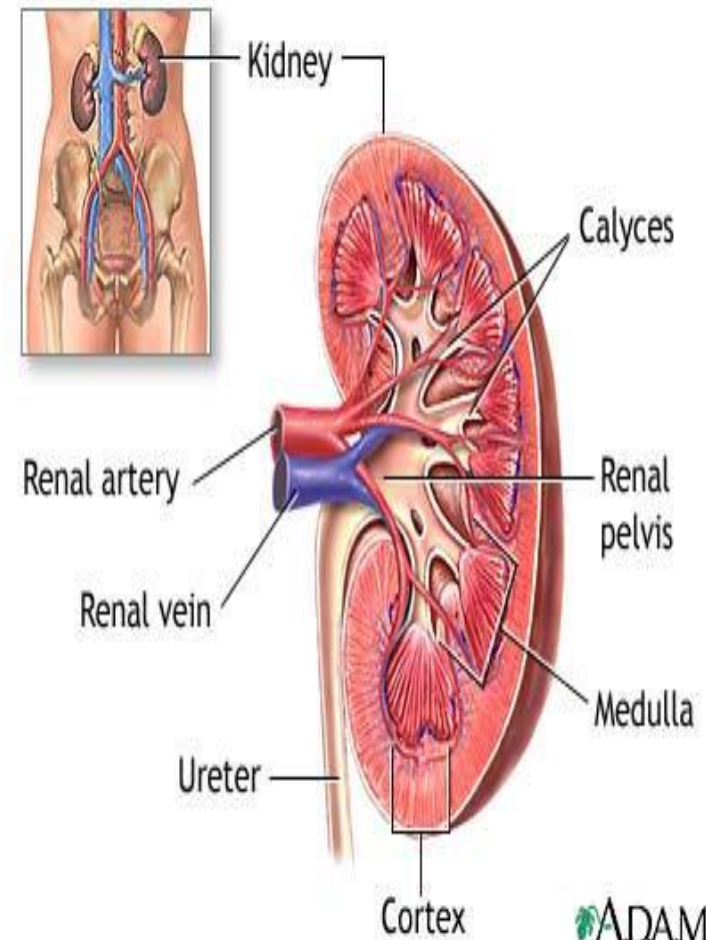


DIURETICS

Prof. Hanan Hagar
Pharmacology Unit

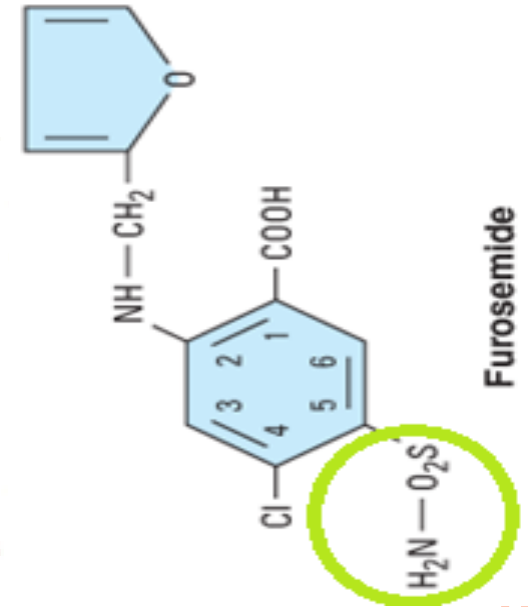
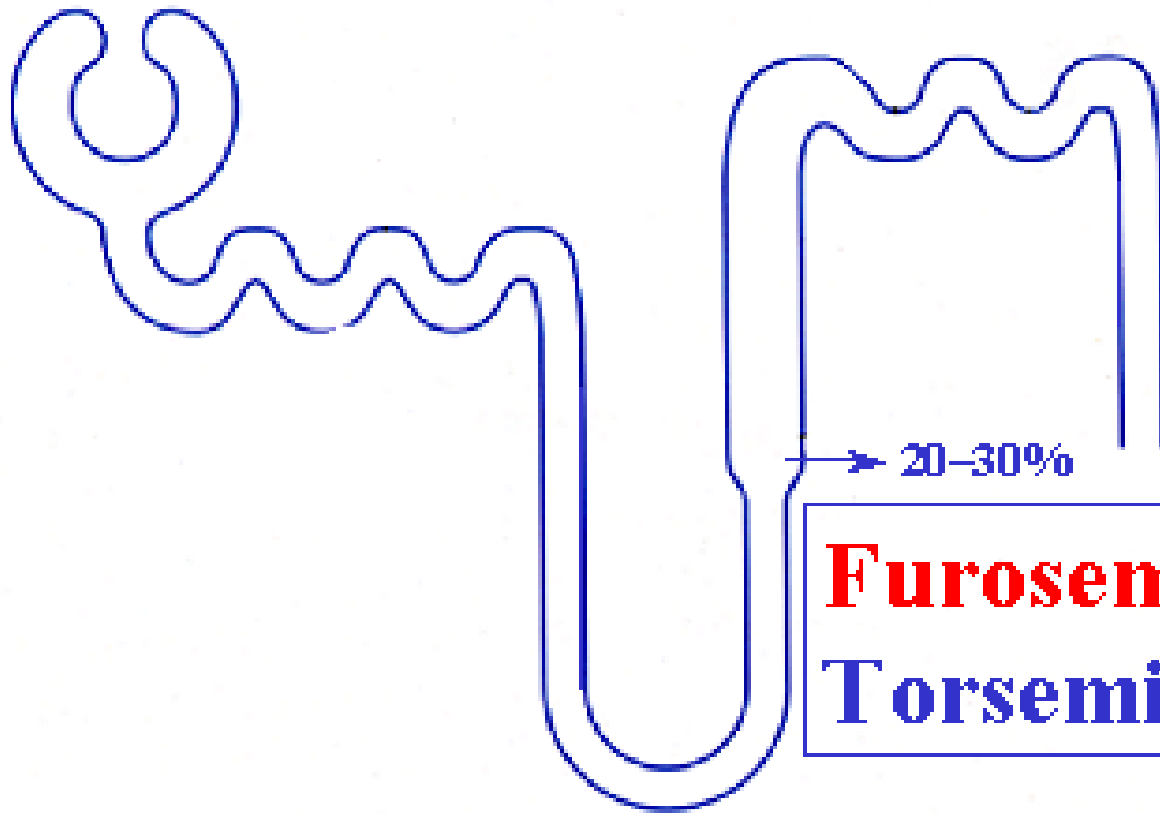


Classification of diuretics

- **Carbonic Anhydrase Inhibitors**
- **Loop Diuretics**
- **Thiazides**
- **Potassium-Sparing Diuretics**
- **Osmotic Diuretics**



Loop Diuretics



LOOP DIURETICS

High Ceiling diuretics

- The most potent diuretic , termed “**high ceiling diuretic**”

Efficacy: High natriuresis as 25-30% Na^+ is reabsorbed.

- **Drugs as:**

- Furosemide - Torsemide
- Bumetanide - Ethcryninc acid



Loop Diuretics

High Ceiling Diuretics

Bumetanide

Potency 40, $t_{1/2}$ 0.8 h

**Ethacrynic
Acid**

Potency 0.7, $t_{1/2}$ 1h

Furosemide

Potency 1, $t_{1/2}$ 1.5h

Torseamide

Potency 3, $t_{1/2}$ 3.5h



LOOP DIURETICS

Mechanism:

- inhibit $\text{Na}^+ / \text{K}^+ / 2 \text{Cl}^-$ co-transporter in the luminal membrane of the thick ascending loop of Henle (TAL).
- inhibit Ca^{++} and Mg^{++} re-absorption.



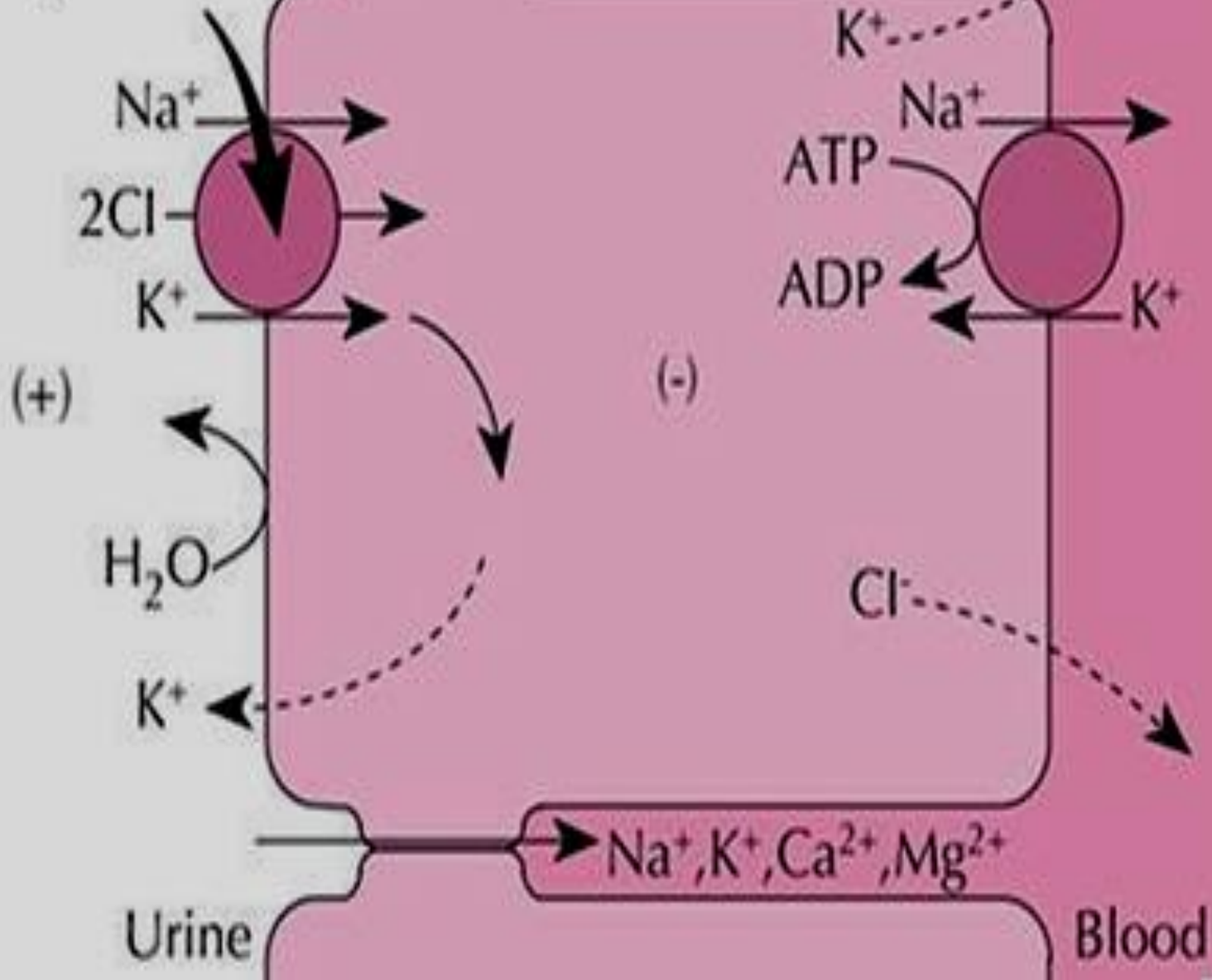
Ascending loop of Henle

- Is impermeable to water
- **In thick ascending loop of Henle (TAL)** is responsible for active re-absorption of Na, K and Cl (**25-30% Na⁺ is reabsorbed**) via transport system in luminal membrane called **Na⁺/ K⁺ / 2Cl⁻ co-transporter**
- Ca and Mg are reabsorbed and enter the interstitial fluid via paracellular pathway

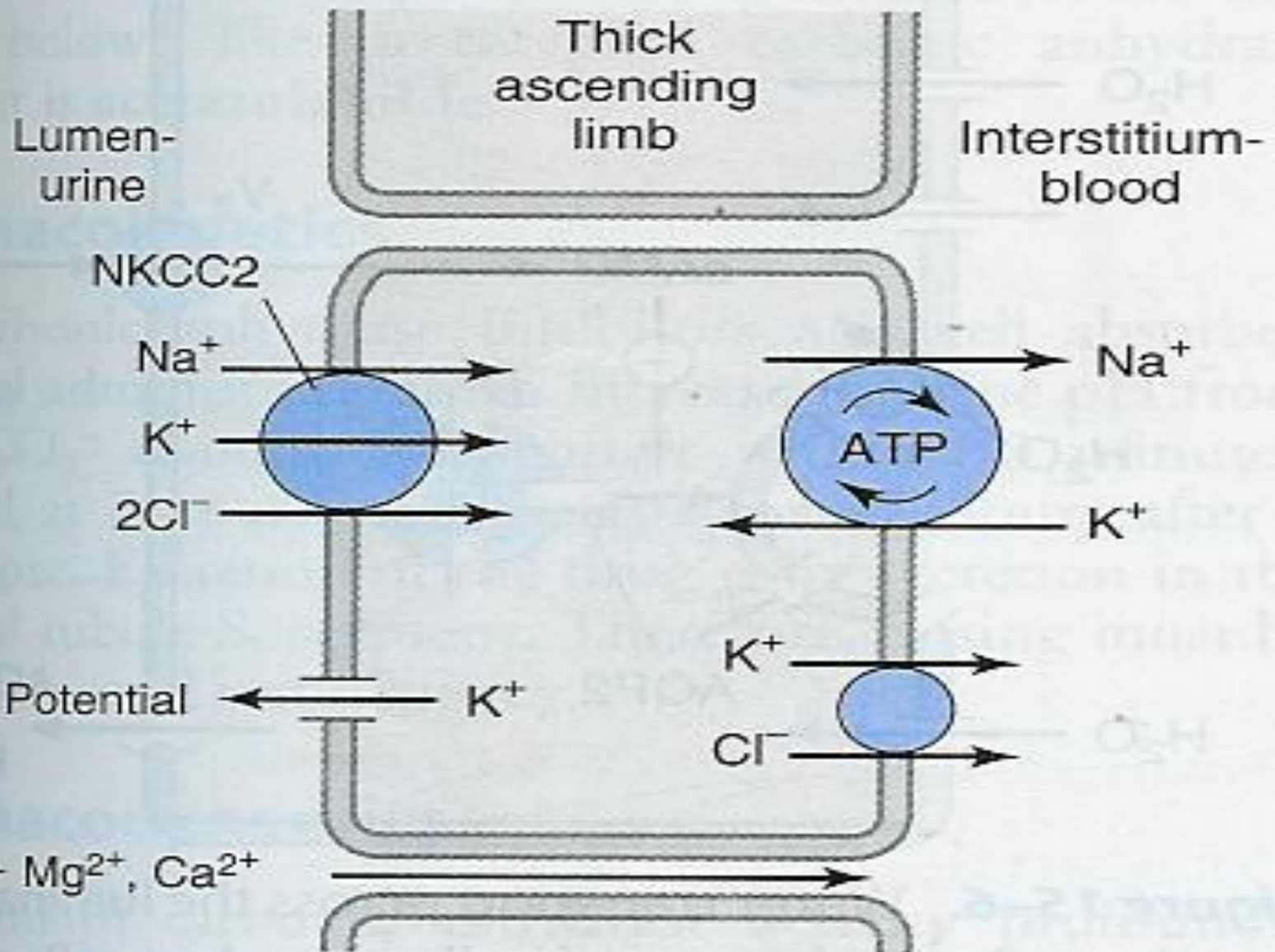


Ascending loop of Henle

Loop diuretics



ASCENDING LOOP OF HENLE



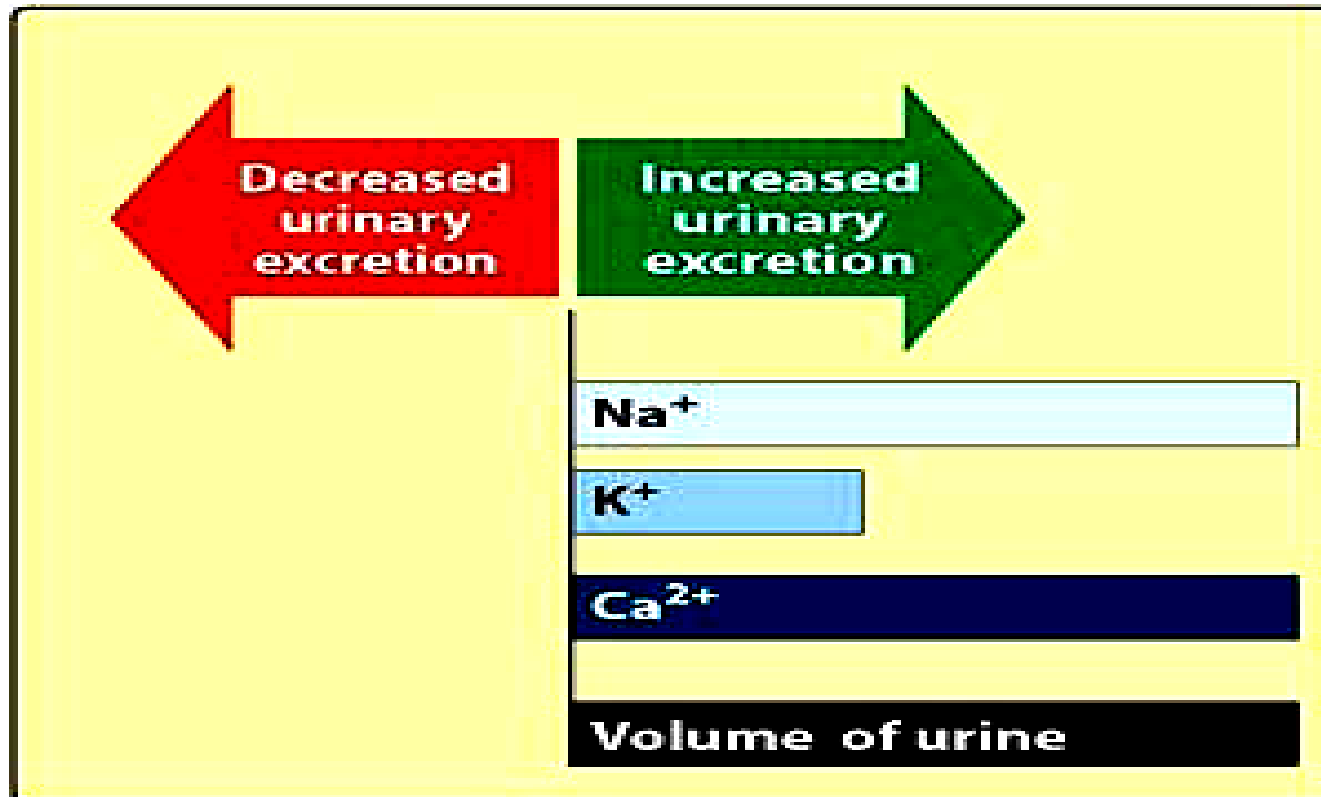
Pharmacokinetics

- Given orally or I. V.
- Have fast onset of action (suitable for emergency)
- Have short duration of action.
- Excreted by active tubular secretion of weak acids into urine
- Interfere with uric acid secretion (hyperuricemia).



Pharmacological effects:

- ↑ urinary excretion of Na^+ and K^+
- ↑ urinary excretion Ca^{++} and Mg^{++}
- ↑ urine volume
- ↑ renal blood flow.



Uses:

are drug of choice for emergency situations as:

- Edema associated with congestive heart failure, nephrotic syndrome
- **Acute** pulmonary edema
- **Acute** hyperkalaemia.
- **Acute** hypercalcemia



ADVERSE EFFECTS

**Volume
Depletion**

Hypokalemia

Hypocalcaemia

Hypomagnesaemia



**Metabolic
Alkalosis**

Ototoxicity

Hyperuricemia

Hyperglycemia



Adverse effects :

- Hypovolemia
- Hyponatraemia (\downarrow blood Na^+).
- Hypokalemia (\downarrow blood K^+)
- Hypomagnesaemia (\downarrow blood Mg^{2+})
- Hypocalcaemia (\downarrow blood Ca^{2+})
- Metabolic alkalosis.
- Postural hypotension
- Dietary K supplementation or K-sparing diuretics should be used to avoid hypokalemia .



Adverse effects :

- **Hyperuricemia** (*increase blood uric acid and gouty attack*).
- **Ototoxicity** (*risk increased if combined with aminoglycosides*)
- **Allergic reactions**

