Pharmacology & Therapeutics

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Definition of Pharmacology

- ***Pharmacology*** is the study of substances that interact with living systems to activate or inhibit normal body processes, to produces biological effects.

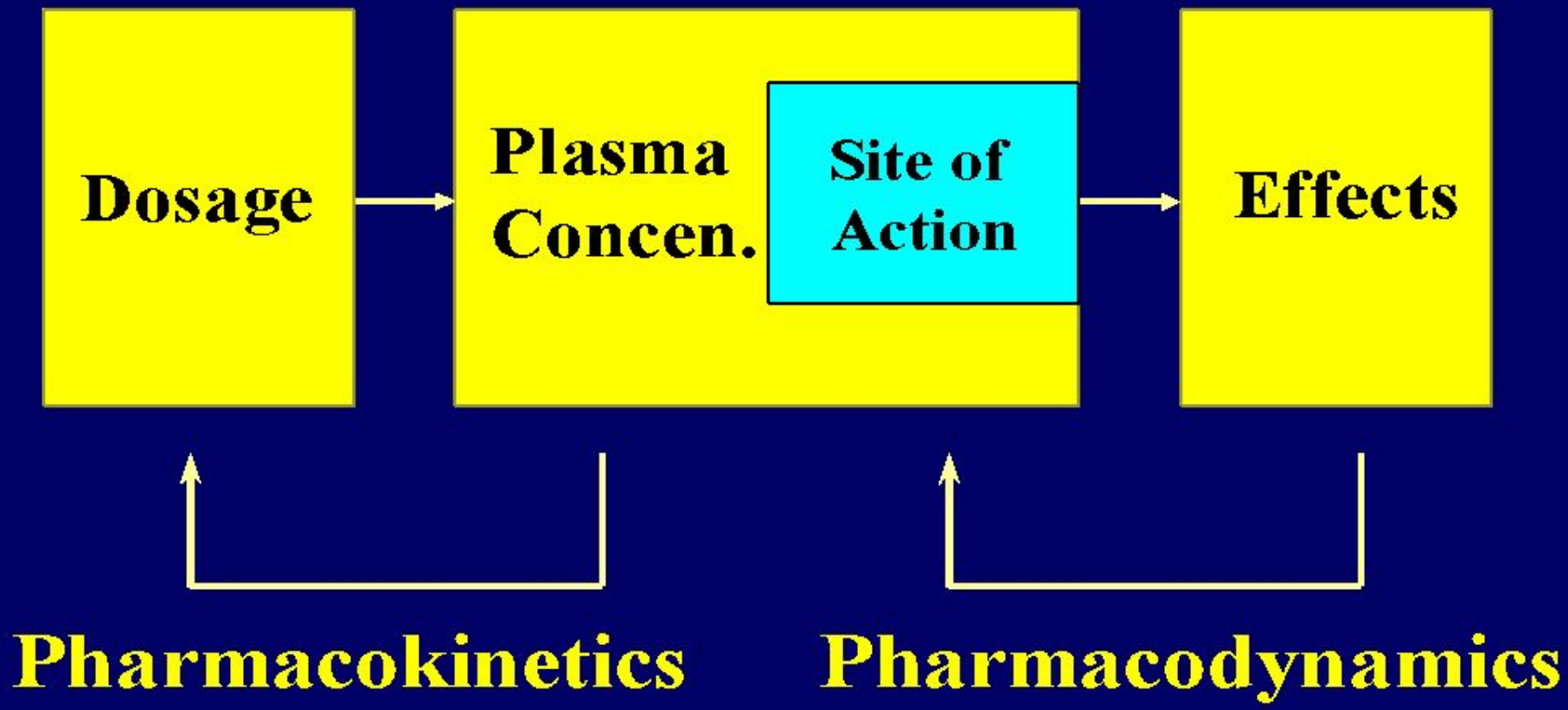
Pharmacology

Pharmacodynamics

PDs means the study of the biological and therapeutic effects of drugs and their mechanism of action. It means what the drug does to the body.

Pharmacokinetics

- It is concerned with the process of drug absorption, distribution, biotransformation (metabolism) and excretion (ADME). *In other words, it means what the body does to drug*
- Pharmacokinetics: the study of the movement of drugs in the body, including the processes of absorption, distribution, localization in tissues, biotransformation and excretion.
- Drugs need to achieve an adequate concentration in their target tissues. So learning pharmacokinetics is of great practical importance in the choice and administration of a particular drug for a particular patient, e.g., one with impaired liver or renal function….


Dosage
Plasma Concen.
Site of Action
Effects
Pharmacokinetics
Pharmacodynamics

Pharmacokinetics

1. Absorption
2. Distribution
3. Metabolism (biotransformation)
4. Excretion (Elimination)

1- Absorption

- It is the process of transfer of drug from site of administration blood stream (systemic circulation).
- The rate and extent of absorption depend on the environment where the drug absorbed, chemical characteristics of the drug and the route of administration (which affect bioavailability)

Handerson-Hassel Balch equation

- Most of the drugs are either weak acids or weak bases
- Handerson-Hassel Balch equation

PH= pKa+ log (non-protonated/protonated)

- Charged/uncharged ratio is determined by PH at the absorption site and the pKa of the drug (Strength of weak acid or weak base).
- The pKa is a measure of the strength of the interaction of compound with a proton. The lower the pKa of a drug the stronger the acid. Conversely the higher the pKa the stronger the base.

1- Absorption

- **Factors influencing absorption**
  - A- Factors related to drug

    a) Physicochemical properties:

    1-Degree of ionization: highly ionized drugs are poorly absorbed.

    2-Degree of solubility: High lipid/water partition coefficient increases absorption.

    3-Chemical nature: inorganic iron is better absorbed that organic iron.

    4-Valency: ferrous salts are more absorbed than ferric,

    -so vitamin C increases absorption of iron.

    b) Pharmaceutical form of drug:

    Absorption of solutions is better than suspensions or tablets.

1- Absorption

- B- Factors related to the patient:

1-Route of administration:

absorption is faster from i.v. > inhaled > i.m. > oral > dermal administration

seconds *minutes* *hours*

2-Area and vascularity of absorbing surface:

absorption is directly proportional to both area and vascularity. Thus absorption of the drug across the intestine is more efficient than across the stomach, as intestine has more blood flow and much bigger surface area than those of the stomach

3-State of absorbing surface: e.g. atrophic gastritis and mal-absorption syndrome decrease rate of absorption of drugs.

4-Rate of general circulation: e.g., in shock, peripheral circulation is reduced and I.V. route is used.

1- Absorption

5-Contact time: diarrhea or increase GE (Parasympathetics) or delayed GE (Sympath; exercise, stress and food also dliutes the drugs and slows GE)

6-Specific factors and presence of other drugs: e.g. intrinsic factor of the stomach is essential for vitamin B12 absorption from lower ileum and adrenaline induces vasoconstriction so delay absorption of local anesthetics.

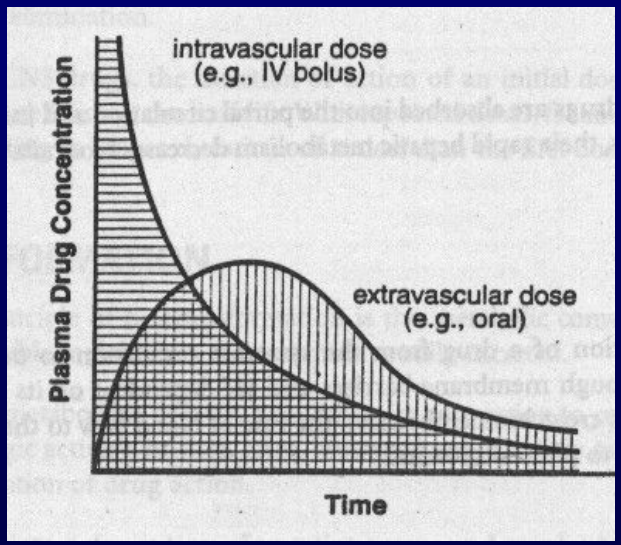
7- Expression of P-glycoprotein (transmembrane transporter protein responsible for transportion various molecules including drugs. It is expressed in tissues throughout the body like liver, kidneys, placenta, intestine, brain capillaries, it pumps drugs out of the cells. Thus in area of high expression, P-glycoprotein reduces absorption

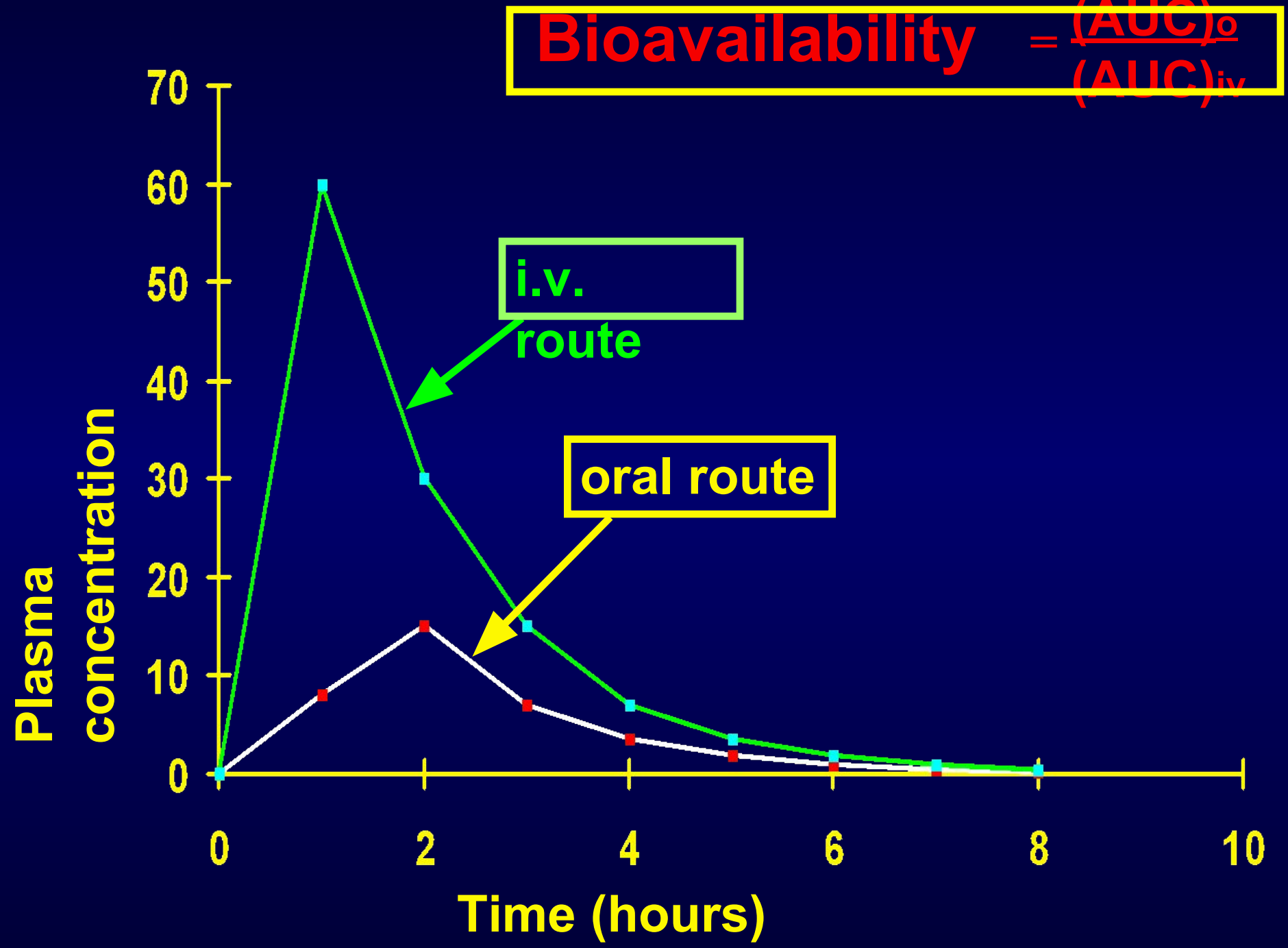
Bioavailability

- It is the rate and extent to which an administered drug reaches the systemic circulation. It is the percentage of drug that reaches systemic circulation in an unchanged form and becomes available for biological effect following administration by any route. It is 100% after IV administration.
- It is calculated by comparison of the area under the plasma concentration time curve (AUC) after IV dose of a drug with that observed when the same dose is given by another route e.g. oral.

$$\text{Oral bioavailability} = \frac{\text{Area under the curve (AUC) oral} \times 100}{\text{Area under the curve (AUC) I.V.}}$$

- Oral bioavailability depends on amount absorbed and amount metabolized before reaching systemic circulation (first pass metabolism)




Bioavailability = (AUC)o / (AUC)iv
i.v. route
oral route
Plasma concentration
70
60
50
40
30
20
10
0
0
2
4
6
8
10
Time (hours)

BIOAVAILABILITY:

For example ,if 100 mg of a drug are administered orally and 70 mg of this drug are absorbed unchanged , the bioavailability is 70% .

FACTORS THAT INFLUENCE BIOAVAILABILITY

1.First-pass hepatic metabolism:

When a drug is absorbed across the GI tract, it enter the portal circulation before entering the systemic circulation. If the drug is rapidly metabolized by the liver, the amount of unchanged drug that gains access to the systemic circulation is decreased. many drugs , such as propranolol or lidocaine , nitroglycerin under go significant biotransformation during a single passage through the liver. FPM limits the efficacy of many oral drugs. So should be administered IV, SL or Transdermal...and in sufficient doses

2-Lipid solubility of the drugs

3- Chemical instability : Some drugs, such as penicillin G, are unstable in the PH of the gastric contents. Others, such as insulin, are destroyed in the GI tract by degradative enzymes.

4-Nature of the drug formulations:
Drug absorptions may be altered by factors unrelated to the chemistry of the drugs. For example, particle size, salt form, crystal polymorphism, and the presence of excipients [such as binders and dispersing agents] can influence the ease of dissolution and, therefore, alter the rate of absorption.

- Bioinequivalent: Two related drugs are bioequivalent if they show comparable bioavailability and similar times to achieve peak blood concentrations. two related drugs with a significant difference in bioavailability are said to be bioinequivalent.

- Therapeutically equivalent: Two similar drugs are therapeutically equivalent if they have comparable efficacy and safety

- Clinical effectiveness of the drug often depends both on *maximum serum drug concentrations and on the time after administration required to reach peak concentration*. Therefore, two drugs that are bioequivalent may not be therapeutically equivalent


Thank You