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.

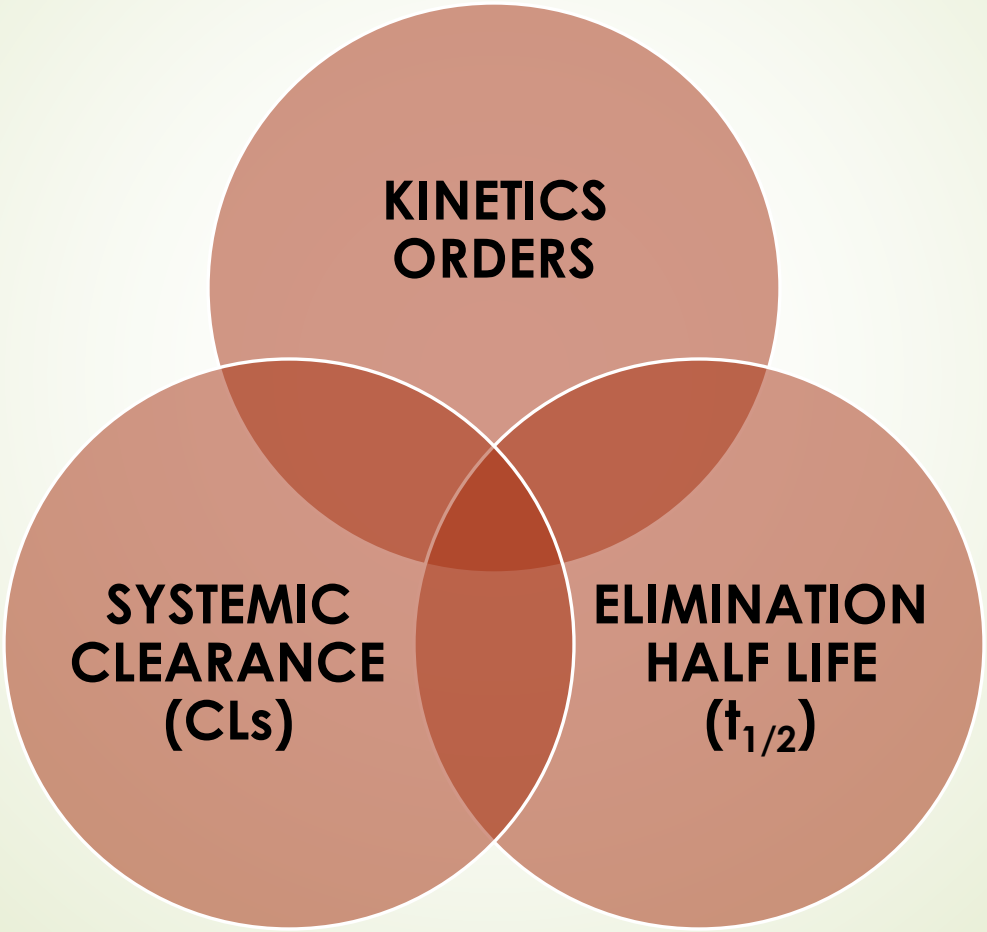
3-Distal convoluted tubules (DCT)

- 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



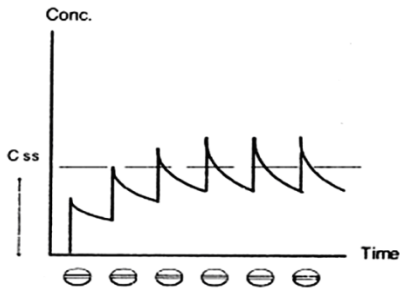
KINETICS ORDERS

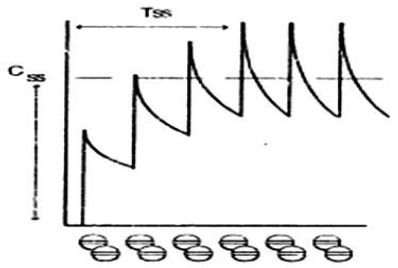
First order **kinetics**

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)

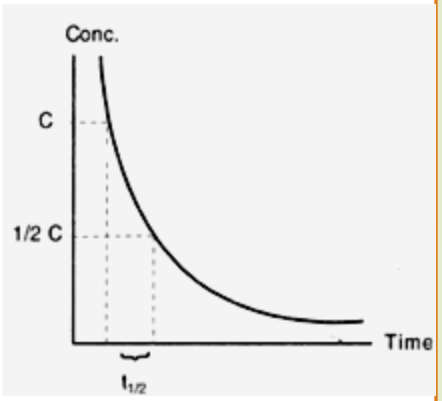
- Rate of drug elimination is constant i.e. ***constant amount*** of drug is eliminated per unit of time.
- "$t_{1/2}$" (half life) is not constant.
- No Css is reached by repeated dosing.
- Any change of the dose may cause toxicity.
- **Some drugs follow 1st order kinetics in small dose and zero order 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 "**$t_{1/2}$**"is very short (minutes),



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

- If "**$t_{1/2}$**"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**tconcentration.

References:

- Lectures in pharmacology part (1) by staff members of clinical pharmacology dep. Faculty of medicine, zagazig university.
- Kadzung B.G., Masters S.B, and Trevor A.J. Basic & Clinical pharmacology 12th edition.
- Wilkins R,Cross S, Megson L and Meredith D (2011):Oxford Handbook of Medical Sciences Second Edition
- Tao Le, Vikas Bhushan Matthew Sochat, Yash Chavda, Kimberly Kallianos, Jordan Abrams, Mehboob Kalani and Vaishnavi Vaidyanathan (2019): FIRST AID for the USMLE Step 1.


Thank you!