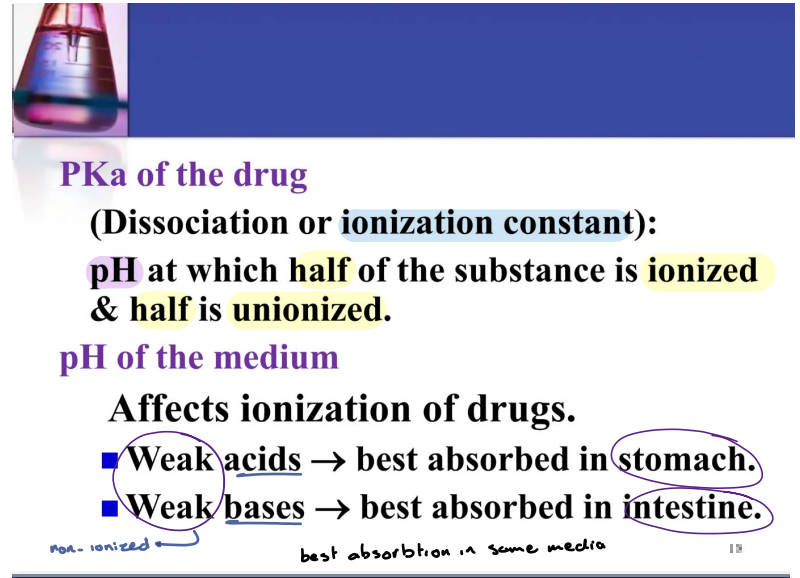
لا يستطيع اختراق الـ (BBB)

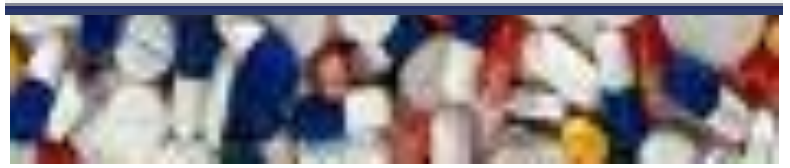


d- **Tertiary amines** "Physostigmine" → Non-ionized → Better absorption.

يخترق الـ (BBB) ويعمل تشنجات







↓ PKa ↑ strong (acid | alkalin) ↑ ionized

Ionization: -

- *Most drugs are weak bases or weak acids*

So, in acidic medium, an acidic drug is less ionized, so more lipid soluble and the easier to pass

In alkaline urine, acidic drug is more ionized, less lipid soluble , difficult to be reabsorbed, so excreted "Ion trapping"

e.g. Aspirin is better absorbed in stomach, trapped in intestine and better excreted in alkaline urine

Aspirin
→ weak acid
→ absorbed in stomach
→ Inonized / trapped in alkaline media (in intestine)
→ overdose treatment is urine alkalinization ($NaHCO_3$)

Ionization: -

- ***Most drugs** are **weak bases or weak acids***

So, in alkaline medium, an alkaline drug is less ionized, so more lipid soluble and the easier to pass

In acidic urine, alkaline drug is more ionized, less lipid soluble , difficult to be reabsorbed, so excreted "Ion trapping"

e.g. Amphetamine is better absorbed in intestine and excreted "trapped" in acidic urine

Amphetamine

→ weak alkaline

→ absorbed in intestine

→ ionized / trapped in acidic media (in stomach)

→ overdose tretment is urine acidification

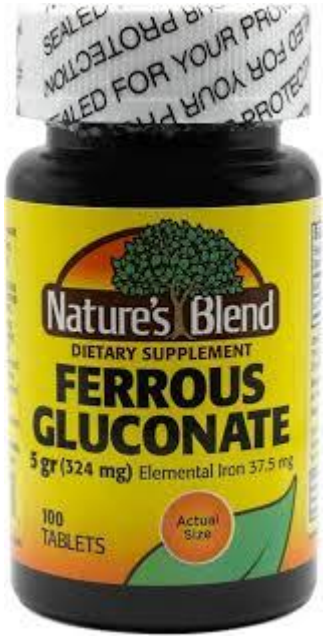
Factors affecting oral absorption

A) Factors Related to the Drug:

3- Valency: Ferrous iron (Fe2+) > Ferric Iron (Fe3+).

تكافؤ هذا الدواء

أفضل بكثير في الامتصاص



4- Nature: Inorganic (small molecules) > Organic (Big molecules).

Factors affecting oral absorption

A) Factors Related to the Drug:

5- Pharmaceutical Preparation:

a- **Dosage form:** Solution > Suspension > Tablet.

b- **Shape & size of particles and rates of disintegration & dissolution of tables:**

Rapid with paracetamol BUT slow with digoxin.

c- **Excipient (Filler): CaCO3 & Ca Phosphate**

→ ⬇ Absorption of Tetracyclines.

Questions

1. The rate of absorption of a drug is affected by all of the following <u>EXCEPT:</u>

(a) Route of drug administration

(b) Solubility of the drug

(c) Site of administration (oral / topical / injection) هو نفس ال route

(d) Distribution of drug

هدول بنفس المعنى اذ انه الامتصاص يتأثر بطريقة أخذ الدواء

injection > tablet

هذه هي المرحلة التي تليها فلا تؤثر عليها إذ انها تبدأ عندما تنتهي عملية الامتصاص

2.What is pKa and its significance? It is affect the ionization of the drug (↓pKa) → (strong / ionized)

It is the pH that which 50% of drug ionized and 50% of it non ionized

3. Which of the following acids has the highest degree of ionization in an aqueous solution?

(a) Aspirin pKa = 3.5

(b) Indomethacin pKa = 4.5

(c) Warfarin pKa = 5.1

(d) Ibuprofen pKa = 5.2

(e) Phenobarbital pKa = 7.4

↓pKa ↑ strong (acid / alkalin) ↑ ionized

Thank You