Pharmacokinetics 1

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ILOS

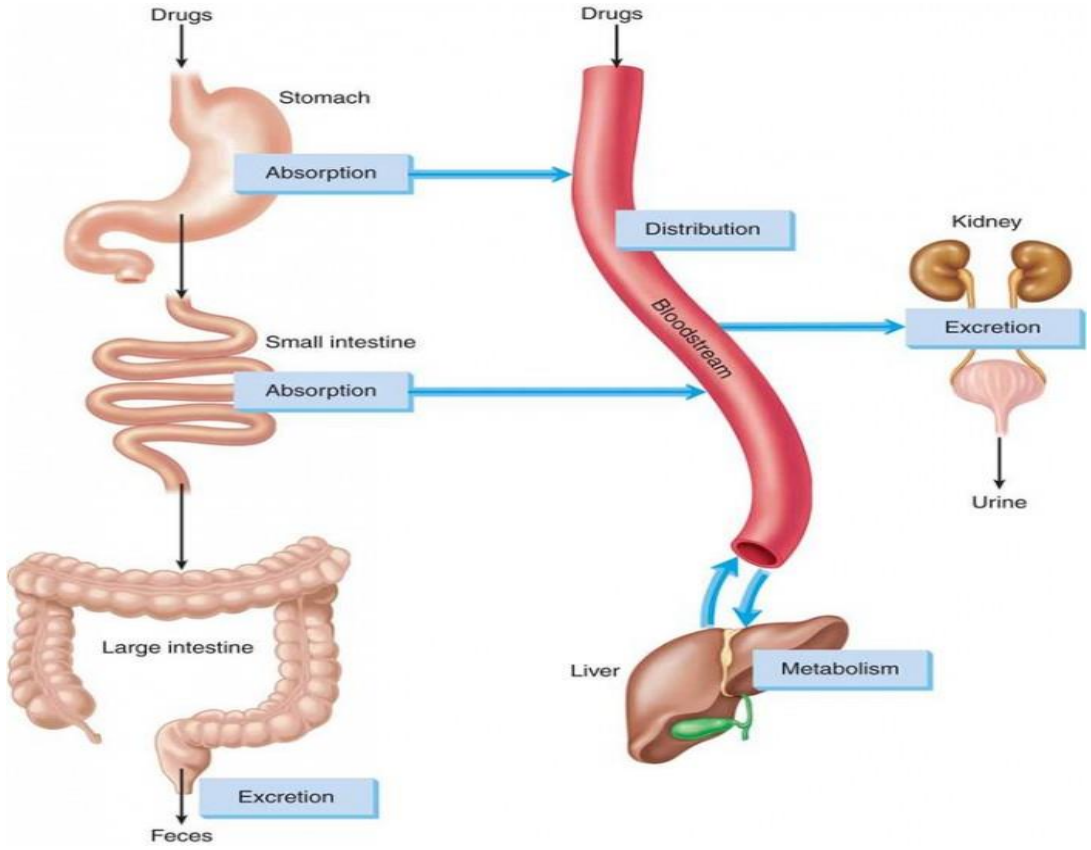
- Recognize the clinical importance of factors affecting drug absorption
- Define bioavailability and First pass effect
- Rationalize importance of bioavailability

1- Introduction

Pharmacokinetics

What the body does to the drug

1. **A**bsorption
2. **D**istribution
3. **M**etabolism
4. **E**xcretion



Pharmacodynamics

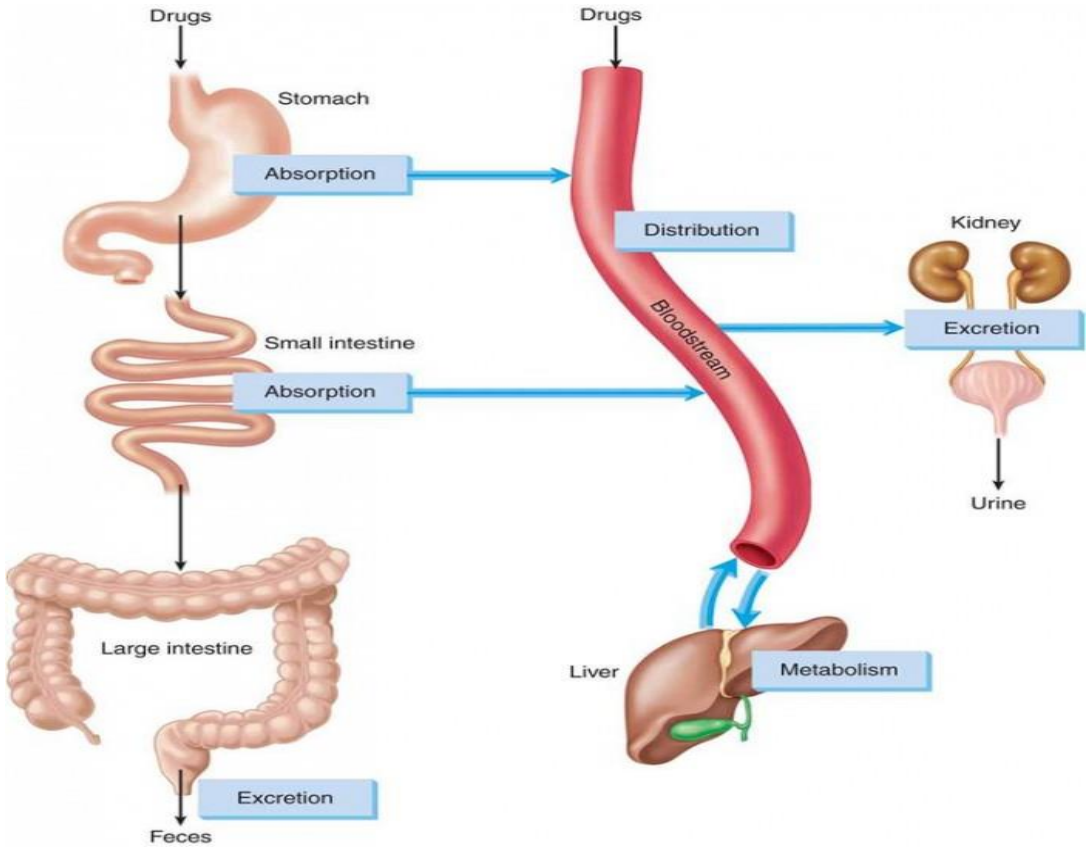
What the drug does to the body

1. Mechanism of action
2. Pharmacological actions

Pharmacokinetics

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 absorption

B) Factors Related to the Patient:

1-Route of Administration: I.V. and inhalation > I.M. > S.C. > Oral > Skin.

Factors affecting absorption

B) Factors related to the patient:

2- Surface area of absorbing surface:

- The intestine has surface area 1000 times that of stomach (due to microvilli) and rich blood flow. **Thus, absorption from intestine > stomach.**

***Alveoli > Intestine > Stomach**

3- State of absorbing surface: Gastritis, Diarrhea& malabsorption syndrome ⇩oral absorption

Factors affecting absorption

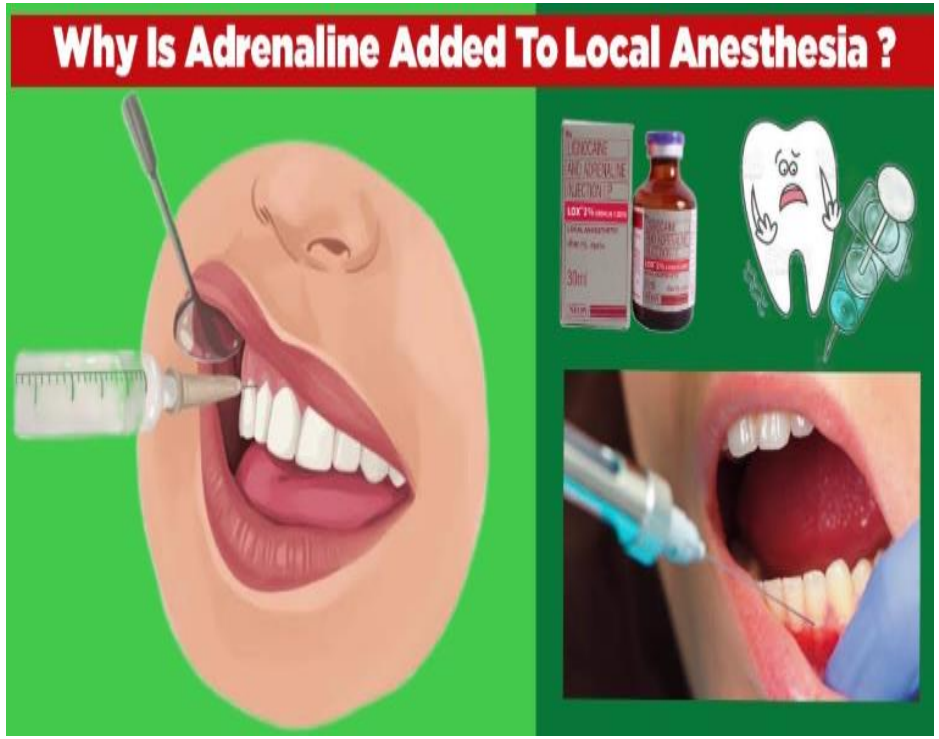
B) Factors Related to the Patient:

4-Systemic circulation: Shock & Heart failure →↓ Absorption.

5-Specific factors: Intrinsic factor for Vit B-12.

6-Presence of other drugs:

- **Adrenaline S.C.** → V.C. → ⬇ Absorption of Local anesthetics → Longer duration of action of local anesthetics.



Factors affecting absorption

B)Factors related to the patient:

7- Motility of the gut and rate of dissolution:

- **Prokinetic drugs increase the gut motility**
  e.g. **Metoclopramide**↑ gut motility →↑ gastric emptying →↑ absorption of rapidly disintegrated drugs (paracetamol) and ↓ absorption of slowly disintegrated drugs (digoxin).

Factors affecting absorption

B)Factors related to the patient:

8- pH within the gut:

- **Weak acids (aspirin)** are better absorbed in an acidic media. So better absorbed in stomach.

- **Weak bases (amphetamine)** are better absorbed in an alkaline media of intestine.

Factors affecting absorption

B)Factors related to the patient:

9- Gut contents: presence of food & other drugs:

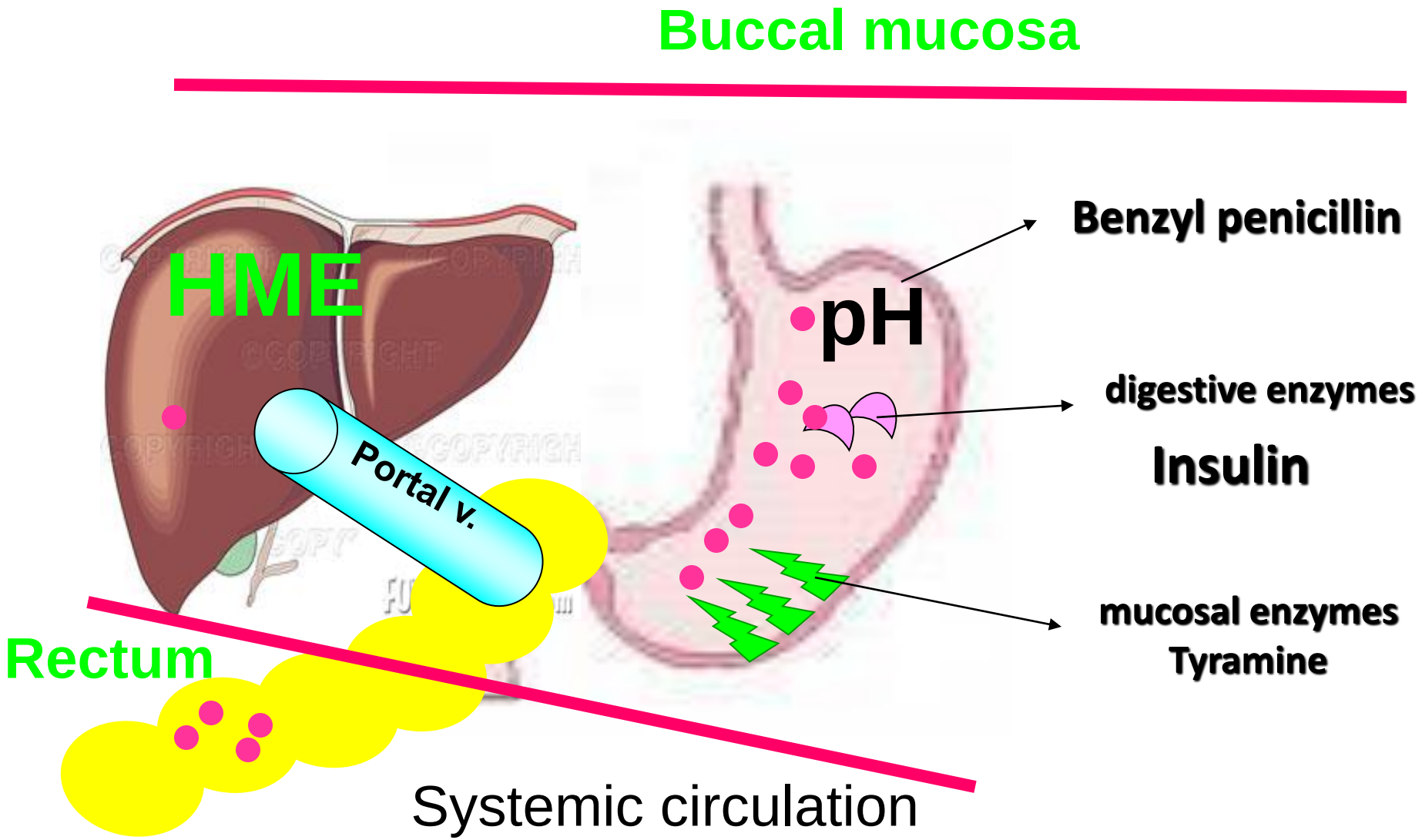
- Presence of food:

  Bad → Food dilutes Drugs & may compete with them for absorption

  Good → with IRRITANT drugs e.g. aspirin.

- **Grape fruit juice** ⬆ absorption of drugs by inhibiting **P. glycoprotein** (which cause reversed transport of drug from gut wall to lumen).
- **Tea** → ⬇ iron absorption by its content of tannic acid.
- **Milk (Calcium)** → ⬇ Oral absorption of Tetracyclines (Antibiotic).

First pass effect (pre-systemic metabolism):



Factors affecting absorption

B)Factors related to the patient:

10- First pass effect:

- **Means metabolism of drug in gut wall or liver before reaching systemic circulation.**

Gut first pass effect:

1. **Gastric acidity:** destroys benzyl penicillin.
2. **Digestive enzymes:** destroy insulin
3. **Mucosal enzymes**

Hepatic first pass effect:

1. **Drugs extensively metabolized**: e.g. Nitroglycerine.

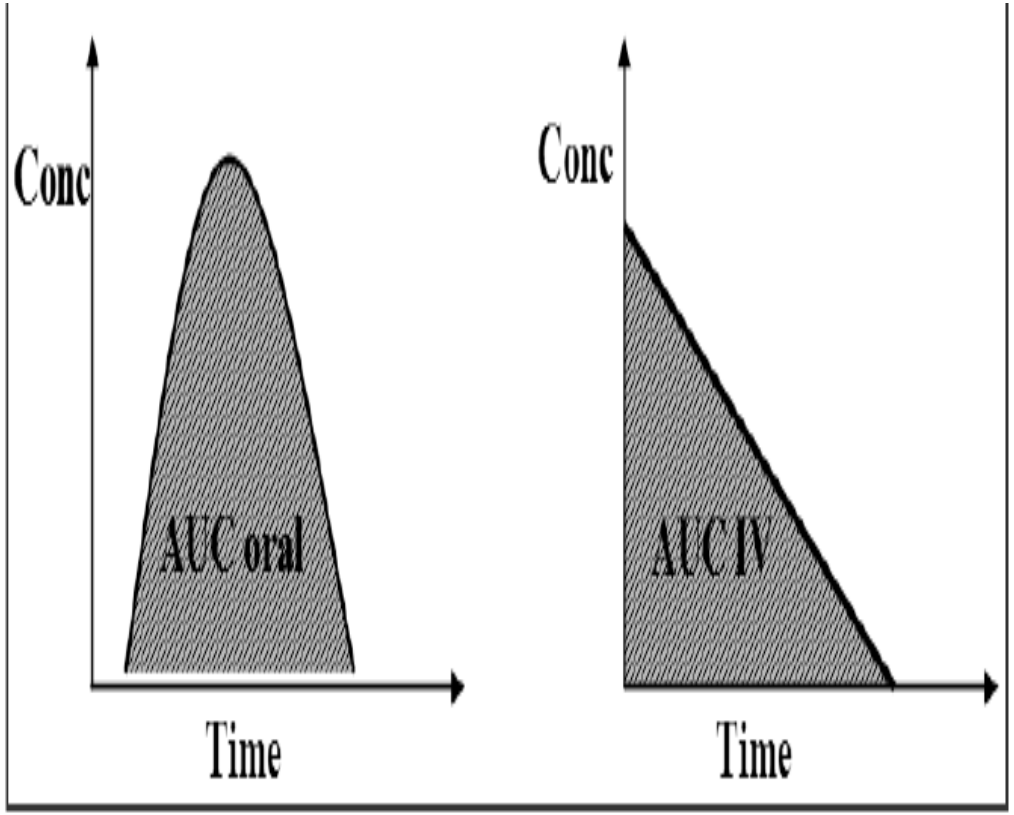
To avoid: change the route of administration: Nitroglycerine SL (sublingual)

2. **Drugs metabolized to a large extent**: e.g. propranolol.

To avoid:⇧ the oral dose.

Bioavailability

- **Bioavailability is the fraction of unchanged drugs reaching systemic circulation after any route of administration.**
- **Bioavailability is 100 % after IV administration and Variable after oral administration.**
- **Oral bioavailability = (AUC oral x100)/AUC iv**



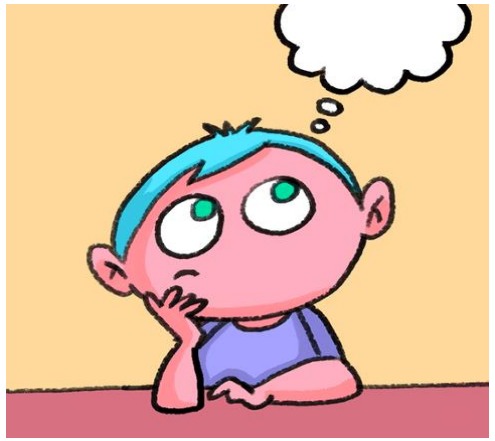
Bioavailability

- **Factors affecting oral bioavailability:**

1. **Amount of drug absorbed = Factors affecting GIT absorption.**

2. **First pass metabolism.**

Questions



1. *Mention factors affecting oral bioavailability.*

2. *Rationalize :*
   a. *Tetracyclines shouldn’t be taken with food.*
   b. *Nitroglycerine is preferred to be taken sublingually.*

Thank You