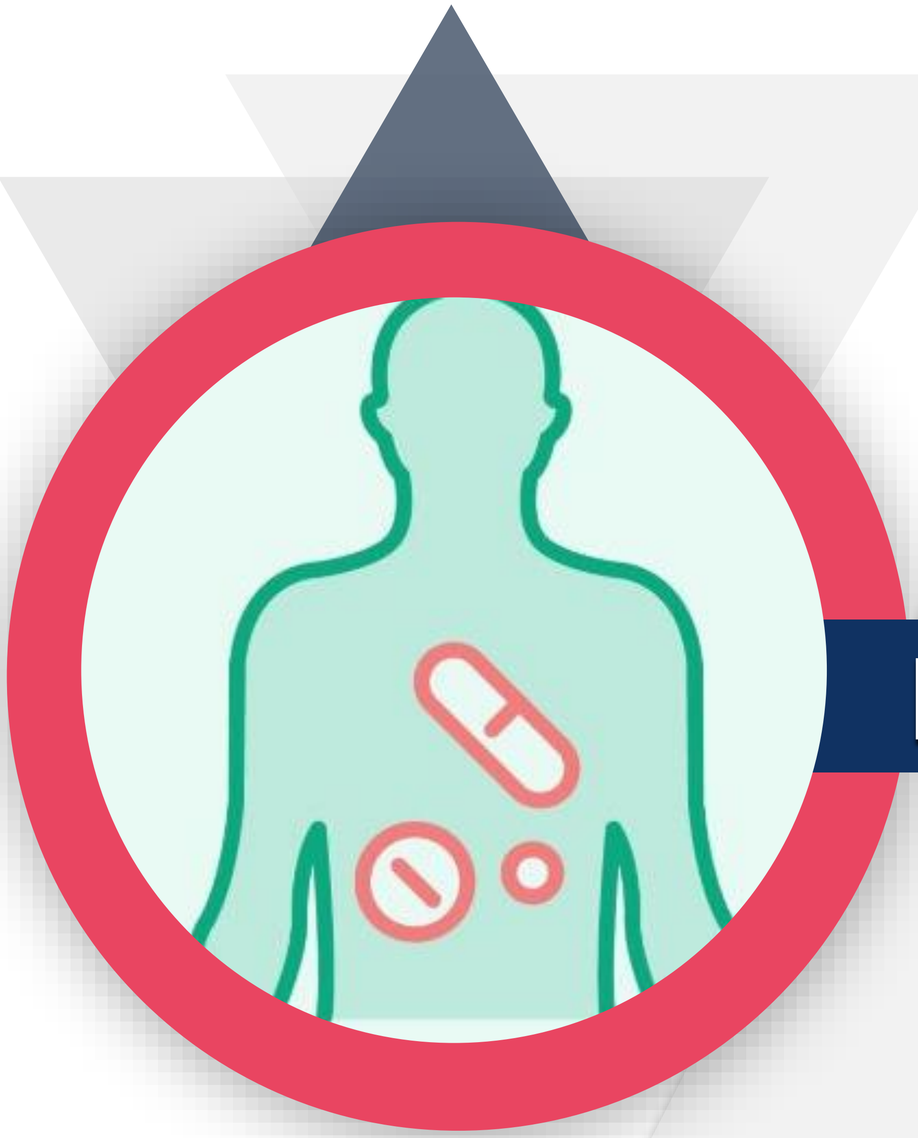


BIOAVAILABILITY

- Bertram G. katzung Basic & Clinical Pharmacology 16th Edition
- Goodman and Gilman’s The Pharmacological Basis of Therapeutics 13th edition.

LEARNING OBJECTIVES

At the end of the academic sessions, students of 3rd Year MBBS will be able to :

01. Define bioavailability

02. Express it mathematically and graphically

03. Describe the clinical significance of bioavailability

04. Define first pass metabolism

05. Recognize the effect of first pass metabolism on bioavailability of drugs

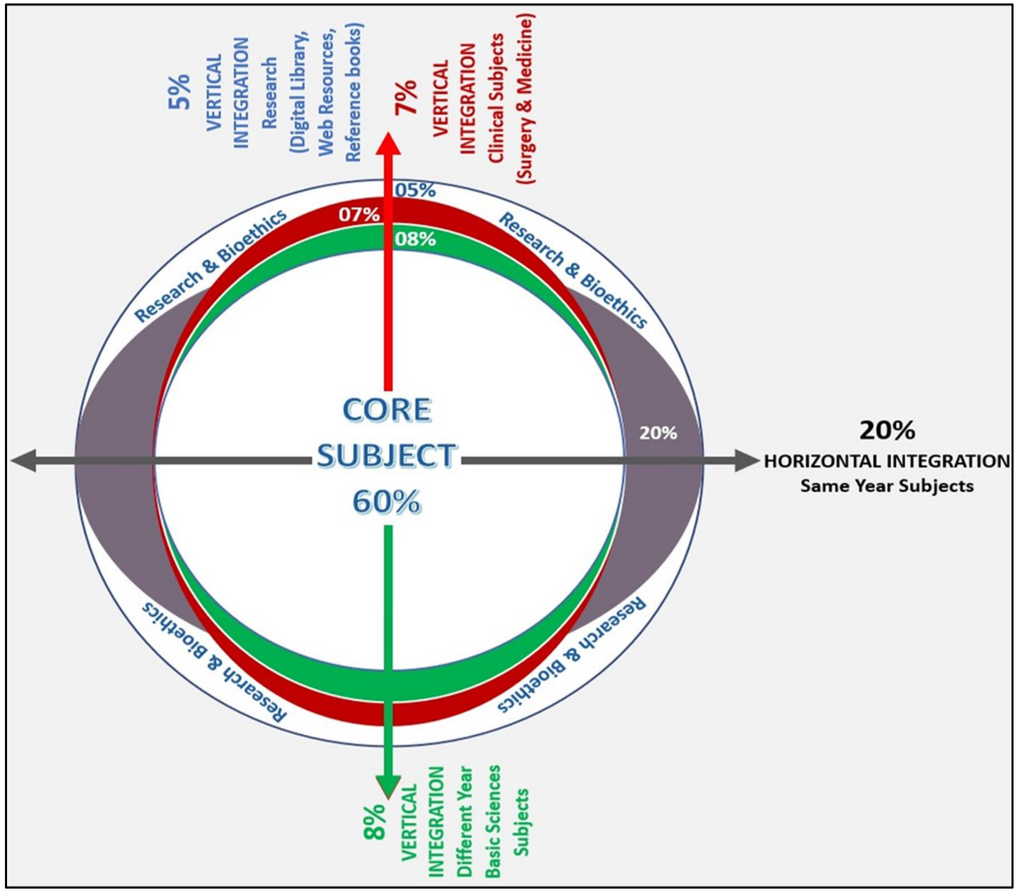
06. Discuss the factors affecting bioavailability of drugs

07. Differentiate between chemical equivalence, bioequivalence & therapeutic equivalence

SEQUENCE OF LECTURE

- Core Subject
- Spiral Integration
- Horizontal Integration
- Vertical integration
- Digital Library References

  (Research & Bioethics)
- EOLA(End of lecture assessment)



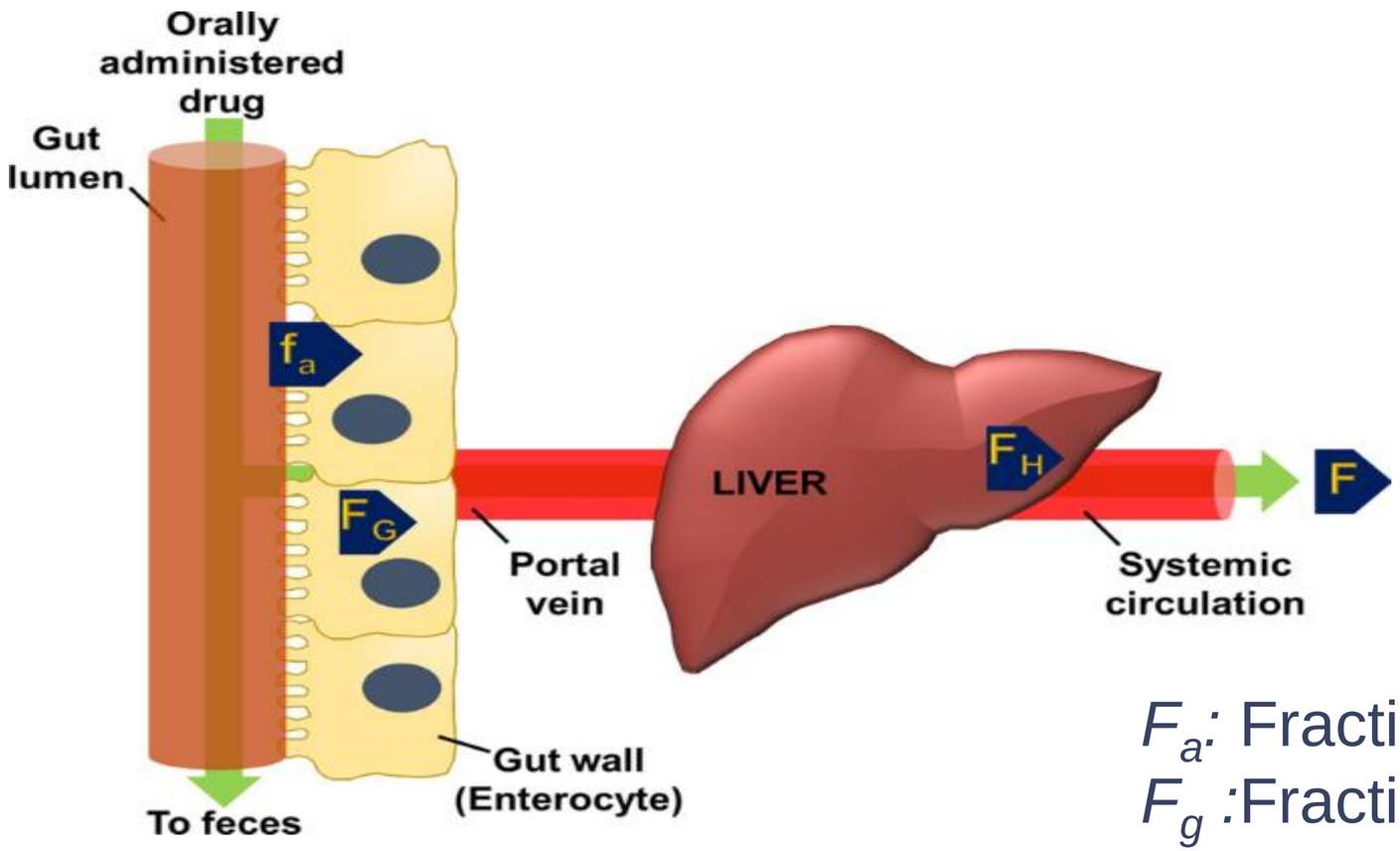
CORE

BIOAVAILABILITY

Fraction of the active drug contained in any dosage form that reaches its site of action or reaches the biological medium that represents its accessibility to the site of action after administration through any route

Fraction of unchanged drug reaching the systemic circulation following administration by any route

BIOAVAILABILITY



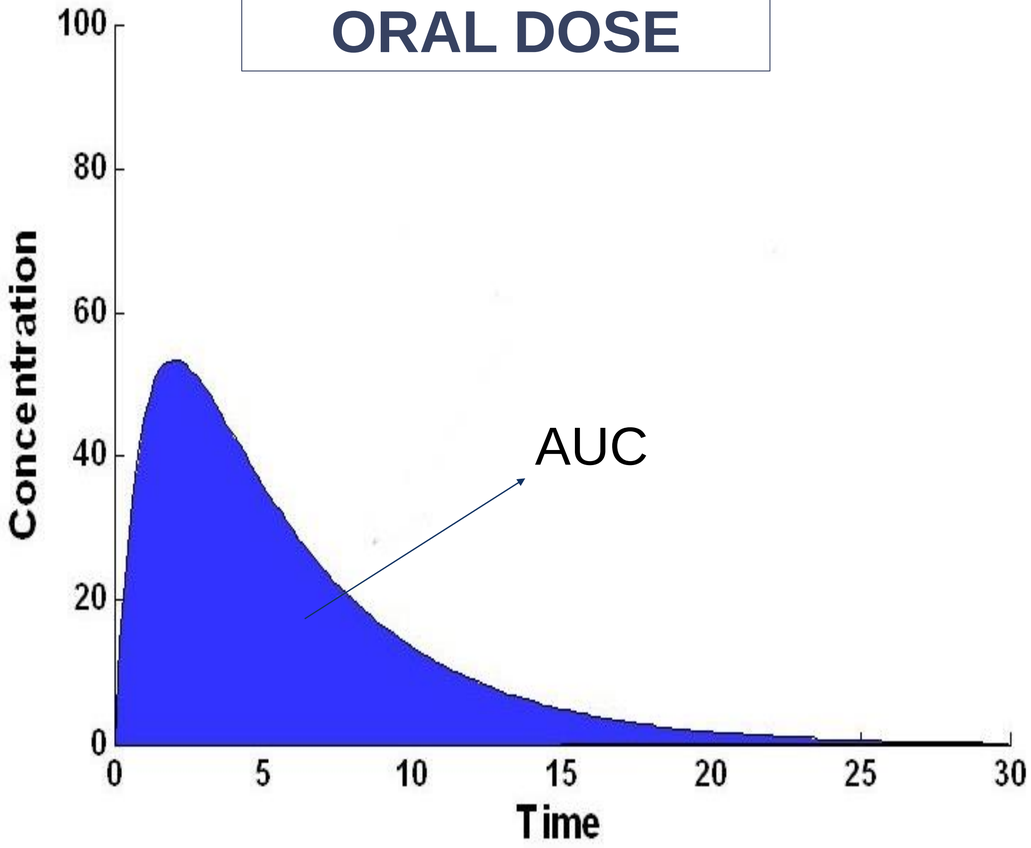
$$F = F_a \cdot F_g \cdot F_h$$

F_a: Fraction absorbed from gut lumen
F_g :Fraction escaping intestinal metabolism
F_h: Fraction escaping hepatic metabolism

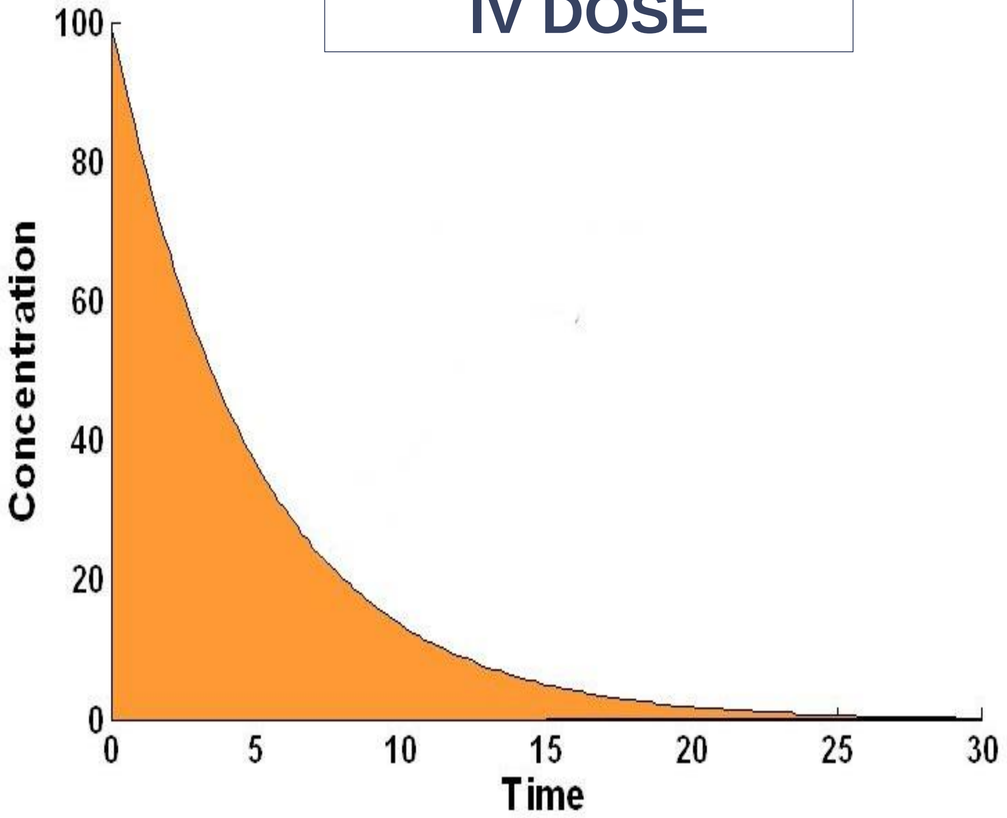
DETERMINATION OF BIOAVAILABILITY

Plasma level time studies

ORAL DOSE



IV DOSE



DETERMINATION OF BIOAVAILABILITY

- Measure area under the curve (AUC) between blood concentration & time.

$$\text{Bioavailability (F)} = \frac{\text{AUC Oral}}{\text{AUC Injected I/V}} \times 100$$

- Bioavailability expressed as *F* is measured on a continuous range from 0 to 1 ($0 < F < 1$) but can be represented as a percentage between 0 and 100 %

TYPES OF BIOAVAILABILITY

Absolute bioavailability :

Compares the bioavailability of the drug following non- intravenous administration

(e.g., oral, rectal, etc.) with the bioavailability following intravenous administration

$$F = \frac{AUC_{oral} \times dose_{i.v}}{AUC_{i.v} \times dose_{oral}}$$

Relative bioavailability:

Compares the bioavailability between test formulations and standard reference.

$$F = \frac{AUC_{test} \times dose_{ref}}{AUC_{ref} \times dose_{test}}$$

DETERMINANTS OF BIOAVAILABILITY

A. Physiochemical properties of drug

B. Biological factors affecting extent of absorption from GIT

C. Quality control in manufacturing and formulation

D. First pass metabolism / effect

E. Route of drug administration

DETERMINANTS OF BIOAVAILABILITY

A. Physiochemical properties of the drug

- Particle size
- Molecular size
- Lipid aqueous solubility coefficient
- Physical form
- Chemical form
- Degree of ionization
- Dosage form
- Formulation excipients

SPIRAL INTEGRATION WITH PHYSIOLOGY

DETERMINANTS OF BIOAVAILABILITY

B. Biological factors affecting extent of absorption from GIT

- Area of absorptive surface
- Vascularity
- pH
- Presence of other substances (e-g food and drugs)
- GI motility
- Functional integrity of absorptive surface (diseases)
- Presence of reverse efflux pumps (P-gp)

DETERMINANTS OF BIOAVAILABILITY

C. Quality control in manufacturing and formulation

- Compression pressure
- Moisture content
- Polymorphism
- Disintegration content

DETERMINANTS OF BIOAVAILABILITY

Depending upon the quality control to related drugs may be:

- **Pharmaceutical equivalent**
  Drug products that contain the same active ingredient(s), are of the same dosage form, route of administration and are identical in strength or concentration.

- **Bioequivalent**
  Pharmaceutical equivalents that display comparable bioavailability when studied under similar experimental conditions.

- **Therapeutic equivalent**
  Drug products that are pharmaceutical equivalents and are expected to produce the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling

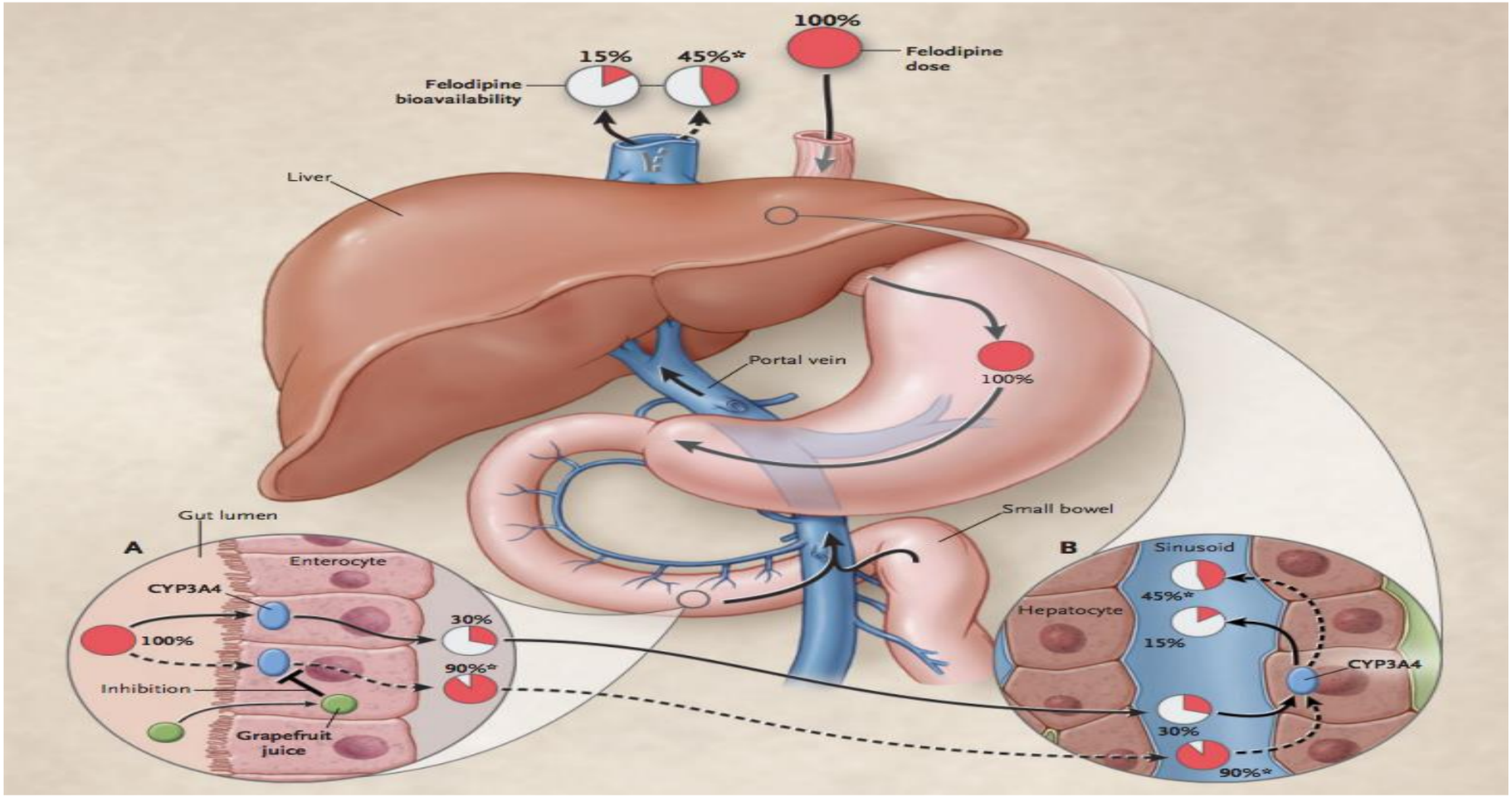
DETERMINANTS OF BIOAVAILABILITY

D. First pass metabolism (pre-systemic hepatic metabolism)

- It is the metabolism / inactivation of drug before it reaches systemic circulation.
- First pass effect depends upon the anatomical site from which absorption takes place & it ↓ Bioavailability .

DETERMINANTS OF BIOAVAILABILITY

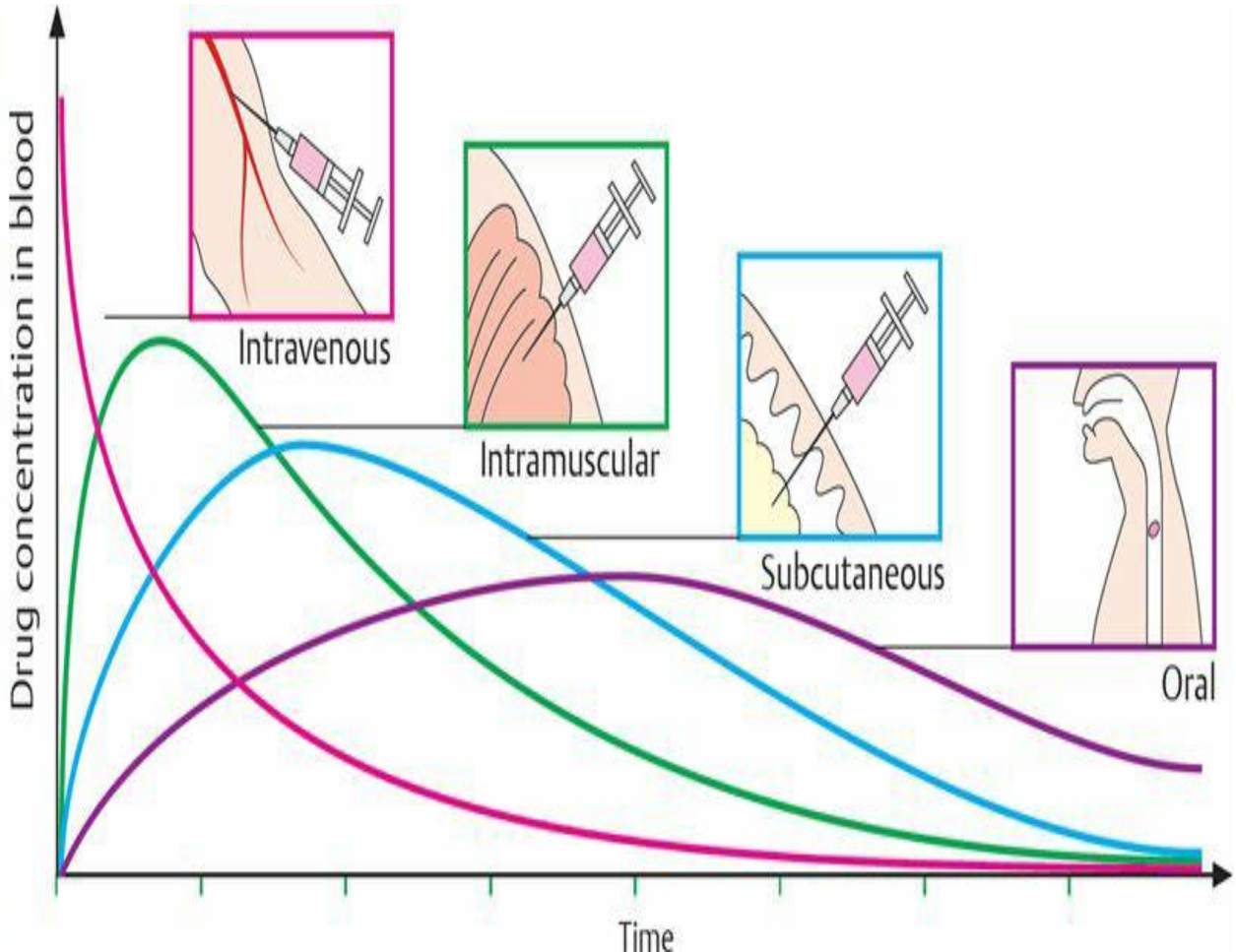
D. First pass metabolism (pre-systemic hepatic metabolism)



DETERMINANTS OF BIOAVAILABILITY

E. Route of drug administration

Route	Biovailability (%)	Characteristics
Intravenous (IV)	100 (by definition)	Most rapid onset
Intramuscular (IM)	75 to ≤100	Large volumes often feasible; may be painful
Subcutaneous (SC)	75 to ≤100	Smaller volumes than IM; may be painful
Oral (PO)	5 to <100	Most convenient; first-pass effect may be important
Rectal (PR)	30 to <100	Less first-pass effect than oral
Inhalation	5 to <100	Often very rapid onset
Transdermal	80 to ≤100	Usually very slow absorption; used for lack of first-pass effect; prolonged duration of action



HORIZONTAL INTEGRATION WITH PATHOLOGY

PATHOLOGICAL STATES

- **<u>Diseases with high BA:</u>**
  In severe hepatic cirrhosis / portal systemic shunts, the dose of the drugs should be ↓ otherwise toxicity due to increased bio-availability

❖High extraction ratio

❖Extensive first pass metabolism

VERTICAL INTEGRATION WITH MEDICINE

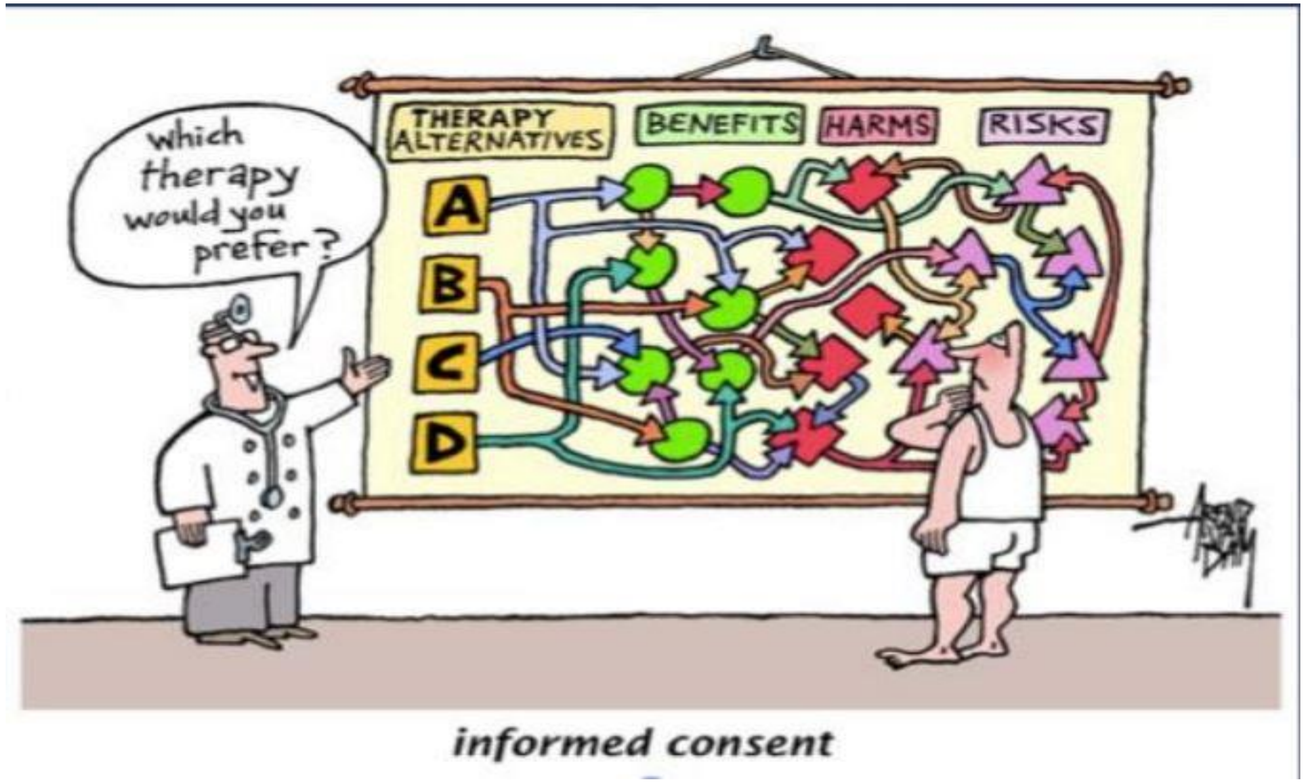
SIGNIFICANCE OF BIOAVAILABILITY

- **Change in F may lead to under medication or over medication**
  - Under medication –**Therapeutic failure**
    Life saving drugs
  - Over medication – **Toxicity**
    Low therapeutic index (cardiac glycosides)

RESEARCH

- Eisenmann, E.D., Talebi, Z., Sparreboom, A. and Baker, S.D., 2022. Boosting the oral bioavailability of anticancer drugs through intentional drug–drug interactions. *Basic & clinical pharmacology & toxicology*, *130*, pp.23-35.

BIOETHICS



“Informed consent is rooted in the fundamental recognition—reflected in the legal presumption of competency—that adults are entitled to accept or reject health care interventions on the basis of their own personal values and in furtherance of their own personal goals.”

END OF LECTURE ASSESSMENT

1. Extraction ratio directly determines:

a) Bioavailability*
b) Clearance
c) Excretion
d) Half Life
e) Volume of Distribution

2. Bioavailability of drug administered via rectal route is

a) 100%
b) 75%
c) 50%*
d) 35%
e) 25%

3. A researcher is studying the bioavailability of commonly used antimuscarinics to treat irritable bowel syndrome. Medication A is administered in a 100 mg daily dose orally and 60 mg of the drug is absorbed from GIT unchanged. Thus, the bioavailability of Medication A is

(A) 50%
(B) 60%*
(C) 70%
(D) 80%
(E) 90%

4. The main factor which affects the drug bioavailability of the drug given orally is:

a) pH of medium
b) Nature of drug
c) **First pass metabolism ***
d) Blood flow
e) Gastric juices

5. Which of the following is not an important parameter of plasma level time studies?

a) Cmax
b) Tmax
c) The area under the plasma level-time curve
d) **Steady state level***