PHARMACOLOGY INTRO DEFINATION

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TOPIC

1) Bioavailability
2) Bioequivalence
3) Therapeutic index
4) Plasma half life
5) Dose response curve
6) Area under curve (AUC)
7) Volume of distribution

PHARMACOKINETICS

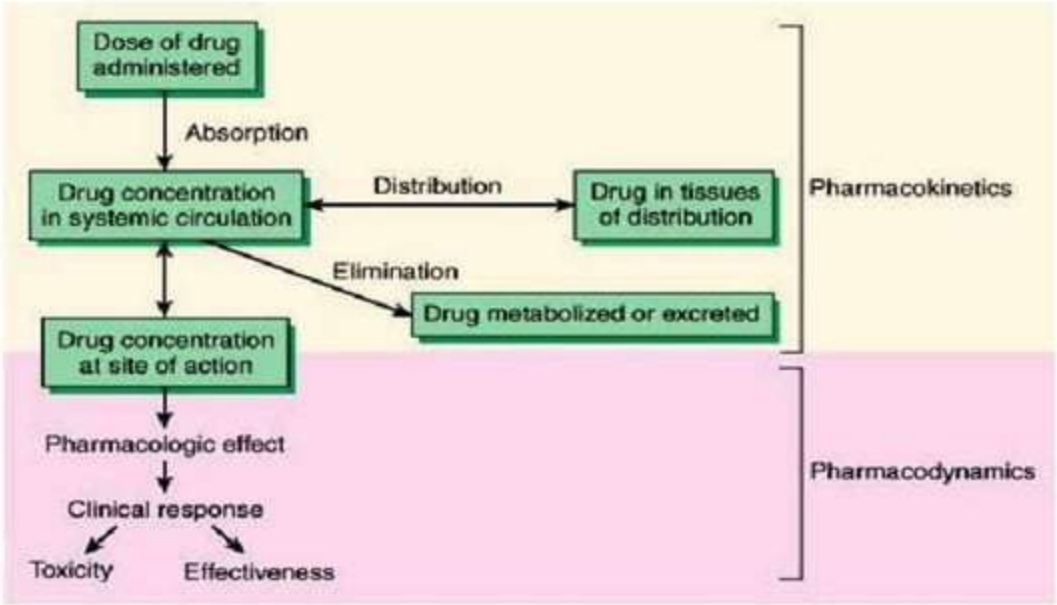
Pharmakon (drug)

Kinetics (motion)

- **Definition** : The actions of the body on an administered drug (dose concentration).

It involves drug absorption , distribution , metabolism and elimination .

PHARMACOKINETICS



Pharmacokinetics
conc. vs time

1) *BIOAVAILABILITY*

- In pharmacology, bioavailability is a measurement of the rate and extent to which a drug reaches the systemic circulation It is denoted by the letter ***f***
- Bioavailability is the ratio of the area calculated for oral route of administration to the intravenous route of administration.
- In pharmacology, **bioavailability** (BA) is a subcategory of absorption and is the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when a medication is administered intravenously, its bioavailability is 100%.
- However, when a medication is administered via other routes (such as orally), its bioavailability generally **decreases** (due to incomplete absorption and first-pass metabolism) or may vary from patient to patient.
- Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration.

- For a non-intravenous drug , it is less than 100% because of :
  1) Absorption Parameters.
  2)First-pass elimination.
- **Bioavailability** is the drug proportion that actually reaches systemic circulation .

Route	Bioavailability (%)	Characteristics
Intravenous (IV)	100	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 significant
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

2) BIOEQUIVALENCE

- Relationship between 2 preparations of the same drug at same dose in same form with similar bioavailability.

OR

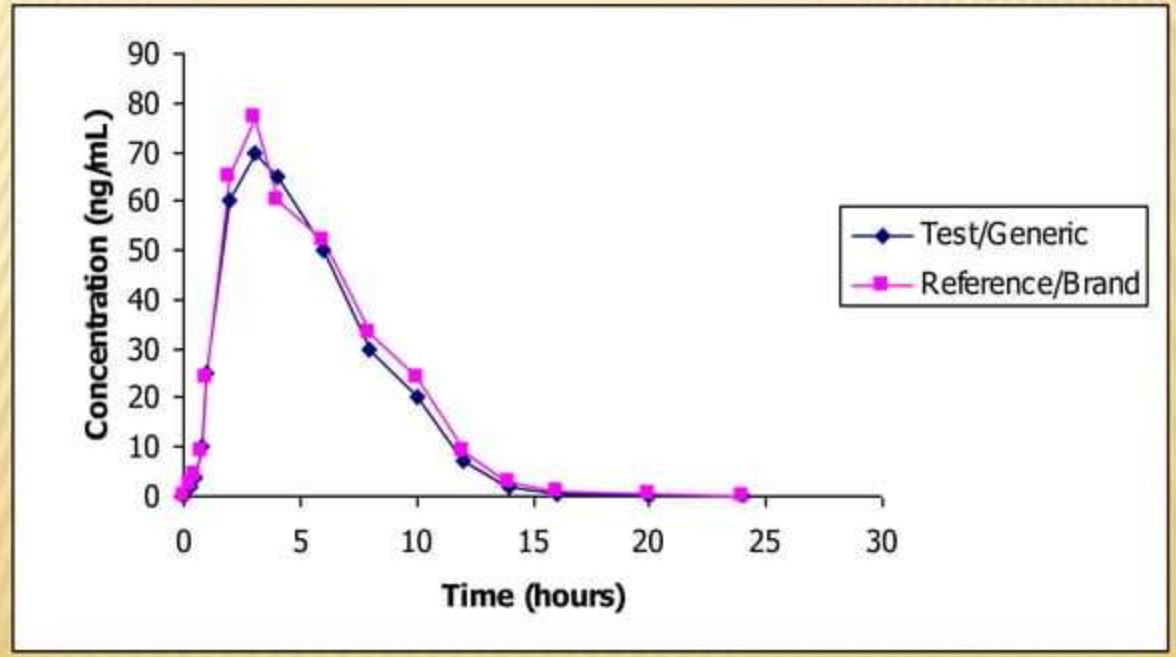
- The relationship between two preparations of the same drug in the same dosage form that have a similar bioavailability.

- **Bioequivalence** is a term in pharmacokinetics used to assess the expected in vivo biological equivalence of two proprietary preparations of a drug. If two products are said to be bioequivalent it means that they would be expected to be, for all intents and purposes, the same.

- two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent and their bioavailabilities (rate and extent of availability) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, can be expected to be essentially the same.

- Pharmaceutical equivalence implies the same amount of the same active substance(s), in the same dosage form, for the same route of administration and meeting the same or comparable standards."[1]

GRAPH SHOWING BIOEQUIVALENCE



3) THERAPEUTIC INDEX

- The difference between the minimum therapeutic and minimum toxic concentrations of a drug.
- Therapeutic index represents the safety of a drug.
- Drugs having low therapeutic index include:

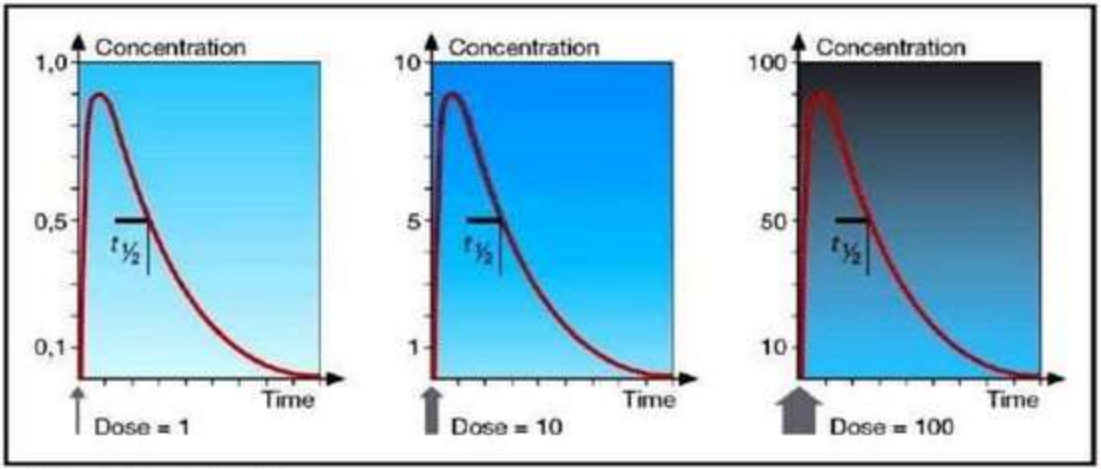
Anticonvulsants, lithium, anticoagulants, corticosteroids and cardio active drugs.

- **therapeutic index** (also known as **therapeutic ratio**) is a comparison of the amount of a therapeutic agent that causes the therapeutic effect to the amount that causes death (in animal studies) or toxicity (in human studies).
- the ratio between the dosage of a drug that causes a lethal effect and the dosage that causes therapeutic effect.
- ***Medical Dictionary :***
  The ratio between the toxic dose and the therapeutic dose of a drug, used as a measure of the relative safety of the drug for a particular treatment.

4) ***PLASMA HALF LIFE***

- The duration of action of a drug is known as its **half life.**
- This is the period of time required for the concentration or amount of drug in the body to be reduced by one-half.
- Drug can be eliminated from the body, or it can be translocated to another body fluid compartment such as the intracellular fluid or it can be destroyed in the blood after it is reduced to half life.
- The removal of a drug from the plasma is known as **clearance** and the distribution of the drug in the various body tissues is known as the **volume of distribution**. Both of these pharmacokinetic parameters are important in determining the half life of a drug.
- Here is the symbol to represent the half-life: $t_{1/2}$

- The **biological half-life** or **elimination half-life** of a substance is the time it takes for a substance (for example a metabolite, drug, signaling molecule, radioactive nuclide, or other substance) to lose half of its pharmacologic, physiologic, or radiologic activity , as per the MeSH definition.
- Biological half-life is an important pharmacokinetic parameter .



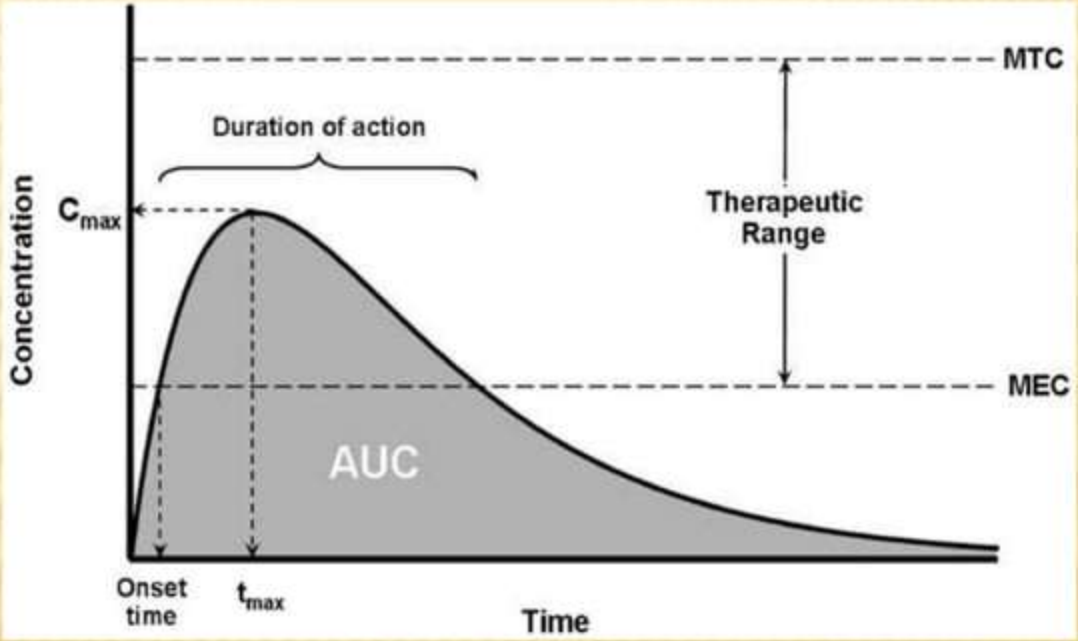
Dose-linear kinetics

5) DOSE-RESPONSE CURVE

- A **dose–response curve** is a simple X–Y graph relating the magnitude of a stressor (e.g. amount of drug) to the response of receptor.
- The measured dose (usually in milligrams, micrograms, or grams per kilogram of body-weight for oral exposures or milligrams per cubic meter of ambient air for inhalation exposures) is generally plotted on the X axis and the response is plotted on the Y axis.
- The **dose–response relationship** , describes the change in effect on an organism caused by differing levels of exposure (or doses) to a stressor (usually a chemical) after a certain exposure time.[1] This may apply to individuals (e.g.: a small amount has no significant effect, a large amount is fatal), or to populations (e.g.: how many people or organisms are affected at different levels of exposure).
- Studying dose response, and developing dose response models, is central to determining "safe" and "hazardous" levels and dosages for drugs, potential pollutants, and other substances to which humans or other organisms are exposed. These conclusions are often the basis for public policy.
- Dose–response relationships generally depend on the exposure time and exposure route (e.g., inhalation, dietary intake); quantifying the response after a different exposure time or for a different route leads to a different relationship and possibly different conclusions on the effects of the stressor under consideration.

6) AREA UNDER CURVE (AUC)

- *The area under the plot of plasma concentration of drug (not logarithm of the concentration) against time after drug administration*
- *The area under the plasma (serum, or blood) concentration versus time curve **(AUC)** has a number of important uses in pharmacokinetics.*
- *The **AUC** is of particular use in estimating bioavailability of drugs, and in estimating total clearance of drugs (**CIT**).*

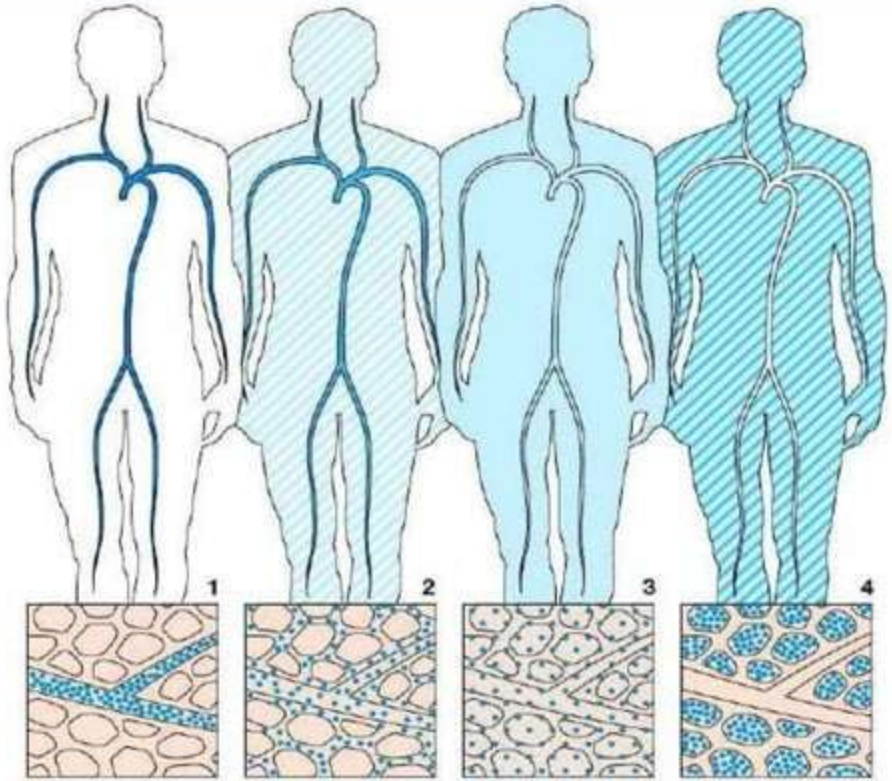

MTC
Duration of action
Therapeutic Range
Concentration
C_{max}
MEC
AUC
Onset time
t_{max}
Time

- **AUC** can be used as a measure of drug exposure. It is derived from drug concentration and time so it gives a measure how much - how long a drug stays in a body.
- The AUC measured after administration of a drug product is an important parameter in the comparison of drug products. These bioequivalence or bioavailability studies can be analyzed by comparing AUC values.
- Drug **AUC** values can be used to determine other pharmacokinetic parameters, such as clearance or bioavailability, F. Similar techniques can be used to calculate area under the first moment curve (AUMC)

7) VOLUME OF DISTRIBUTION

- Volume of distribution is the measure of the apparent space in the body available to contain the drug.
- Volume of distribution relates the amount of drug in the body to the concentration of drug in blood or plasma .
- Formula for volume of distribution is , total amount of drug in the body divided by drug blood plasma concentration.
- It is not a real but a theoretical volume.
- if VD is greater, it shows that the drug is more diluted than it should be (in the blood plasma), meaning more of it is distributed in tissue (i.e. not in plasma).
- It is defined as the distribution of a medication between plasma and the rest of the body after oral or parenteral dosing.

- Volume of distribution may be increased by renal failure (due to fluid retention) and liver failure (due to altered body fluid).
- Conversely it may be decreased in dehydration.


1
2
3
4
Distribution in tissue

REFERENCE

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★THANK YOU...

ANY QUESTION ???