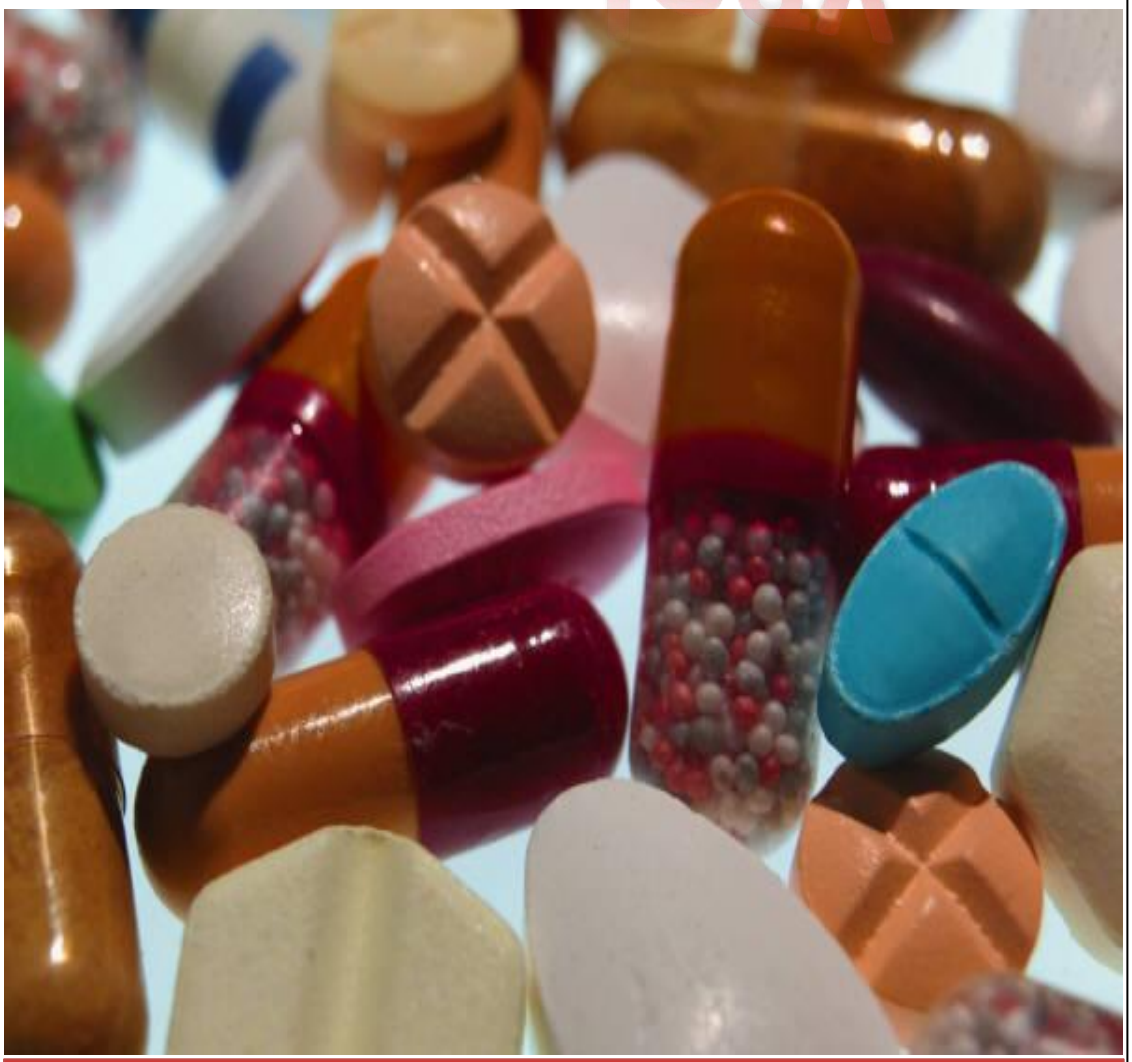
pharmacology



By:.

Team of pharmacology

- 7th pharmacology lecture “Concepts of drug disposition (Metabolism)”

Lecture’s objectives:

1. The definition and importance of metabolism.

2. The sites of metabolism.

3.The types and results of metabolic reactions.

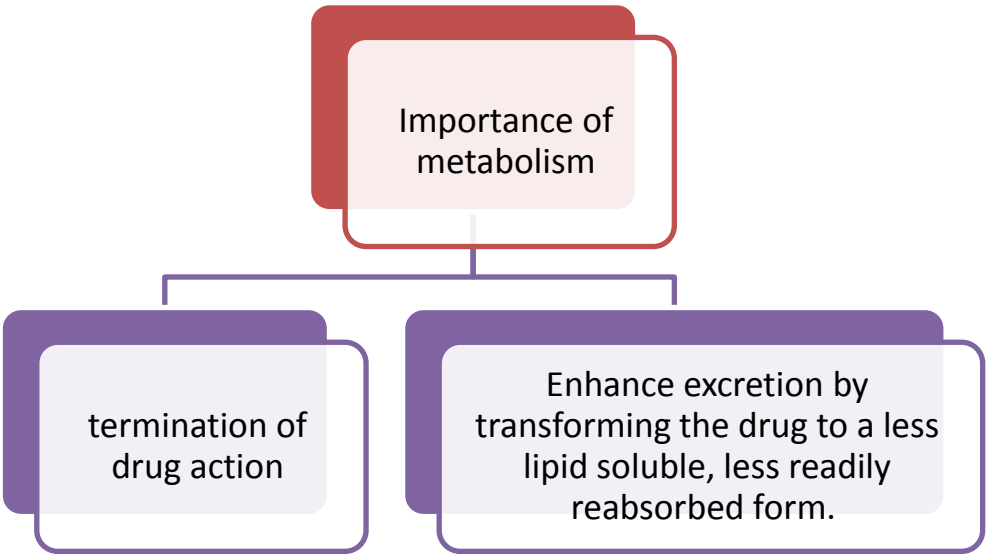
4.Routes of excretion.

5.What is the meaning of Enter hepatic circulation and plasma half-life (t1/2)

6.The factors which affecting metabolism and half-life.

7.The meaning of steady state levels.

- Definition: Chemical reactions which lead to modification of drugs.

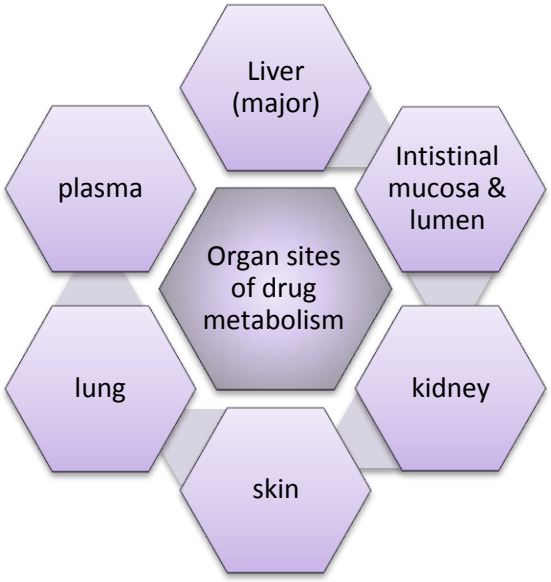


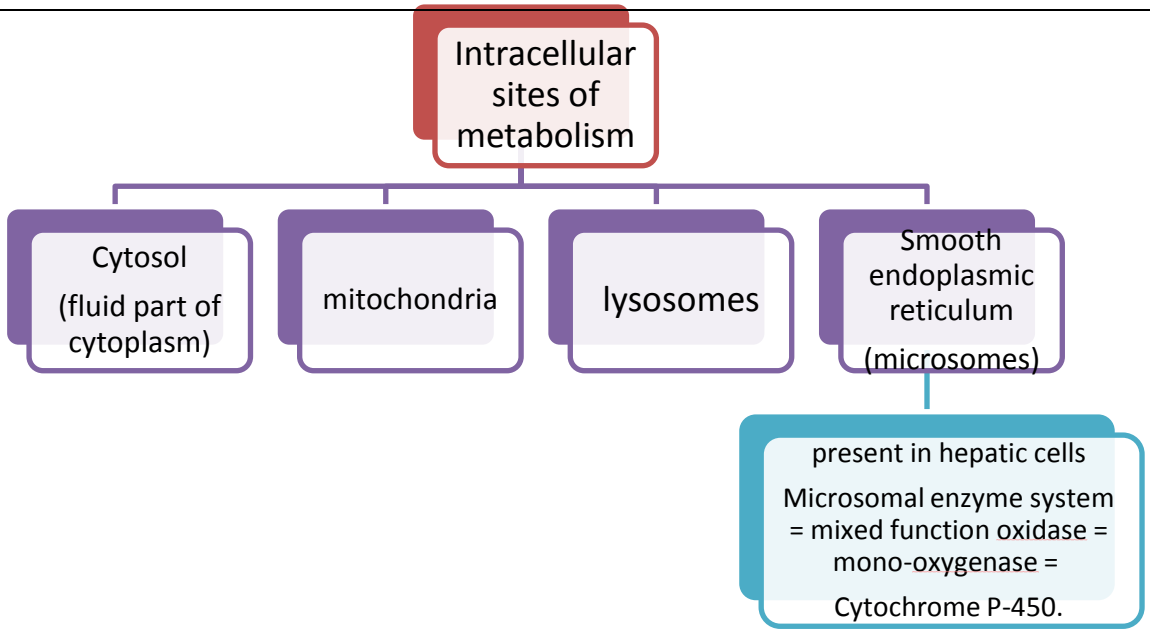
Lipid soluble Metabolism → Water soluble

Lipid soluble in

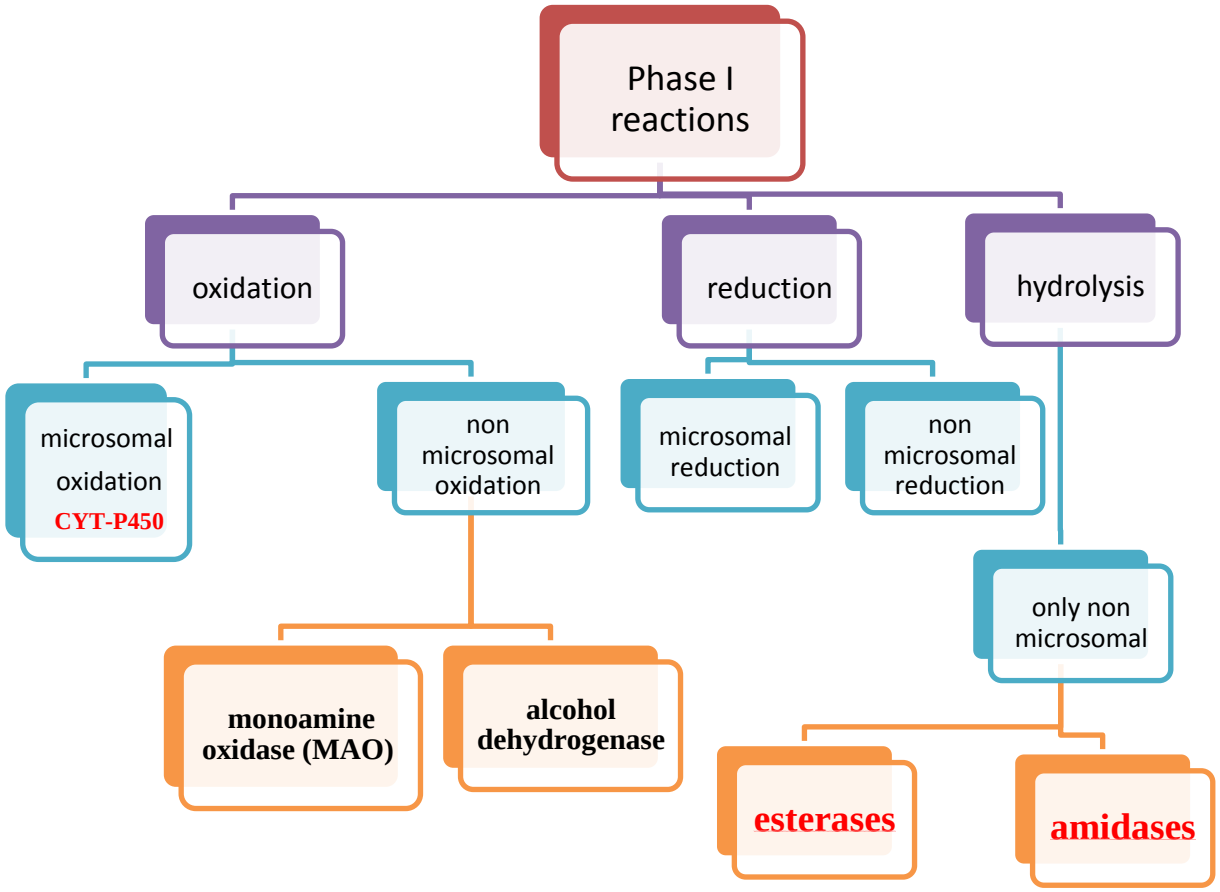
a) Absorption
b) Enter the membrane
c) Distribution
d) Metabolism

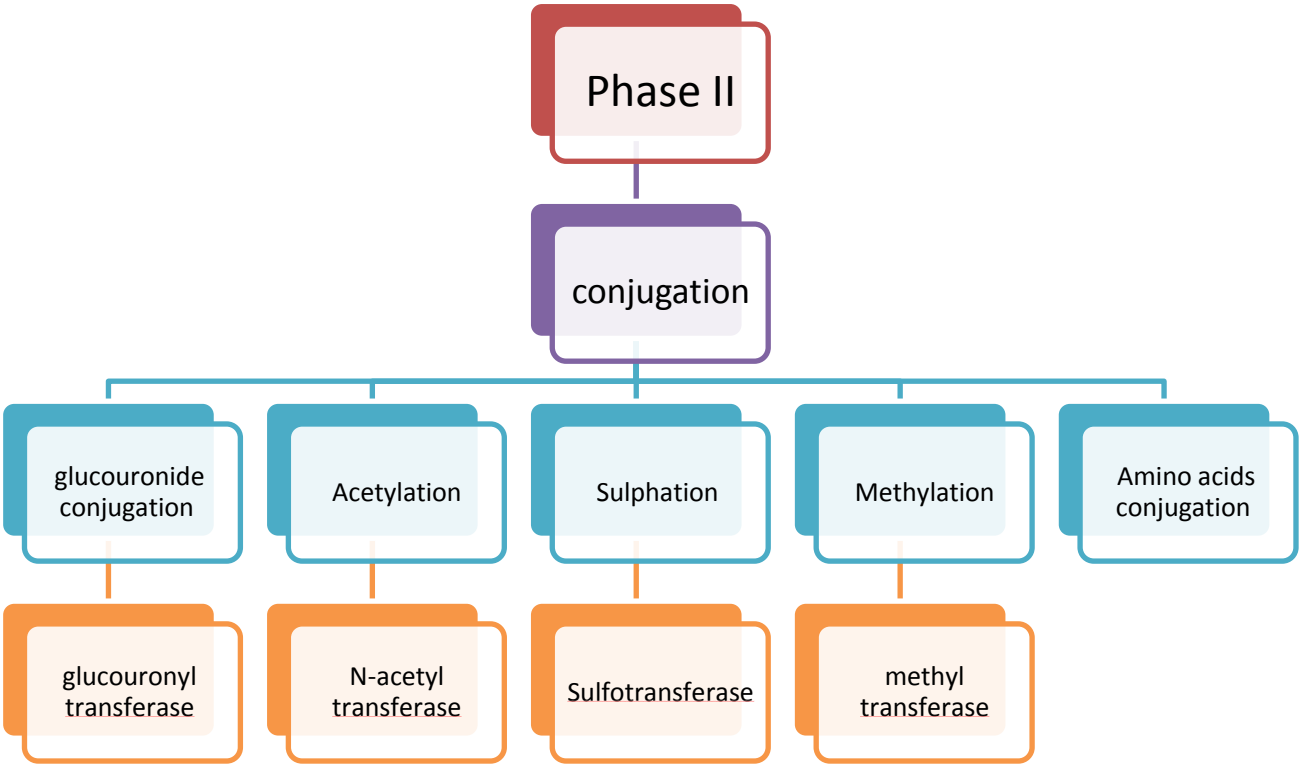
Water soluble in the **excretion**





Types of metabolism reactions: Phase I & Phase II reactions



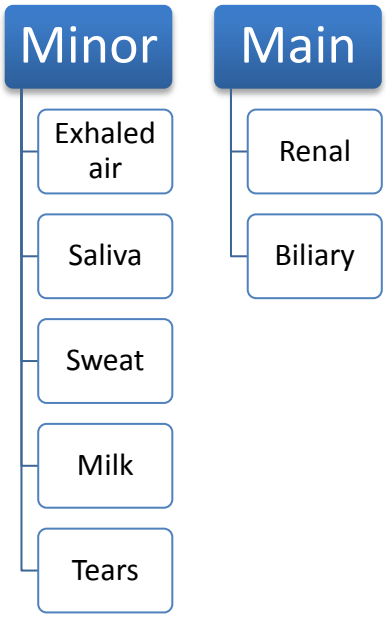


Notes for Phase II:

- **All are non-microsomal except glucuronidation**
- **Deficiency of glucuronyl transferase results into toxicity with chloramphenicol (gray baby syndrome)**

Results of metabolism	
Phase I	Phase II
Inactivation of drug (termination of action)	Make drug inactive
Conversion of active drug to another active metabolic	Polar
Conversion of drugs to toxic metabolic	More water soluble
Activation of pro-drug	More readily exerted in urine
Product might undergo phase II (if the drug not completely water soluble)	

Routes of drug excretion



***Renal excretion include:**

1.Glomerular filtration:

- ✓ Occurs to free drugs, low MW drugs
- ✓ Depends on renal blood flow (20%)

2.Active tubular secretion:

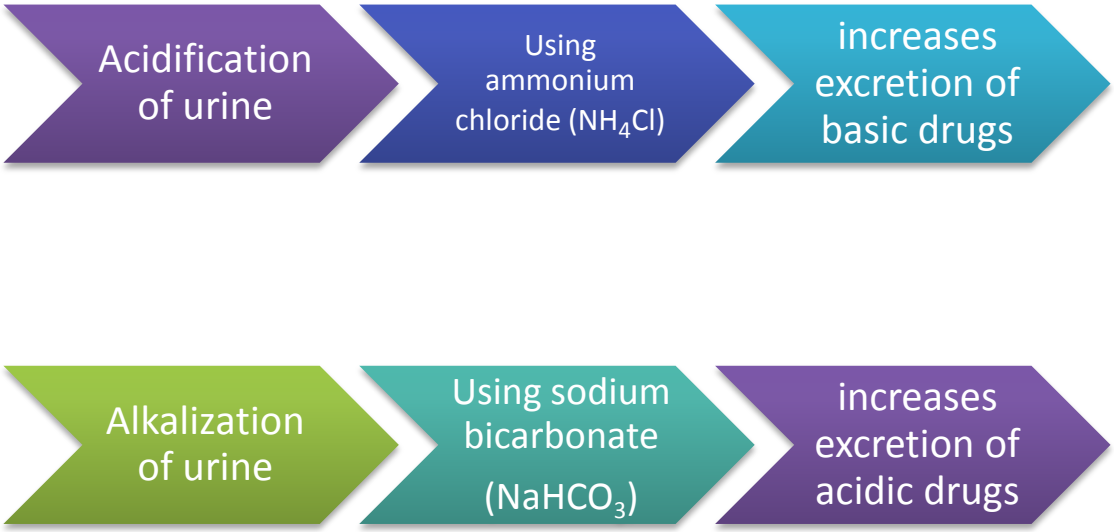
- ✓ Occurs in proximal tubules (increases drug concentration in tubular lumen)
- ✓ Organic anionic & cationic transporters mediate active secretion of anionic & cationic drugs

3.Passive tubular reabsorption:

- ✓ Occurs in distal convoluted tubules & collecting ducts
- ✓ Passive diffusion of unionized, lipophilic drugs

***Urinary pH trapping (Ion trapping)**

Urine is normally slightly acidic & favors to excretion of basic drugs.



Renal Excretion

Drugs excreted mainly by the kidney include:

- **Aminoglycosides antibiotics (Gentamycin).**
- **Penicillin.**
- **Lithium.**

These drugs are contraindicated (should NOT be used) **in:**

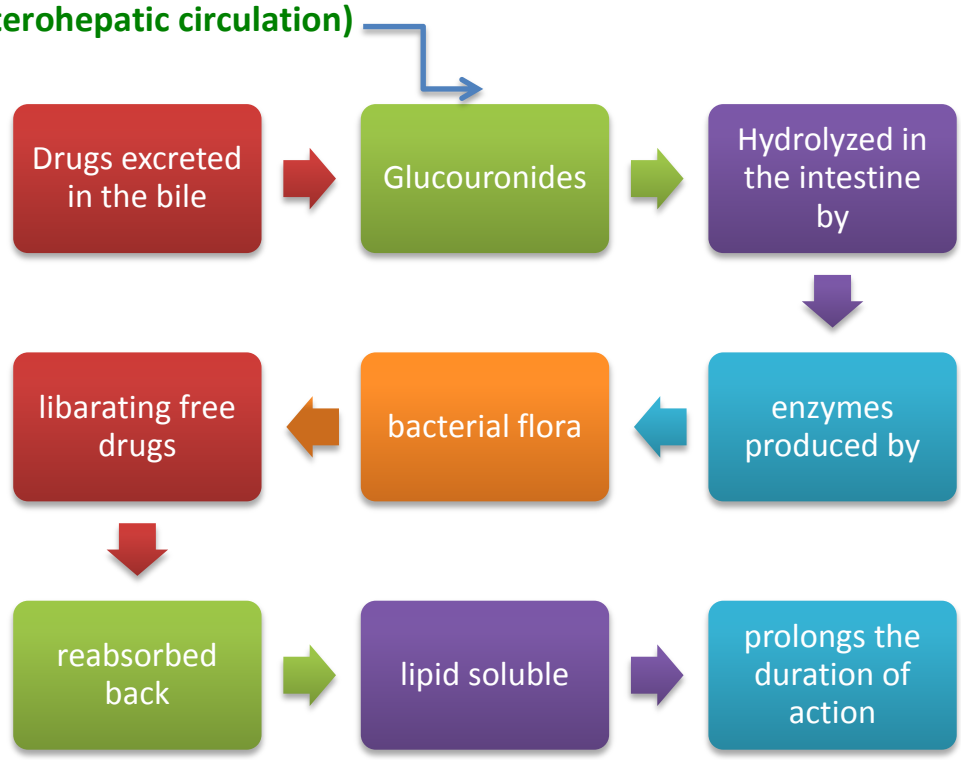
- **Renal disease.**
- **Elderly people.**

***Biliary excretion:**

Occurs to drugs that excreted into feces.

Such drugs are secreted from the liver into bile by active transporters then into duodenum.

Some drugs reabsorbed back into systemic blood circulation (Enterohepatic circulation)



***Plasma half-life (t1/2):**

- ✓ The time required to decrease the blood concentration of the drug by 50%.
- ✓ Determine the dosing interval.

Factors affecting Metabolism	Half-life (increased)
Age	Decreased metabolism **(liver disease)**
Nutrition	Decreased clearance: ***Renal disease** ***Congestive heart failure**
Genetic variation	
Gender	
Diseases	High binding of drugs: ***Plasma proteins** ***Tissue binding**
Degree of protein binding	
Enzyme induction and inhibition	
Route of drug administration	Enterohepatic recycling

***Steady state level:**

(Rate of drug administration = Rate of drug elimination).