Lecture (4)

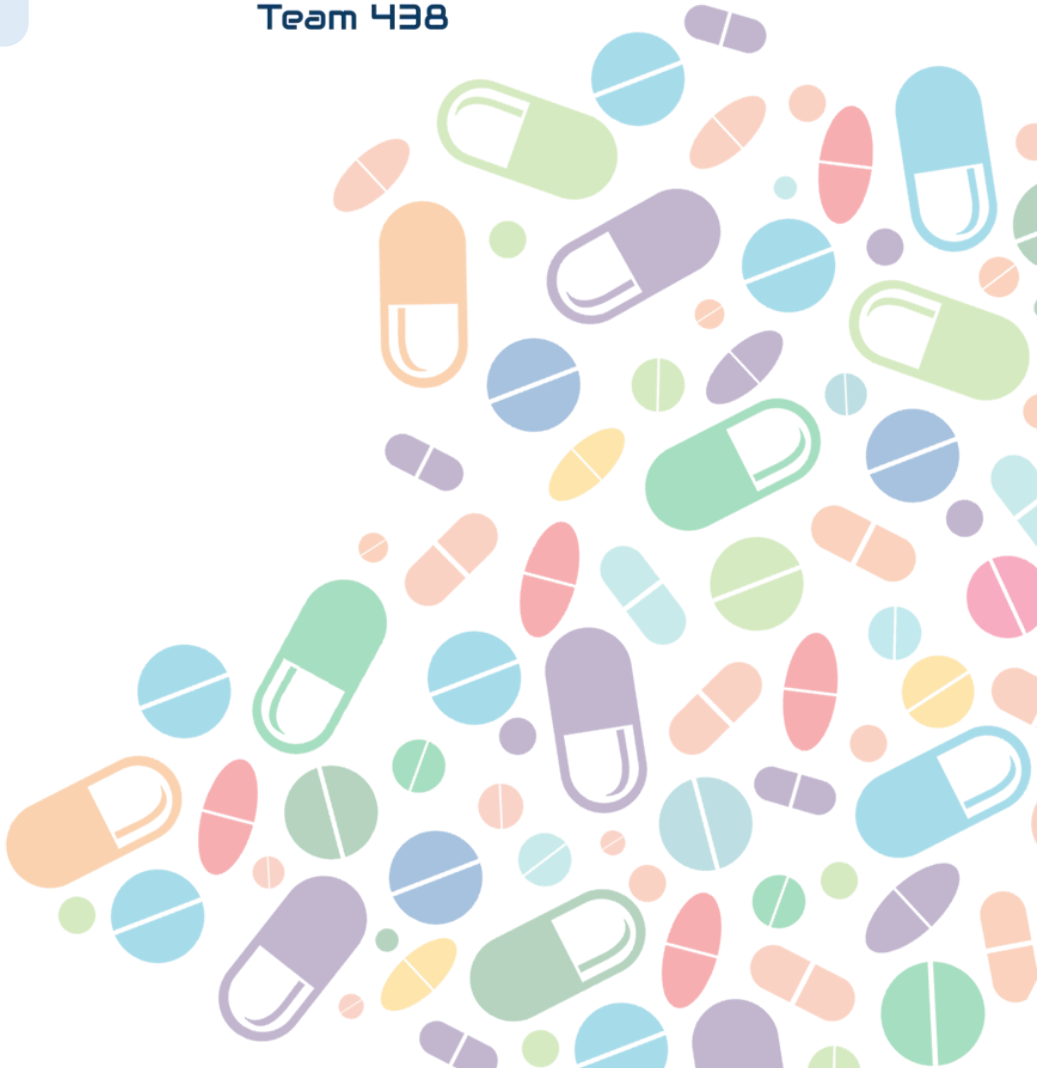
Excretion of Drugs

pharmacology
Team 438

MED438
KING SAUD UNIVERSITY

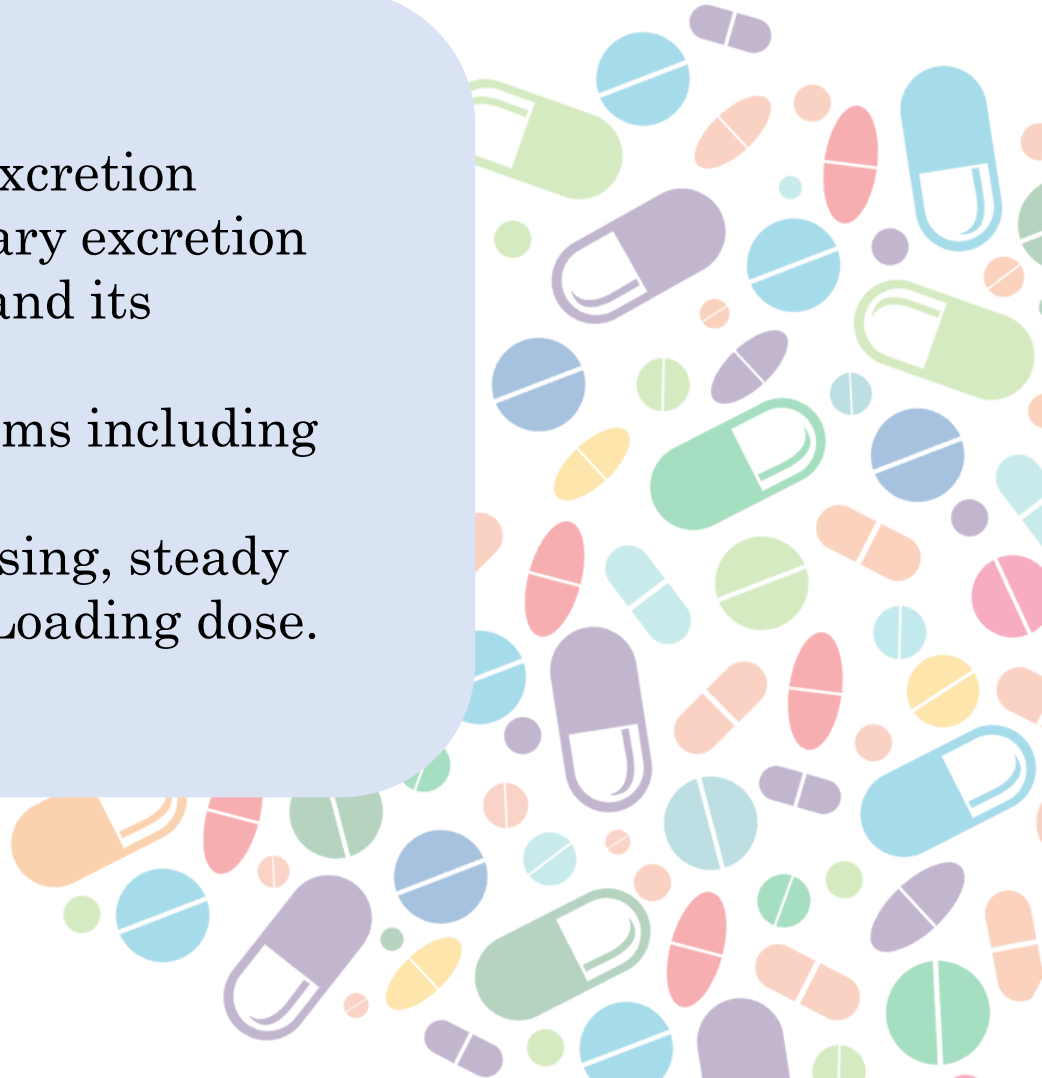
- Red : important
- Black : in male / female slides
- Pink : in girls slides only
- Blue : in male slides only
- Green : notes, Extra

Reviewed by Razan AlRabah & Khalid Alkhani



Objectives:

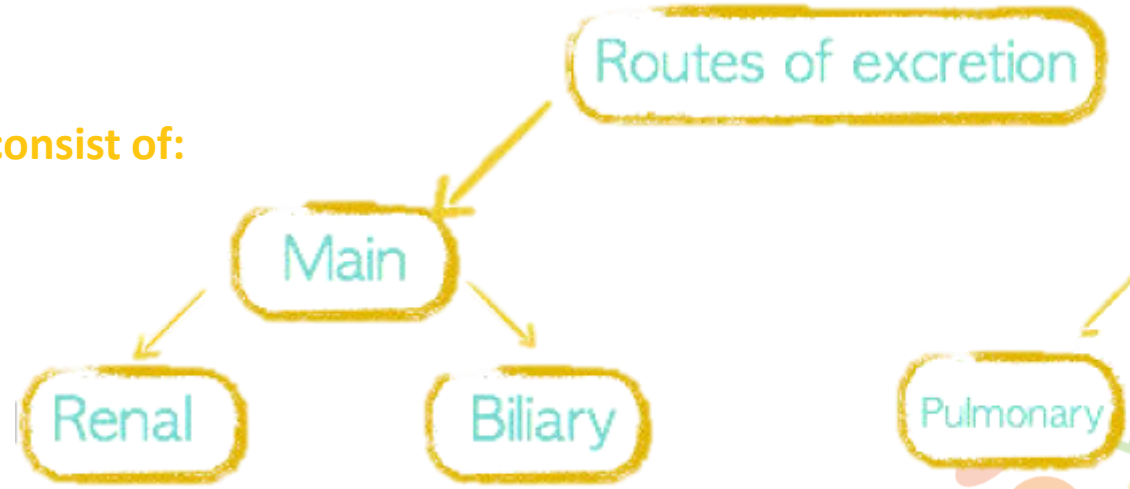
- Identify main and minor routes of Excretion including renal elimination and biliary excretion
- Describe enterohepatic circulation and its consequences on duration of drugs.
- Describe some pharmacokinetics terms including clearance of drugs.
- Biological half-life (t ½), multiple dosing, steady state levels, maintenance dose and Loading dose.



Excretion:

Nephron(the structure unit of kidney)consist of:

- Glomerulus
- Proximal convoluted tubules
- Loop of Henle
- Distal convoluted tubules
- Collecting



The principle processes that determine the Urinary excretions of drugs are:

Glomerular filtration (GFR):

- Depends upon renal blood flow (600 ml/min)
- GFR 20% of renal blood flow = 125 ml/min.
- Glomerular filtration occurs to low molecular weight drugs
- Only free drugs (unbound to plasma proteins) are filtered

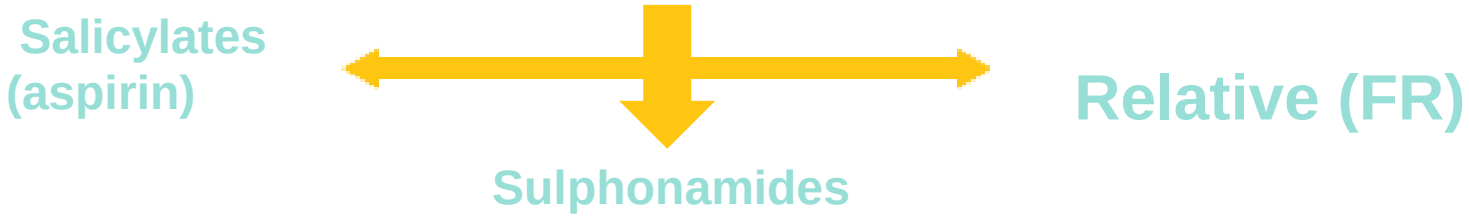
Active tubular secretion:

- occurs mainly in proximal tubules; increases drug concentration in lumen
- organic anionic and cationic transporters mediate active secretion of anionic and cationic drugs.
- can transport drugs against conc. gradients.
- e.g. **Penicillin**

Passive tubular re-absorption

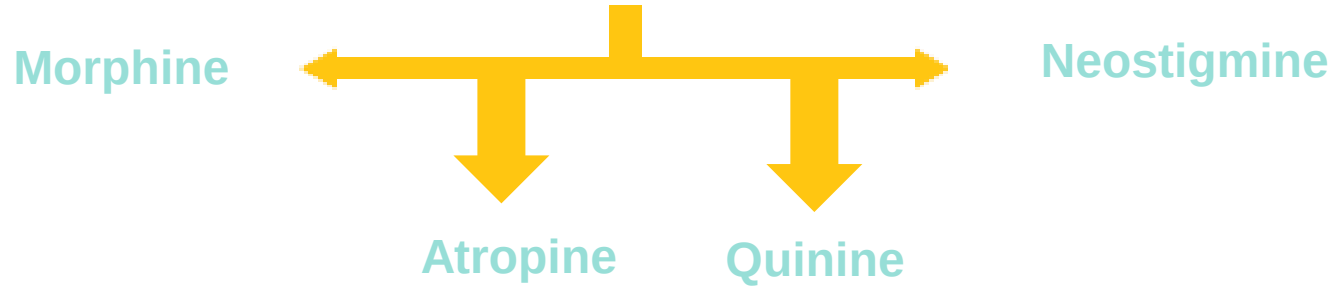
- In distal convoluted tubules & collecting ducts.
- Passive diffusion of unionized, lipophilic drugs
- Lipophilic drugs can be reabsorbed back into blood circulation and excretion in urine will be low.
- Ionized drugs are poorly reabsorbed so urinary excretion will be high.

System for Acidic Drugs



Transport of acidic drugs is blocked by probenecid (It inhibits the tubular reabsorption of urate,
thus increasing the urinary excretion of uric acid and decreasing serum urate levels).

System for Basic Drugs



The suffix -ine means that the drug is coming from natural sources (glands) and it is basic

Urinary pH trapping (Ion trapping)

• Changing pH of urine by chemicals can inhibit or enhance the drug reabsorption from renal tubules back into blood circulation.
• Ion trapping is used to enhance renal clearance of drugs during toxicity.
• Urine is slightly acidic and favors excretion of basic drugs.
• Acidification of urine using **ammonium chloride (NH4Cl)** increases excretion of basic drugs as *amphetamine*.
• Alkalization of urine using **sodium bicarbonate (NaHCO3)** increases excretion of acidic drugs as *aspirin*.

Renal Excretion

Drugs excreted mainly by the kidney include:

- Aminoglycosides antibiotics (as gentamycin)
- Penicillin
- Lithium

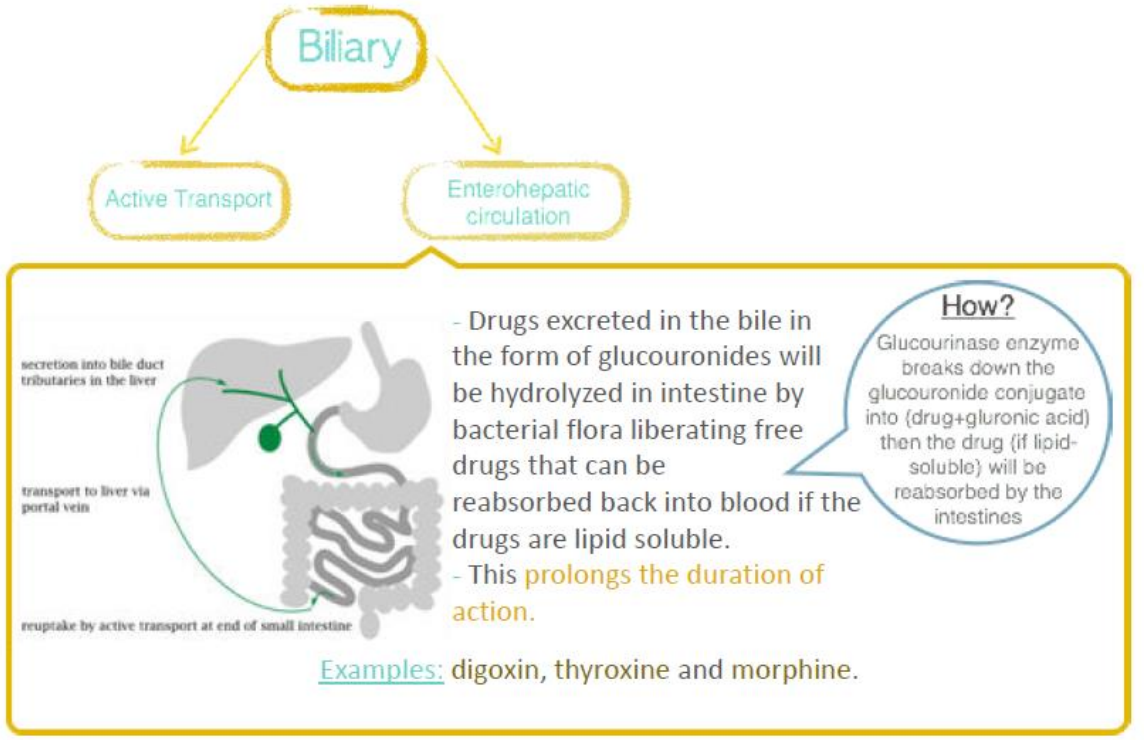
These drugs should be prescribed carefully in:

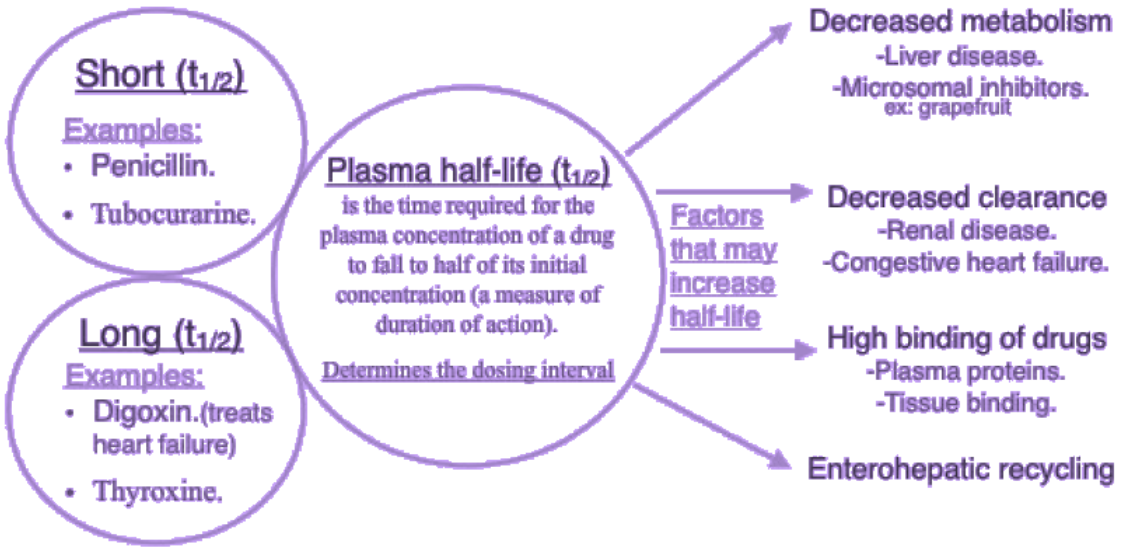
- Patients with renal disease
- Elderly people

Biliary Excretion

- Occurs to few drugs that are excreted into feces.
- Such drugs are secreted from the liver into bile by active transporters, then into duodenum.

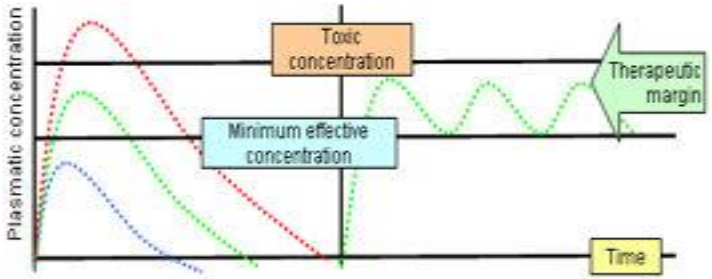
Some drugs undergo enterohepatic circulation back into systemic blood circulation.





Steady State level

A state at which the therapeutic plasma concentration of the drug (mg/ml) remains constant with the therapeutic window (the range between effective and toxic levels of drugs).
rate of drug administration = elimination rate



Therapeutic window:

The range at which the state of the drug is steady, (drug in= drug out) without reaching toxicity level

3-5 half lives would be necessary to reach the steady state concentration.
E.g. Morphine

Loading dose:

is the initial dose that is given to achieve rapid therapeutic plasma level.

- After administration of the drug, the plasma concentration decreases due to distribution of drug to other tissues
- These doses balance the drug distribution
- This is important for drugs with long half lives
- important for drugs with long halve lives.

Clinical application for the loading dose:

- A loading dose may be desirable if the time required to attain steady state of drug (4 elimination t1/2 values) is long and rapid relief is required in the condition being treated.
- E.g. t1/2 of *Lidocaine* (antiarrhythmic drug) is usually 1-2 hours and Arrhythmias after myocardial infarction are life-threatening. One cannot wait 4-8 hours to achieve a therapeutic concentration.
- So we use a loading dose of *Lidocaine* in the coronary care unit.

Maintenance dose:

- Are the doses required to maintain the therapeutic level of the drug constant or the steady state of the drug.
- - These doses balance the amount of drug lost during metabolism and clearance.
- - The patient needs to take regular doses of a drug such as *Amoxicillin* (500 mg) / 8 hours to maintain the therapeutic level

Quiz (MCQ) :

Q1.Which one of these drugs does not require to be absorbed ?

A)Oral B)intravenous C)rectal

Q2.A drug is distributed through 2 compartments is found in ? From 437

A)Plasma B)ICF C)ECF

Q3.Drugs with very high molecular weight are most likely to be found in ?

A)Plasma B)interstitial fluid C)ICF

Q4.A drug with large Vd mean that the drug has ?

A)Short duration of action B)Long duration of action C)No action

Q5.The Vd for Ethanol is ?

A)45 B)38 C)27

Q6.Drugs are distribute rapidly to ?

A)Kidney B)Fat C)Skeletal muscle

Q7.Tetracycline drug bind to ?

A)Heart B)Muscle C)Bone

ANSWER : 1)B - 2)C - 3)A - 4)B - 5)B - 6)A - 7)C

Quiz (SAQ) :

Q1.When the rate and extent of bioavailability of active ingredients in two products are the same the two pharmaceutically products called ?

Q2.What are the factors that affect the bioavailability ?

Q3.What is the ratio of drug amount in the body (dose) to the concentration of drug in blood ?

Q4.How many compartments the drug with low molecular weight may distribute with?

Q5.Give an example to a drug with high Vd ?

Q6.What type of drugs that do not readily cross membranes ?

Q7.What type of drugs that can cross the blood brain barrier (BBB)?

Q8.Give an example to a plasma protein has affinity for acidic drugs ?

Q9.Which type of drug bindings will have high volume of distribution (Vd)?

10.What can the inflammation as in meningitis cause to the permeability of the drug?

Answer(SAQ) :

1. bioequivalent
2. -are the same factors controlling drug absorption -first pass effect
3. Apparent volume of distribution
4. Two compartment
5. digoxin, phenytion, morphine
6. Hydrophilic drugs (ionized, charged, polar)
7. lipid soluble drugs or actively transported drugs
8. Albumin
9. Tissue binding
10. increase permeability to hydrophilic drugs

Good luck

Thanks to the pharma team 435

PHARMACOLOGY 435

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