DIURETICS

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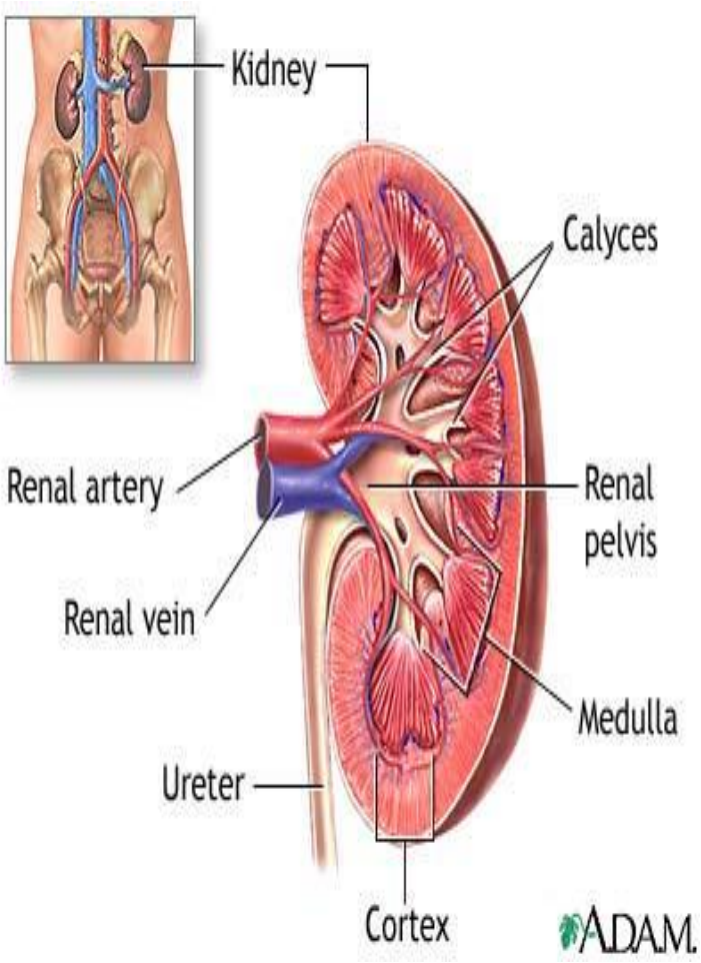
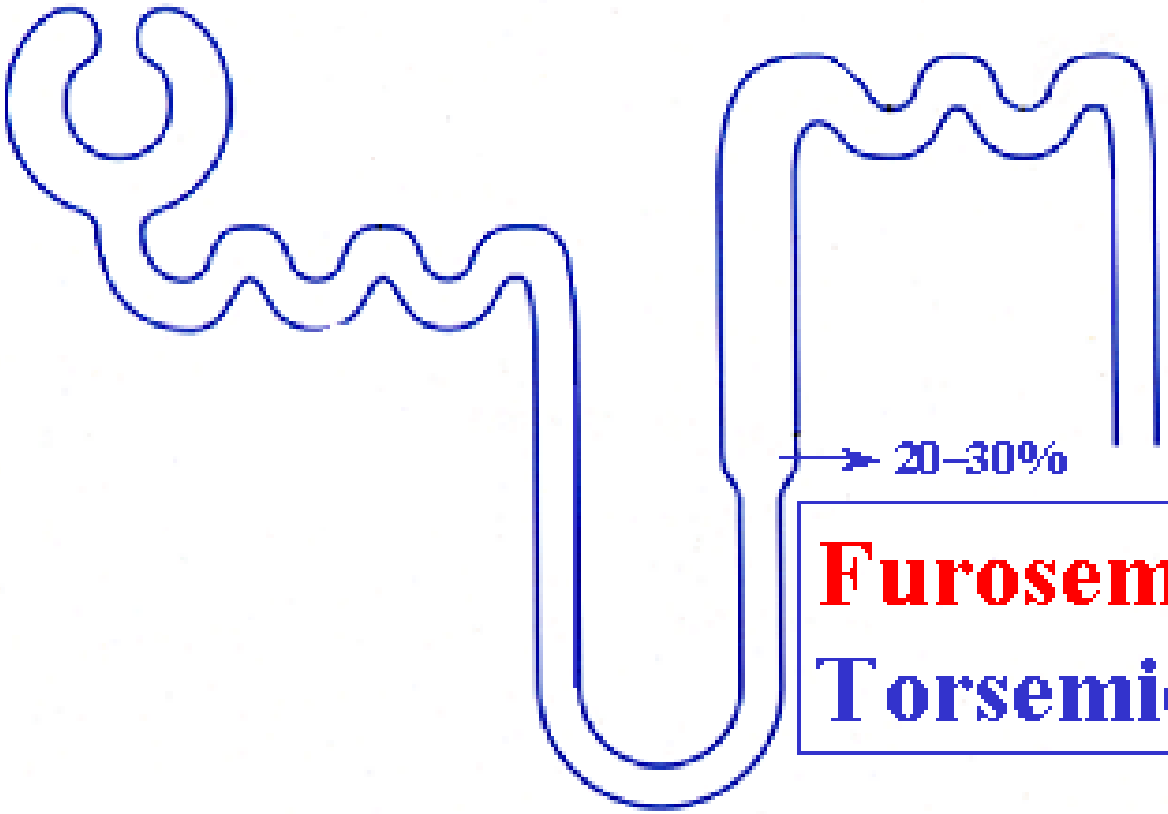


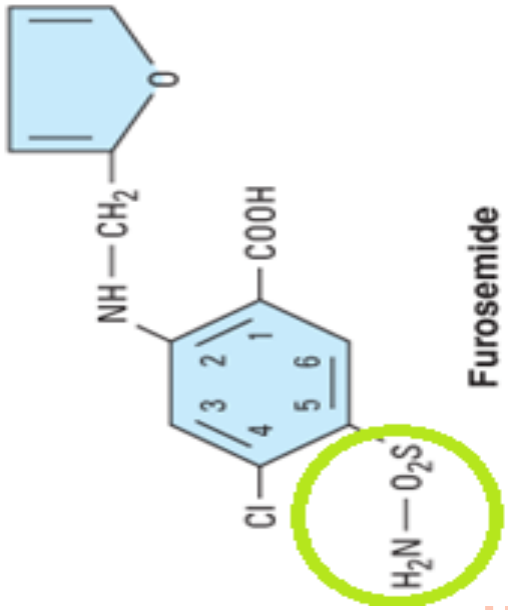
Classification of diuretics

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

Loop Diuretics



Furosemide
Torsemide



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 - Ethcrynic acid

Loop Diuretics
High Ceiling Diuretics

Bumetanide
Potency40 ,t½ 0.8 h

Ethacrynic Acid
Potency 0.7, t½ 1h

Furosemide
Potency 1, t½ 1.5h

Torsemide
Potency 3, t½ 3.5h

LOOP DIURETICS

Mechanism:

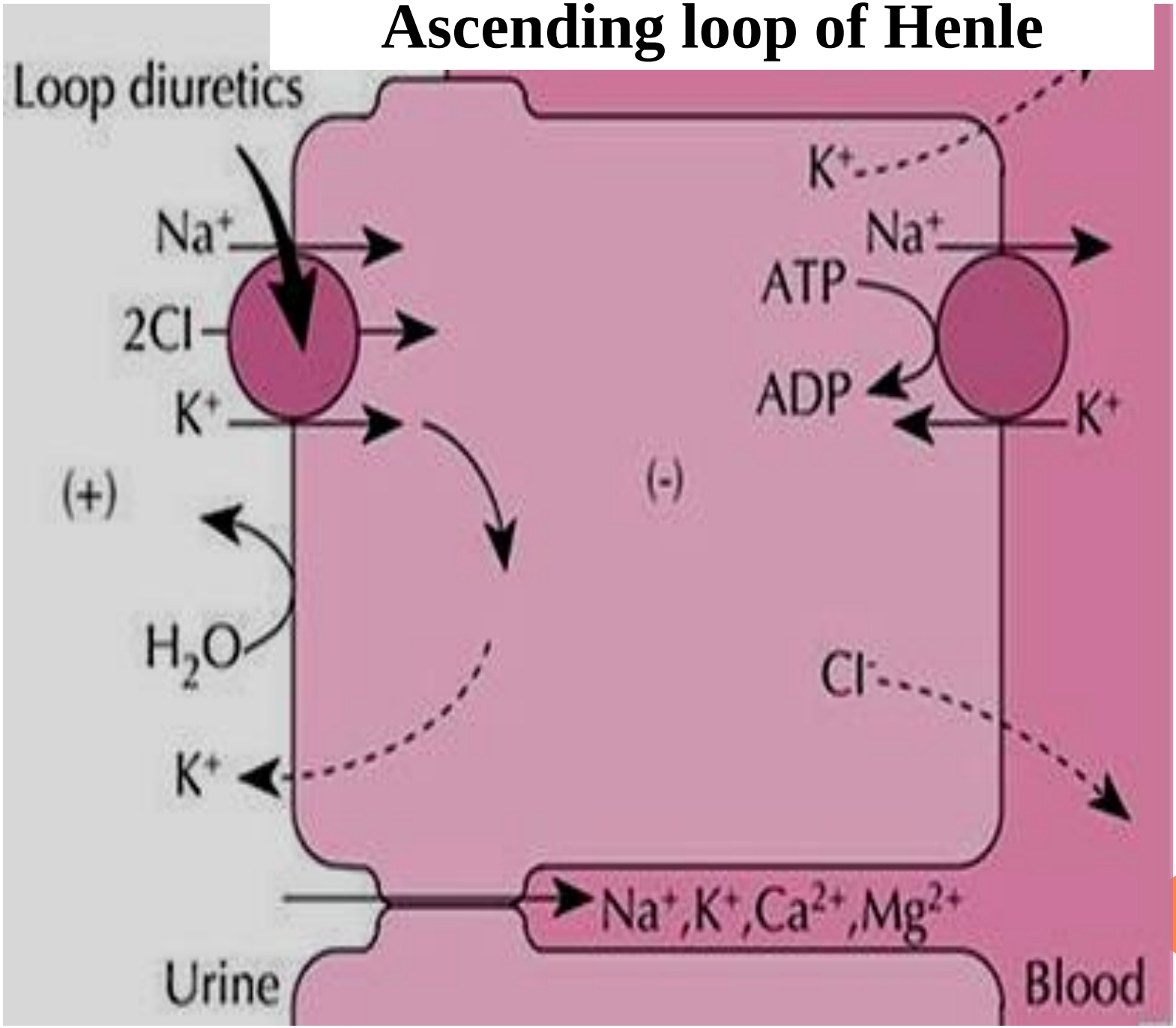
- inhibit Na^+ / K^+ / 2 Cl^- co-transporter in the luminal membrane of the thick ascending loop of Henle (TAL).
- inhibit Ca^{++} and Mg^{++} re-absorption.

Ascending loop of Henle

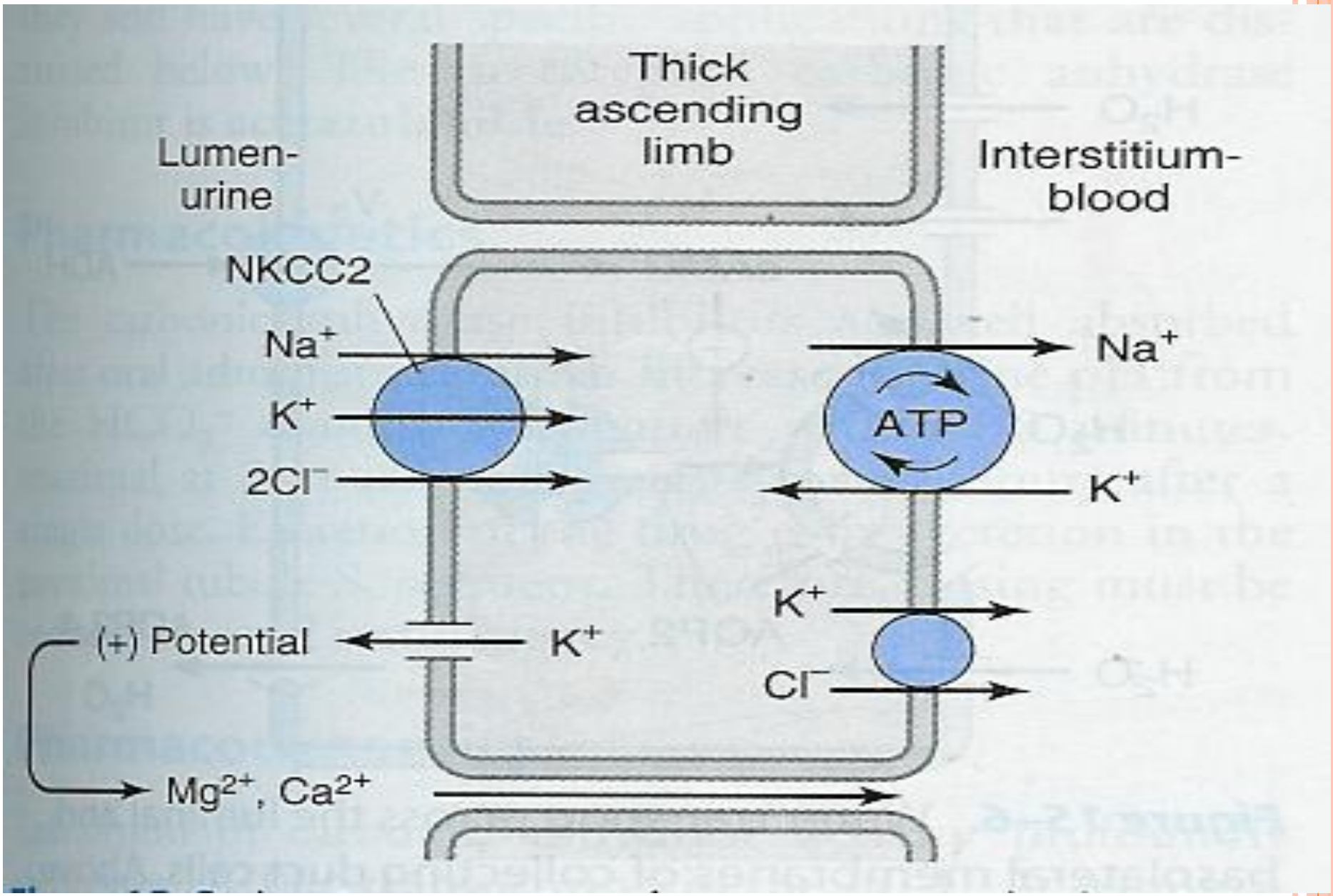
- Is impermeable to water
- **In thick ascending loop of Henle (TAL)** is responsible for active re-absorption of Na, K and Cl **(25-30% Na^+ is reabsorbed)** via transport system in luminal membrane called **Na^+/ K^+ / $2Cl^-$ co-transporter**

- Ca and Mg are reabsorbed and enter the interstitial fluid via paracellular pathway

Ascending loop of Henle



Ascending loop of Henle

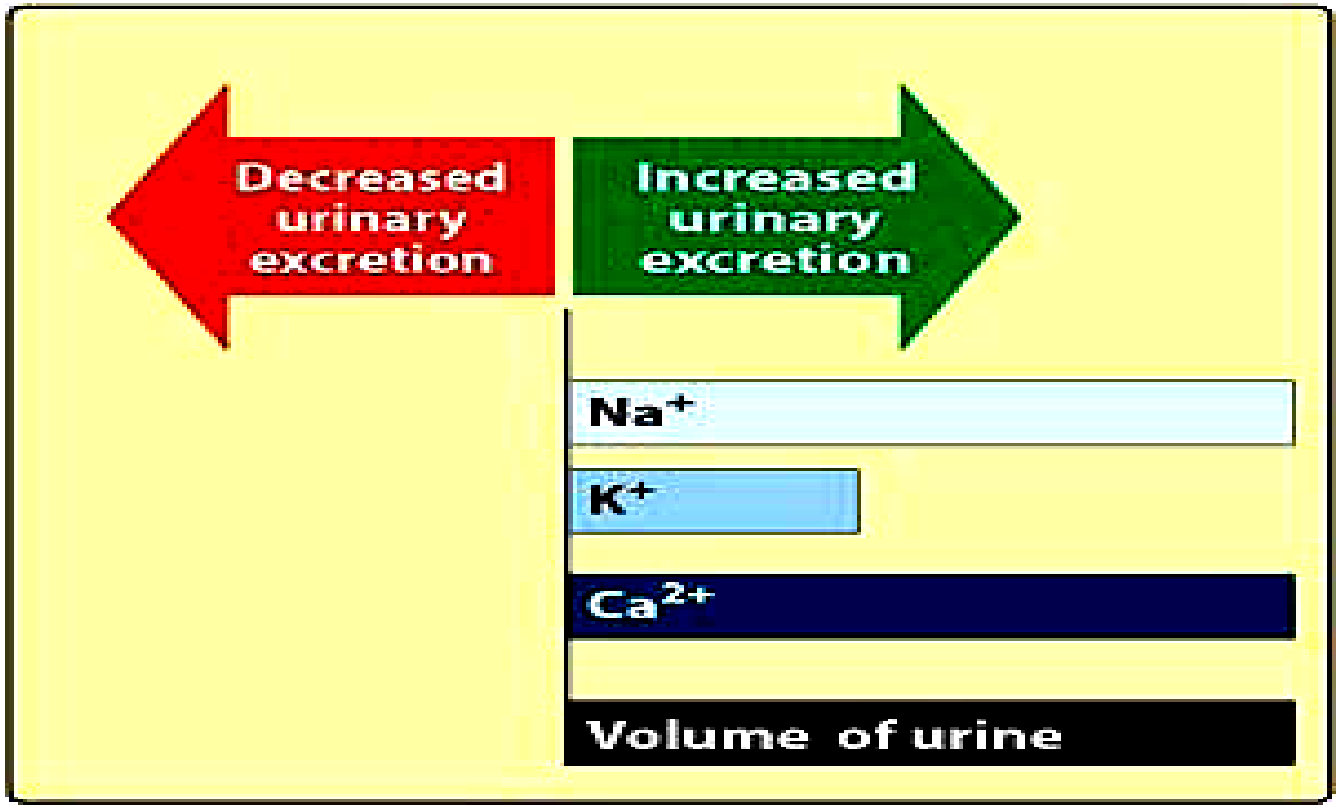


Pharmacokinetics

- 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

LOOP DIURETICS

DRUG- DRUG INTERACTIONS

NSAIDS → ↓Diuretic Response

Digitalis → Arrhythmias

Aminoglycosides → ↑ Ototoxicity of Loop Diuretic

Adverse effects :

- **Hypovolemia**
- **Hyponatraemia (↓ blood Na^+).**
- **Hypokalemia (↓ blood K^+)**
- **Hypomagnesaemia (↓ blood Mg^{2+})**
- **Hypocalcaemia (↓ 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**

Thiazide diuretics

Drugs as:

- **Chlorothiazide**
- **Hydrochlorothiazide**
- **Chlorthalidone**
- **Metolazone**
- **Indapamide**

THIAZIDE DIURETICS

Chlorothiazide
Potency 0.1, t½ 2h

Chlorthalidone
Potency 10, t½ 26h

Metolazone
Potency 5, t½ 5h

Hydrochlorothiazide
Potency 1 , t½ 3h

Indapamide
Potency 20, t½ 16h

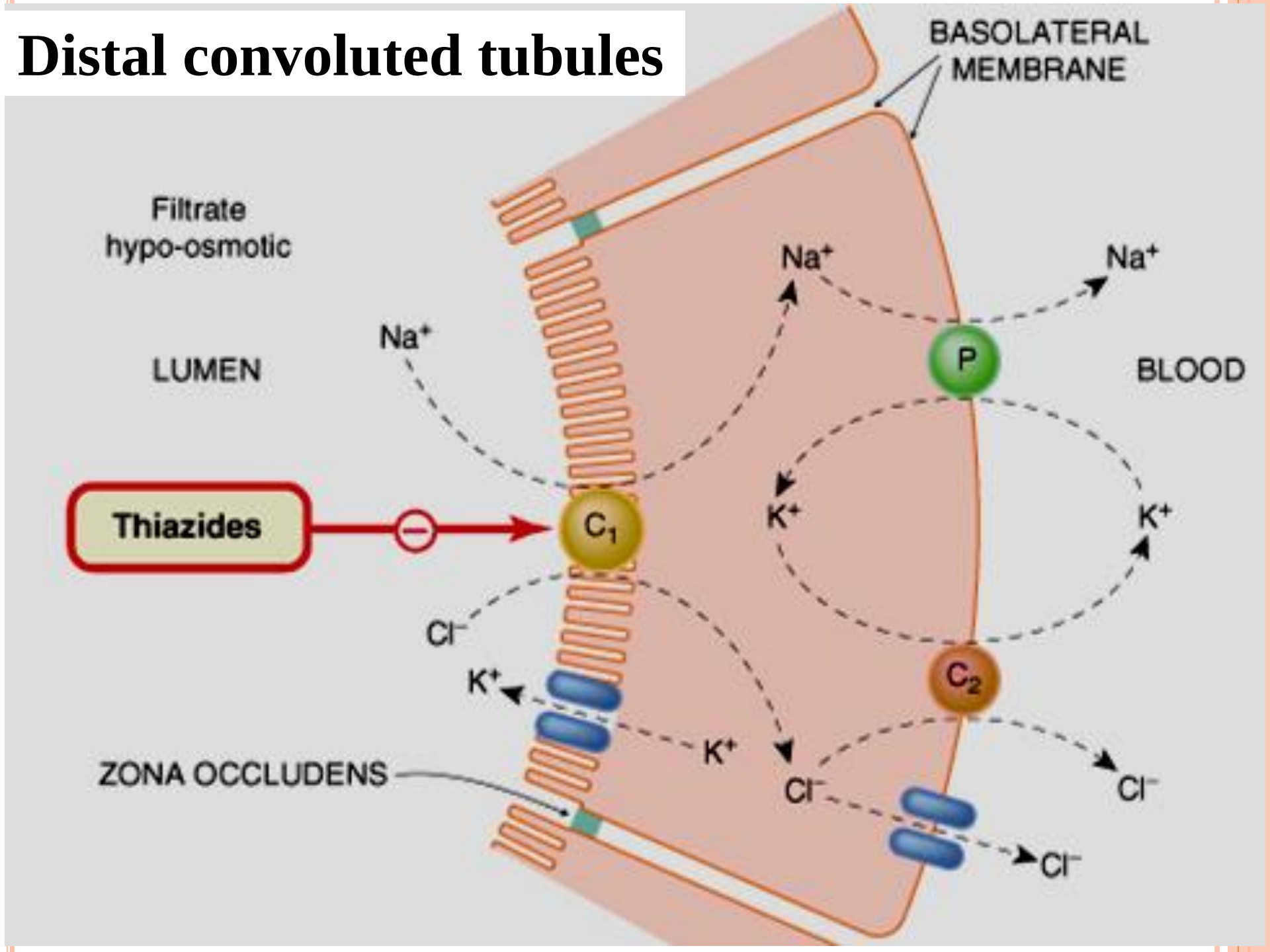
Thiazide diuretics

Mechanism of action:

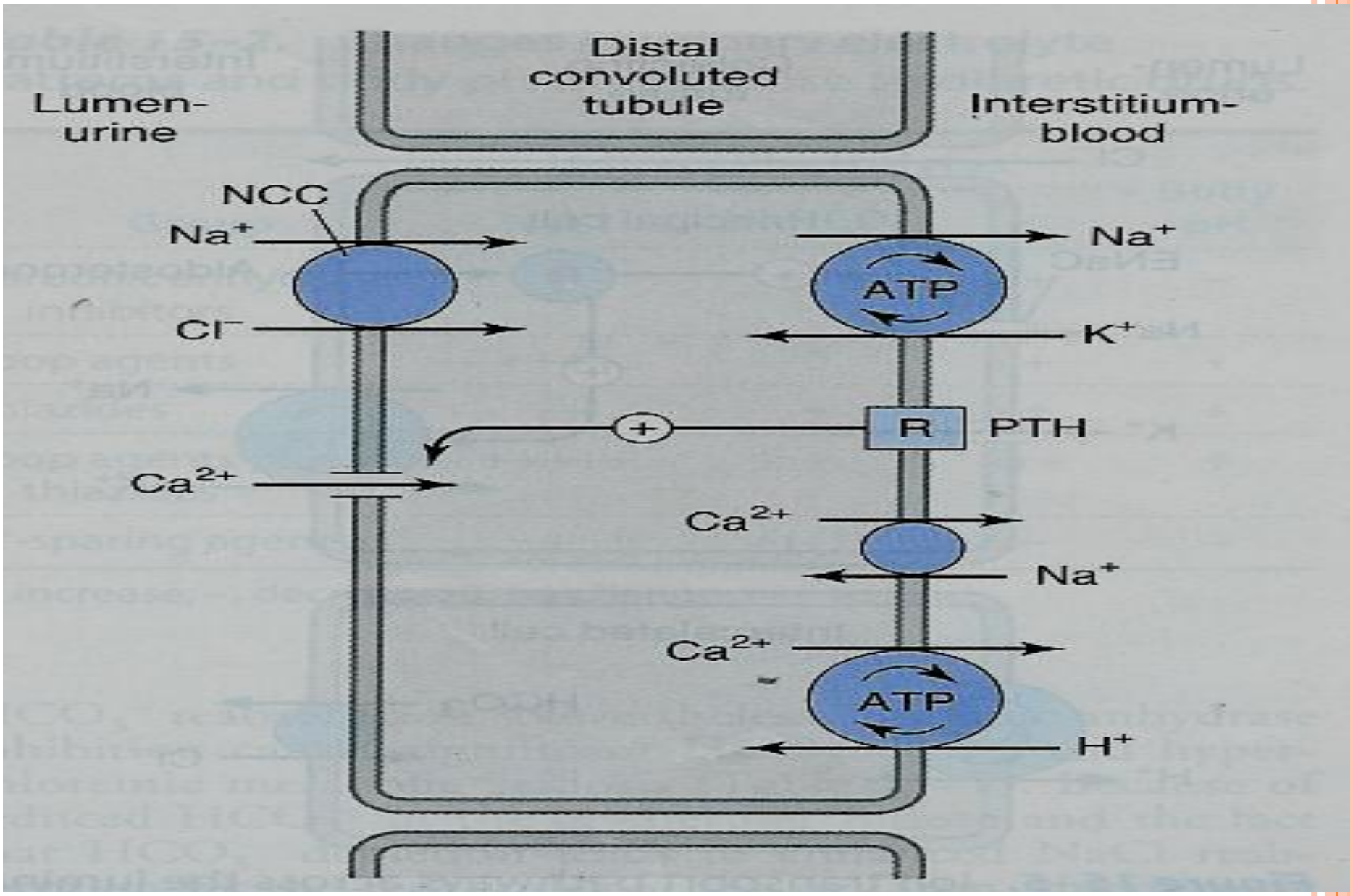
- **acts via inhibition of Na/Cl co-transporter on the luminal membrane of distal convoluted tubules.**

- Efficacy: **Moderate natriuresis (5-10% of filtered load of sodium is reabsorbed).**

Distal convoluted tubules



Mechanism of action of thiazide diuretics



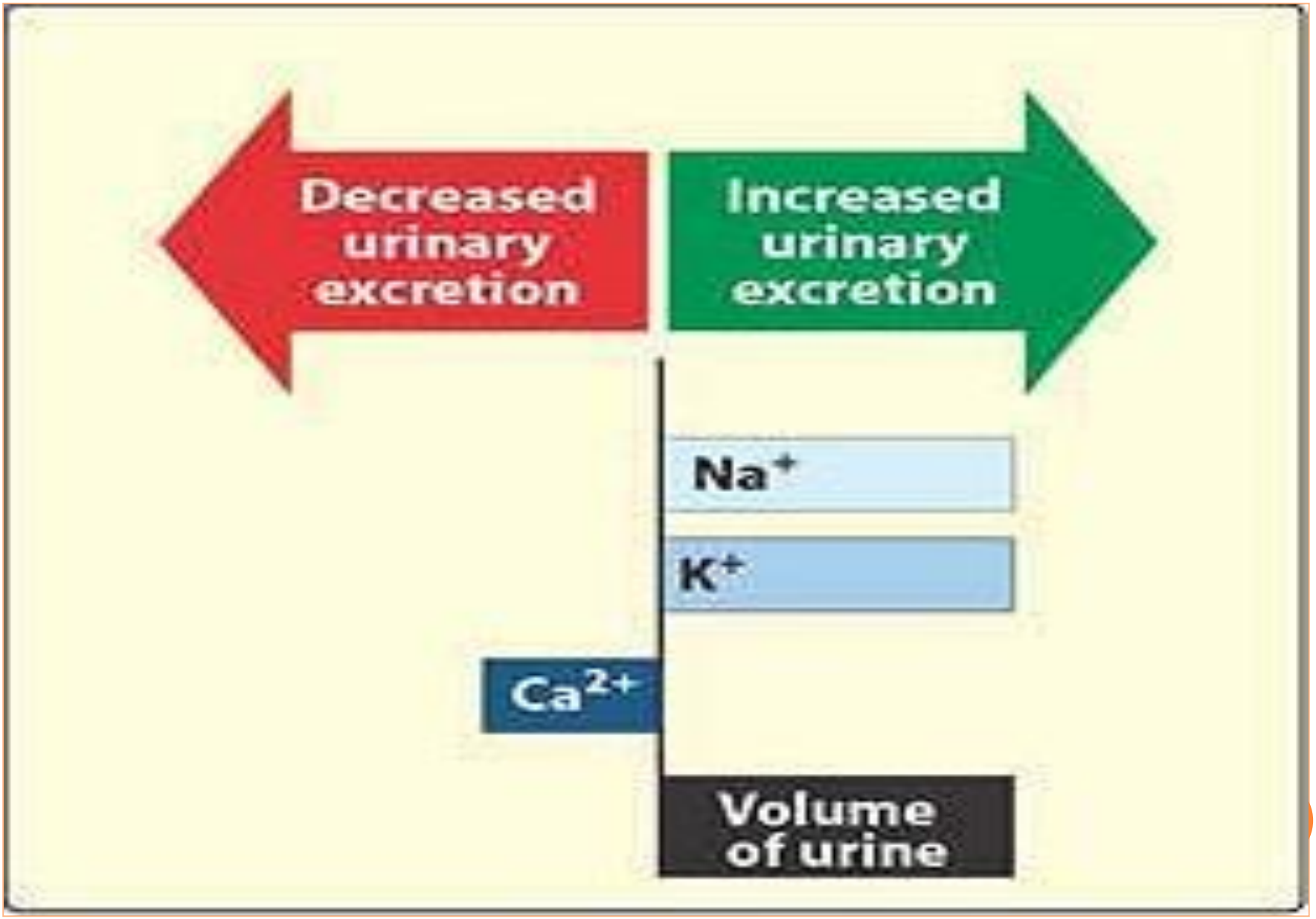
Pharmacokinetics:

- Given orally, slow of onset
- long duration of action (40 h)
- are secreted by active tubular secretory system of the kidney
- may interfere with uric acid secretion and cause *hyperuricemia*

Pharmacological effects:

- ↑ urinary NaCl excretion
- ↑ urinary K excretion **(Hypokalemia)**
- ↑ urinary magnesium excretion
- ↓ urinary calcium excretion
- ↑ calcium re-absorption **hypercalcemia**

Thiazide diuretics



Uses:

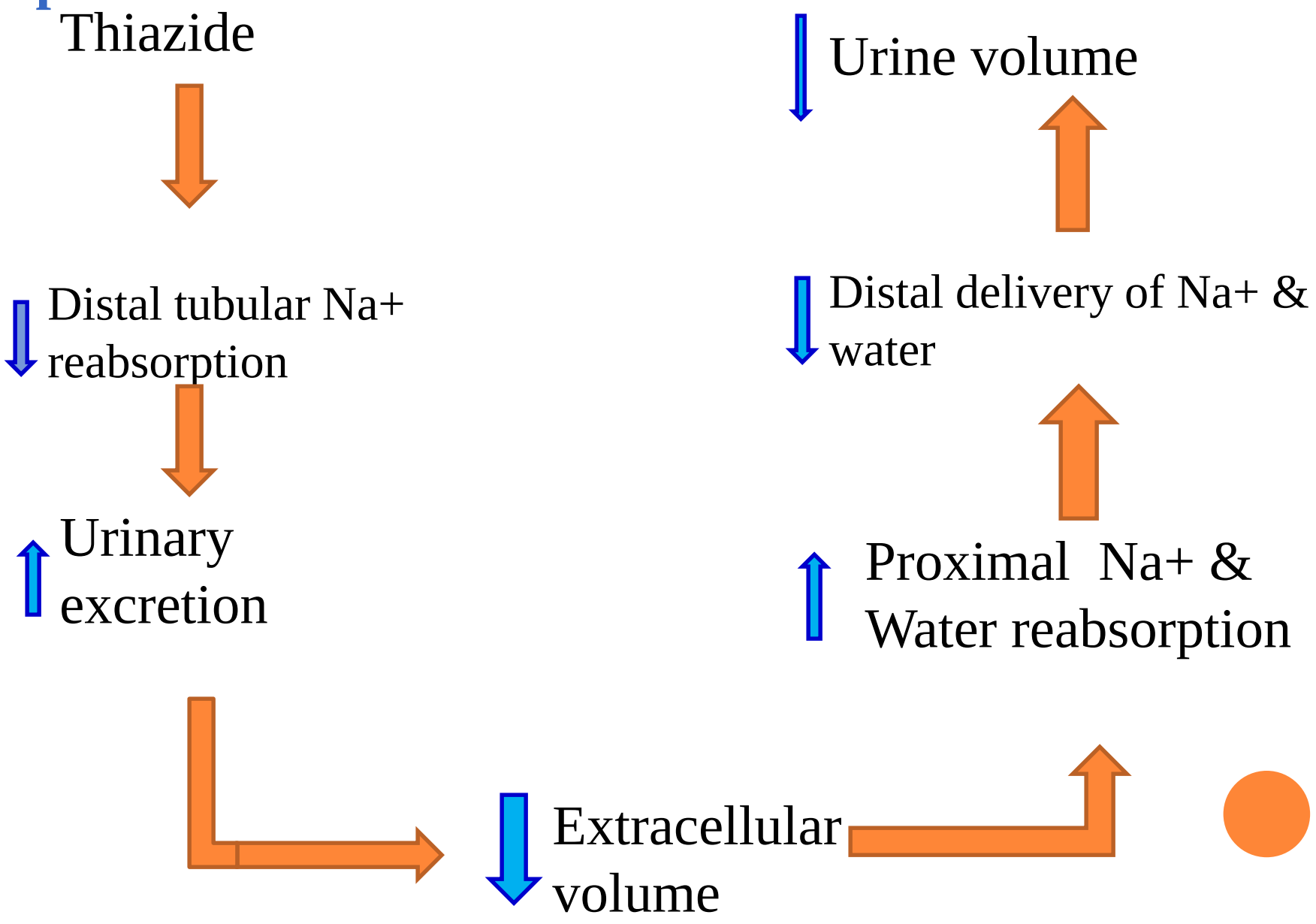
- **Treatment of essential hypertension *(cheap-well tolerated).***
- **Treatment of mild heart failure *(to reduce extracellular volume).***
- **Treatment of osteoporosis**

Uses:

- **Calcium nephrolithiasis due to hypercalciuria *(to increase calcium re-absorption and decrease renal calcium stones)***

- **Nephrogenic diabetes insipidus *(decrease blood volume and GFR)***

Mechanism of antidiuretic effect of thiazide in diabetes insipidus



Adverse effects:

- Fluid and electrolyte imbalance
- Hyponatremia
- Hypovolemia (volume depletion)
- Hypokalemia
- Metabolic alkalosis.
- Hyperuricaemia (gout)
- Hypercalcemia
- Hyperglycaemia
- Hyperlipidemia

ADVERSE EFFECTS

Volume Depletion

Metabolic Alkalosis

Hypokalemia

Hypocalcaemia

Hyperuricemia

Hypomagnesaemia

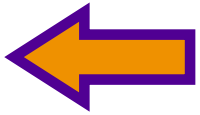
Hyperglycemia

Hyperlipidemia

THIAZIDE DIURETICS

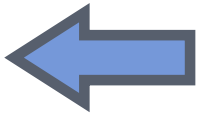
DRUG- DRUG INTERACTIONS

Uricosurics
Sulphonylurea



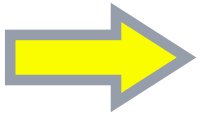
Thiazides
Diminish
effect

Digitalis
Diazoxide



Thiazides
Increase effect

NSAIDs



Reduce thiazide
efficacy