NOVA

Charting New Horizons in Education

Pharmacokinetics IV

06

pharmacology

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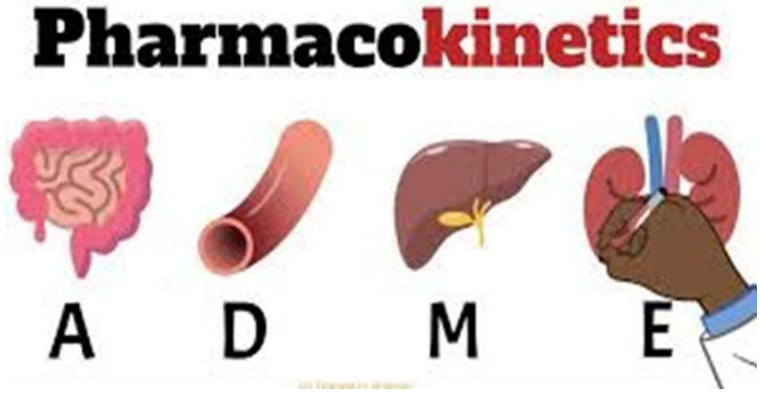
Objectives:

- **kinetics orders (order of elimination)**
- **Elimination half life**
- **Steady state plasma concentration (Css)**
- **Systemic clearance**

Pharmacokinetics

what the body does to the drug?

- Absorption
- Distribution
- Metabolism
- Excretion.



EXCRETION OF DRUGS

Kidney: is the most important organ for excretion

- Excretion occurs through:

  - Glomerular filtration
  - Proximal convoluted tubules (PCT)
  - Distal convoluted tubules (DCT)

1- Glomerular filtration

All free drug molecules whose size is less than the glomerular pores are filtered into Bowman's capsule.

2- Proximal convoluted tubules (PCT)

Active secretion occurs either through :

1- acid carrier .e.g. for penicillin, probenicid, salicylic acid.

2- basic carrier for amphetamine and quinine.

3- Distal convoluted tubules (DCT)

- Lipophilic drugs may be reabsorbed back to systemic circulation.

- Alkalinization of urine keeps acidic drugs ionized and increases their excretion.

- Acidification of urine keeps basic drugs ionized and increases their excretion.

Other sites of excretion:

- **Bile**: e.g. Doxycycline, Azithromycin.
- **Lungs** e.g. Volatile anesthetics.
- **Saliva** e.g. Iodides.
- **Sweat** e.g Rifampicin.
- **Milk**: this is important in lactating mothers.

(Nalbuphine(an opiod) during breastfeeding leading to prolonged sleep, lethargy, or reduced alertness in the infant)

PARAMETERS OF ELIMINATION

- KINETICS ORDERS
- ELIMINATION HALF LIFE (t1/2)
- SYSTEMIC CLEARANCE (CLs)

KINETICS ORDERS

- **First order kinetics**
- **Zero order kinetics**(phenytoin ,alcohol , Salicylates)

First order kinetics (most drugs):

- Rate of elimination is directly proportionate to the blood concentration of drugs (constant percentage of the drug is eliminated per unit of time) (Constant "t1/2“)

- Repeated dosing increases drug concentration and accordingly the rate of elimination increases till the rate of administration equals the rate of elimination.

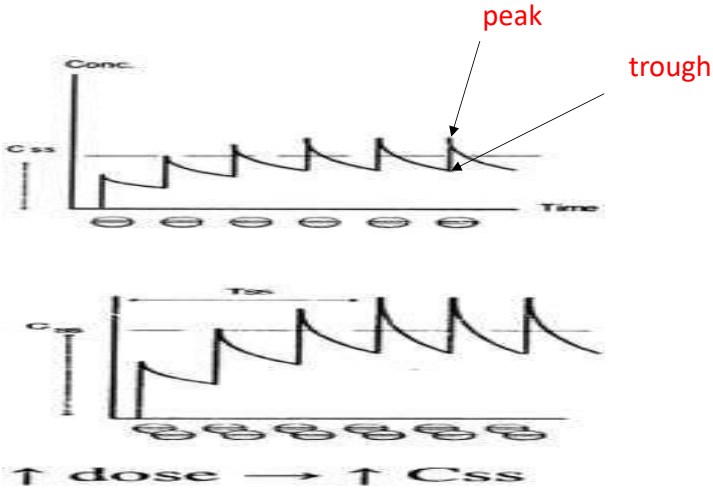
- Steady state plasma concentration (Css)can be reached after 4-5 t1/2.

- Css is directly proportionate to the dose.

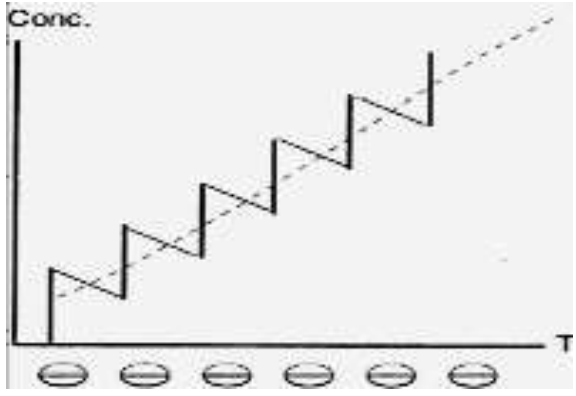
Zero order kinetics

- Rate of drug elimination is constant i.e. constant amount of drug is eliminated per unit of time. "t1/2" (half life) is not constant.
- No Css is reached by repeated dosing.
- Any change of the dose may cause toxicity.
- Some drugs follow 1st order kinetics in small dose and zero order kinetic at large doses i.e. the elimination mechanism is said to be saturated (saturation kinetics).

First order



Zero order



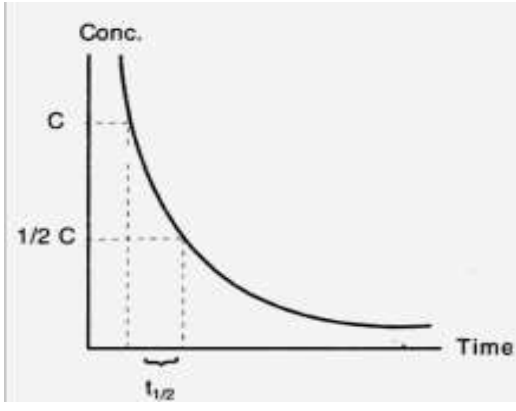
- The **therapeutic range** is the interval between the **peak concentration (Cmax)**, which is the highest level of the drug in the bloodstream after administration, and the **trough concentration (Cmin)**, which is the lowest level just before the next dose

Characteristic	First-Order Kinetics	Zero-Order Kinetics
Rate of Elimination	Proportional to the drug concentration	Constant amount eliminated per unit time
Percentage or Amount	Percentage of drug eliminated remains constant (e.g., 50% of remaining drug)	Fixed amount eliminated (e.g., 10 mg/hour)
Half-Life	Constant half-life regardless of concentration	Half-life varies based on drug concentration
Reach Steady-State Concentration (Css) ?	YES	NO
Toxicity Risk	NO	YES

ELIMINATION HALF LIFE (T1/2)

- It is the time required to reduce the plasma concentration of the drug to half the initial concentration (the time required for drug concentration to be changed by 50%).

- T1/2 = 0.7 * Vd /CLs



- **The therapeutic effect is not achieved after the first half-life; it occurs after 4 to 5 half-lives of continuous dosing.**

Importance of elimination T1/2:

- It determines the dosage interval (T).
- It indicates time required to attain Css (about 4-5 t1/2):
- If "t1/2“ is very short (minutes), the drug should be given by IV infusion [dopamine].
- If "t1/2“ is long [digoxin], the drug should be administered in loading dose followed by maintenance dose.

Factors affecting elimination "t1/2":

- State of eliminating organs i.e. liver & kidney function.
- Delivery of drugs to the eliminating organs affected by:

1-plasma protein binding : Highly bound drugs are typically eliminated more slowly, while drugs with low binding are cleared more rapidly.

2-Vd of the drug : Drugs with a high volume of distribution may take longer to eliminate, while those with a low volume of distribution are usually cleared more quickly.

Systemic clearance (CLs)

- It is the volume of fluid cleared from the drug per unit of time.
- Systemic CLs = Renal clearance (CLr) + non-renal clearance (CLnr)

Significance of clearance: Calculation of the maintenance dose

- **Loading dose**: The dose required to achieve a desired plasma concentration (desired Css) rapidly, followed by routine maintenance dose.
- **Loading dose** = Vd×TC
- **Maintenance dose**: The dose given to maintain the desired Css.
- **Maintenance dose** = CLs×TC (Target concentration).

«Education is the passport to the future, for tomorrow belongs to those who prepare for it today»

- Maclom X-

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