PHARMACOKINETICS 4

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Pharmacokinetics

what the body does to the drug?

- Absorption
- Distribution
- Metabolism
- Excretion.

EXCRETION OF DRUGS

- **Kidney:** most important organ for excretion
- Excretion occurs through:

1. **Glomerular filtration**
2. **Proximal convoluted tubules (PCT)**
3. **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

- acid carrier e.g. for penicillin, probenicid, salicylic acid.
- basic carrier for amphetamine and quinine.

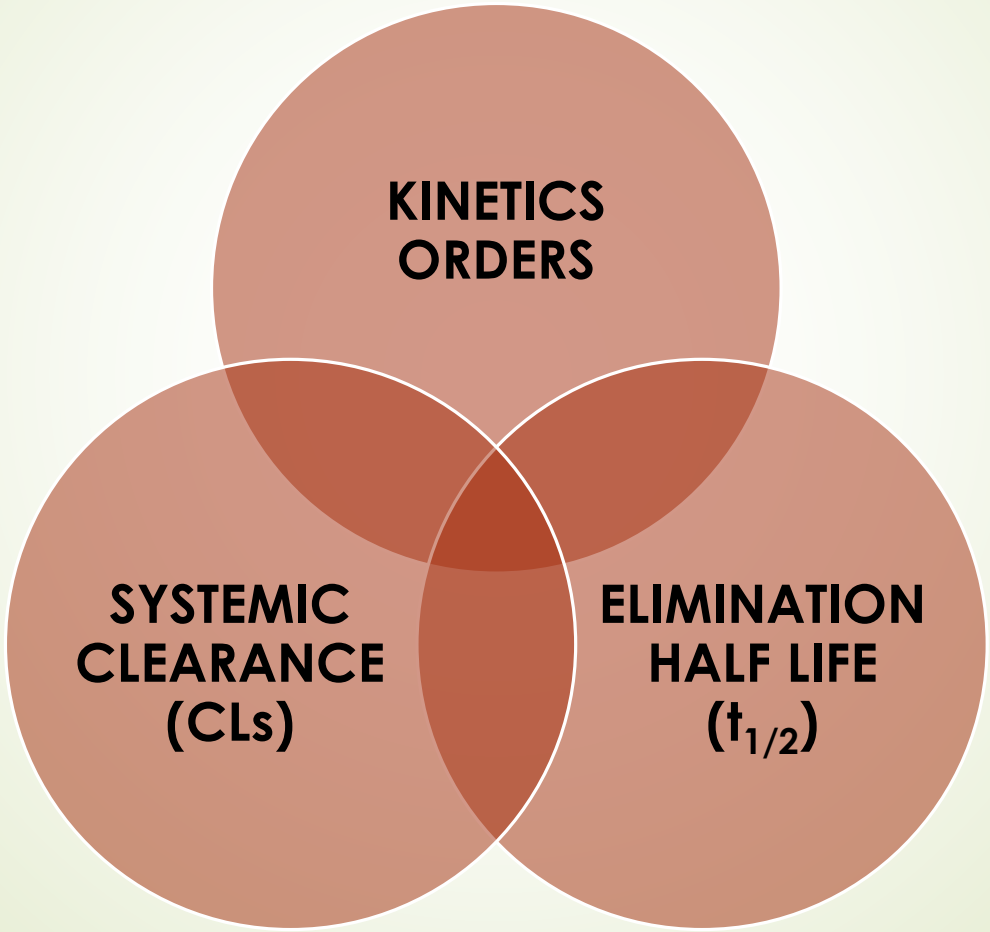
3-Distal convoluted tubules (DCT)

- 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.

PARAMETERS OF ELIMINATION



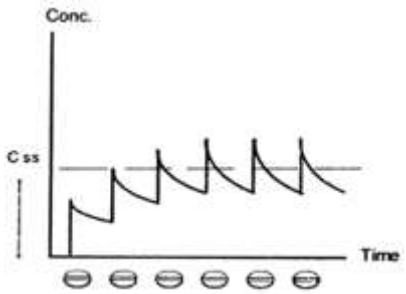
KINETICS ORDERS

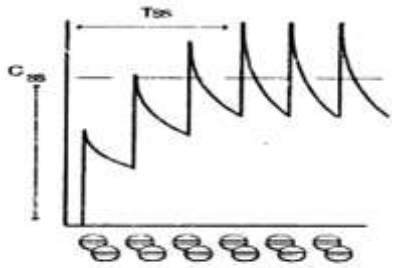
First order **kinetics**

Zero order kinetics

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 "$t_{1/2}$"**
- Repeated dosing increases drug concentration and accordingly the rate of elimination increases till the rate of administration equals the rate of elimination.
- Css can be reached after 4-5 $t_{1/2}$
- Css is directly proportionate to the dose.





↑ dose → ↑ Css

Zero order kinetics
(phenytion and salicylate)

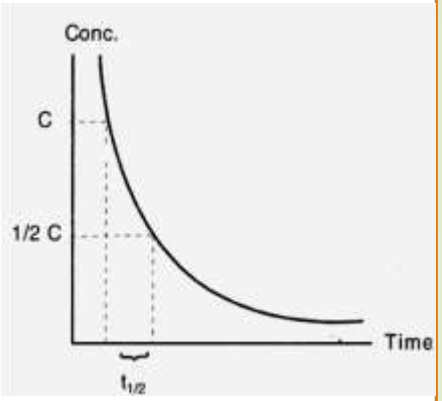
- Rate of drug elimination is constant i.e. ***constant amount*** of drug is eliminated per unit of time.
- "$t_{1/2}$" (half life) is not constant.
- No Css is reached by repeated dosing.
- Any change of the dose may cause toxicity.
- **Some drugs follow 1st order kinetics in small dose and zero order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

ELIMINATION HALF LIFE ($T_{1/2}$)

- 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%).
- $T_{1/2} = 0.7\ V_d/CLs$

Importance of elimination $T_{1/2}$:

- It determines the dosage interval (T).
- It indicates time required to attain Css (about 4-5 $t_{1/2}$):
- If "$\mathbf{t_{1/2}}$"is very short (minutes),



the drug should be given by IV infusion [dopamine].

- If "$\mathbf{t_{1/2}}$"is long [digoxin], the drug should be administered in loading dose followed by maintenance dose

Factors affecting elimination "$t_{1/2}$":

- State of eliminating organs i.e. liver & kidney function.
- Delivery of drugs to the eliminating organs: affected by plasma protein binding and Vd of the drug.

SYSTEMIC CLEARANCE (CLs)

- *It is the volume of fluid cleared from the drug per unit of time.*
- ***Systemic CLs*** *= Renal clearance (*CL_r*) + 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).

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Thank you!