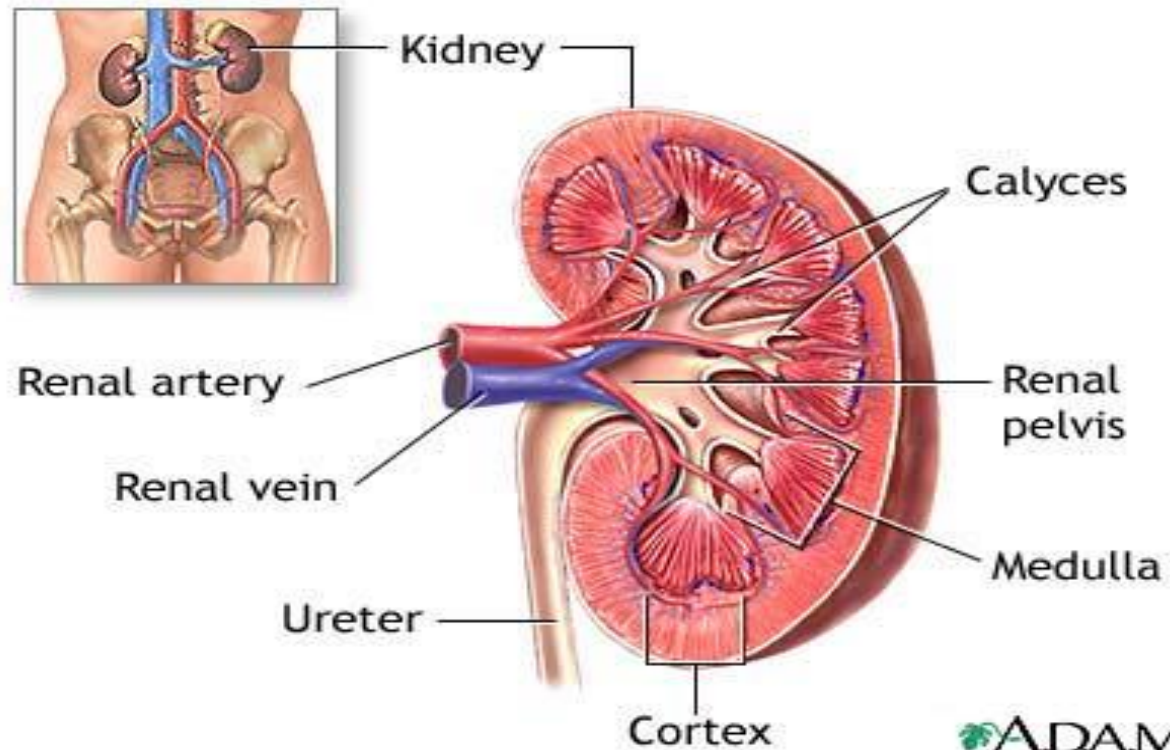


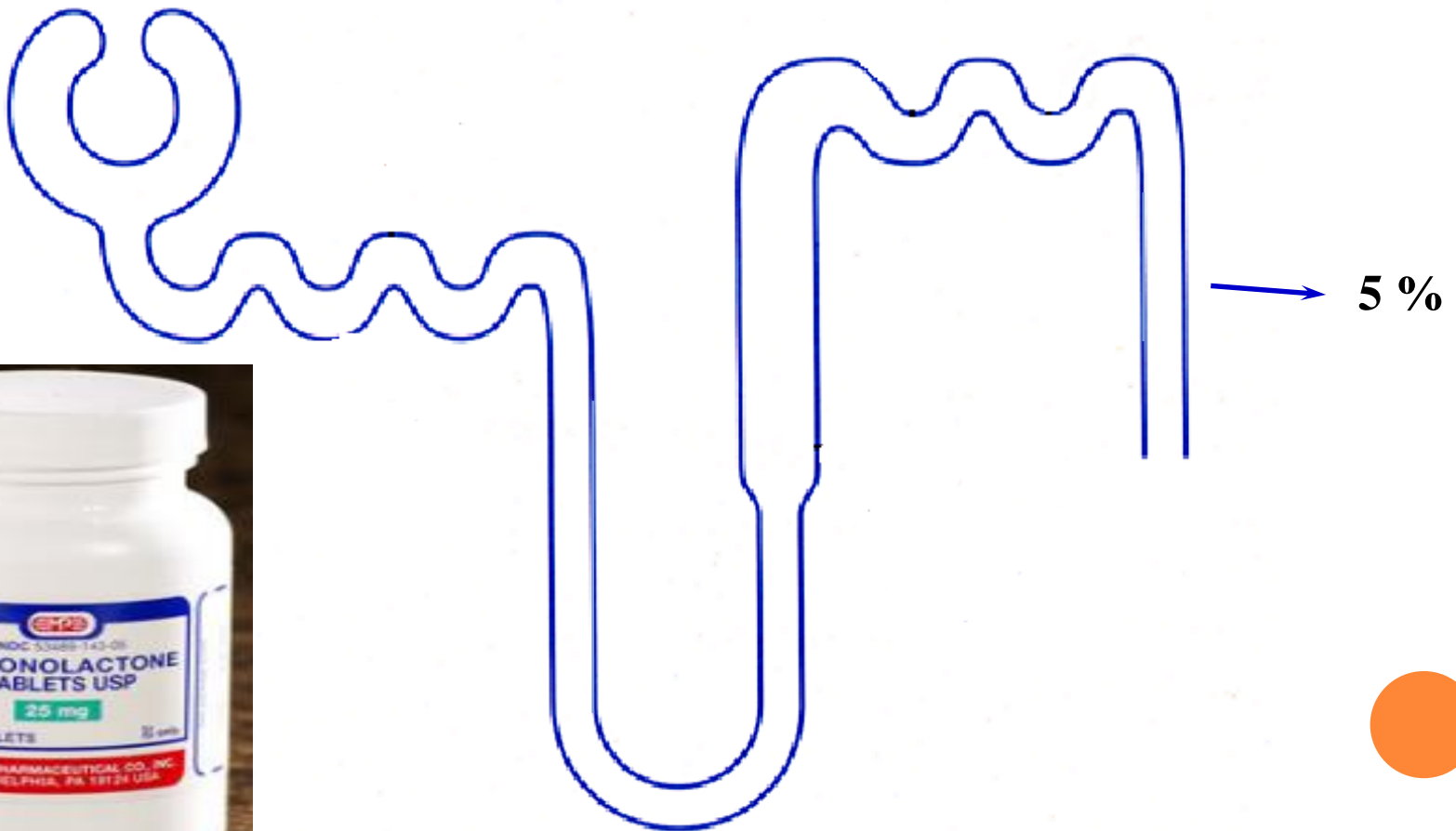
DIURETICS

Prof. Hanan Hagar
Pharmacology Unit



Potassium-sparing diuretics

Amiloride
Triamterene
Spironolactone



Potassium-sparing diuretics

Steroids

Competitive aldosterone antagonists

- **Spirolactone**

Nonsteroids

Na⁺ channels inhibitors

- **Amiloride**
- **Triamterene**

Aldosterone Antagonists

Also Called:

- K-Sparing Diuretics
- Mineralocorticoid receptor antagonists



Spironolactone

Eplerenone

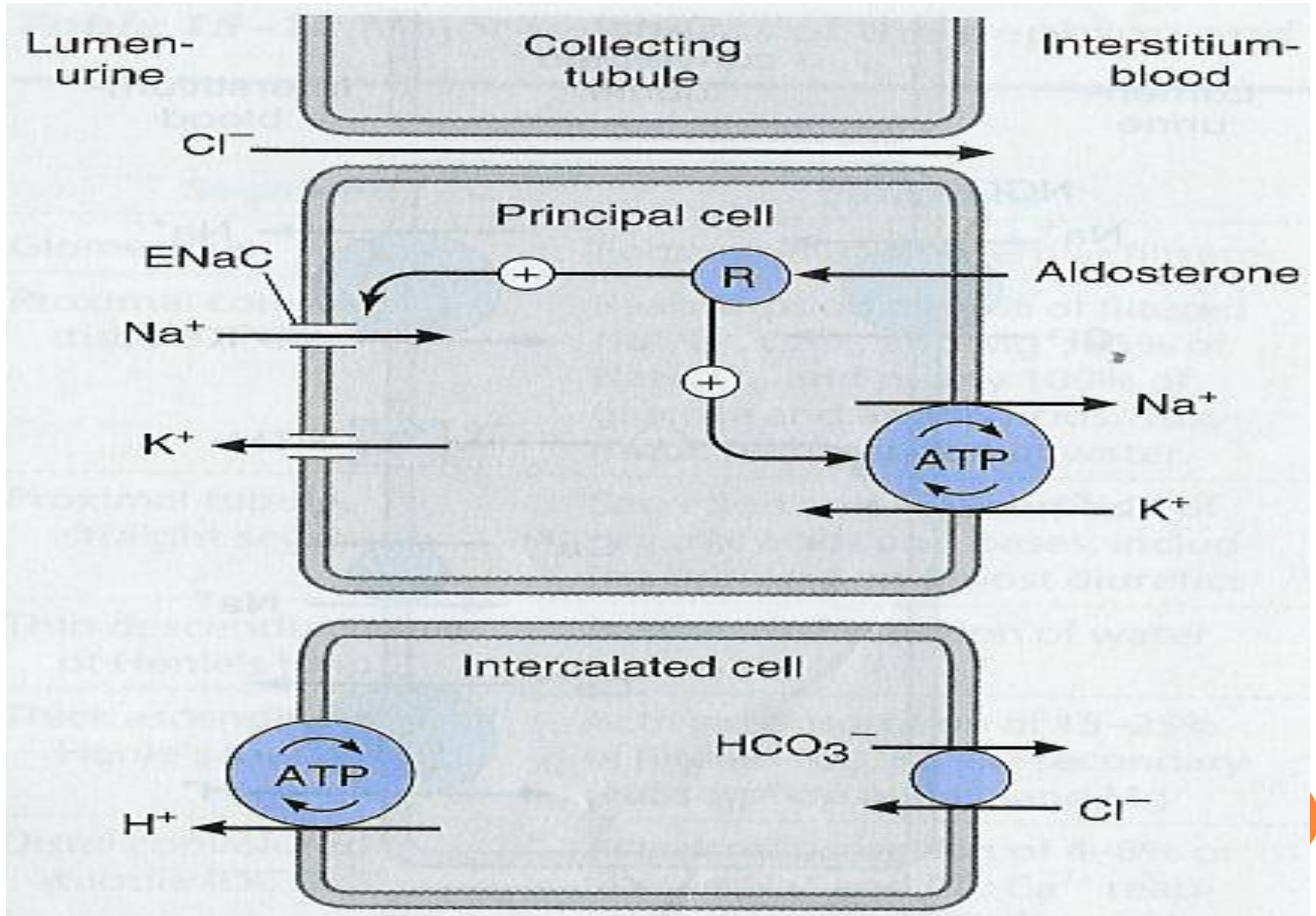
Mechanism of action

Spironolactone:

act at the collecting duct by
competitive inhibition of cytoplasmic
aldosterone receptors \rightarrow \uparrow Excretion of
 Na^+ , Cl^- & \downarrow Excretion of K^+ , H^+



COLLECTED TUBULES (CT)



Pharmacokinetics of spironolactone

- Well absorbed from the GIT , $t_{1/2}=1.6\text{h}$
- Highly protein-bound
- Undergoes enterohepatic recycling
- Delayed onset of action (nuclear receptor), maximum diuretic action 4 days.
- Converted in gut & liver to active metabolite, $t_{1/2}=16\text{h}$]



Pharmacodynamics:

- **↑** urinary Na^+ excretion
- **↓** urinary K^+ excretion **Hyperkalemia**
- **↓** H^+ excretion (**acidosis**).
- has antiandrogenic action.



Therapeutic uses:

- **Treatment of hypertension**

Usually used combined with thiazide or loop diuretics to:

- **Enhances natriuresis caused by other diuretics**
- **Correct for hypokalemia.**



Therapeutic uses of aldosterone antagonists:

- **Treatment of primary hyperaldosteronism**
(Conn's syndrome)
- **Treatment of secondary hyperaldosteronism in diseases as**
 - **CHF**
 - **Edema of hepatic cirrhosis**
 - **Nephrotic syndrome**

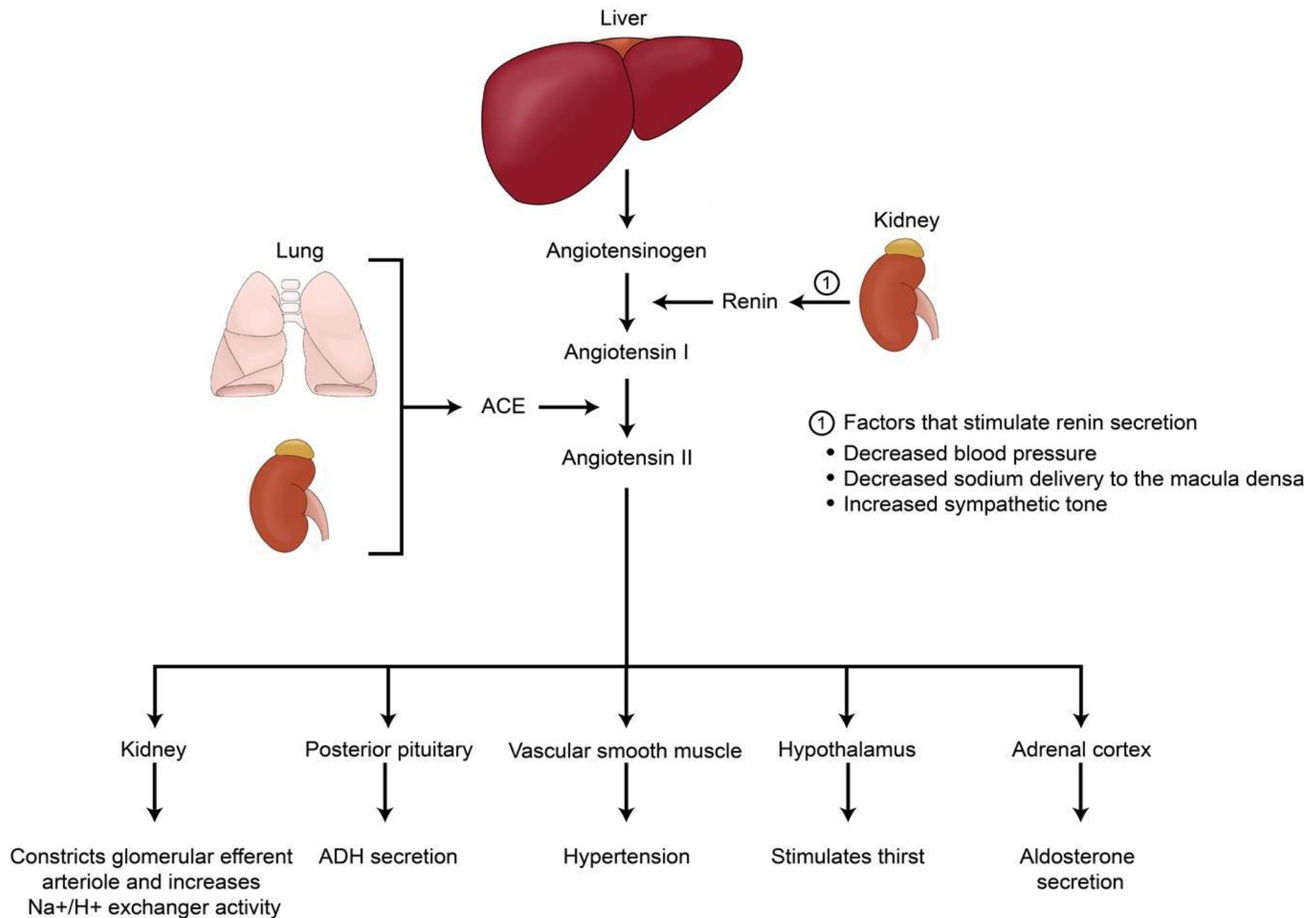


Therapeutic uses of aldosterone antagonists:

- **Treatment of hirsutism, acne due to the antiandrogenic effects.**

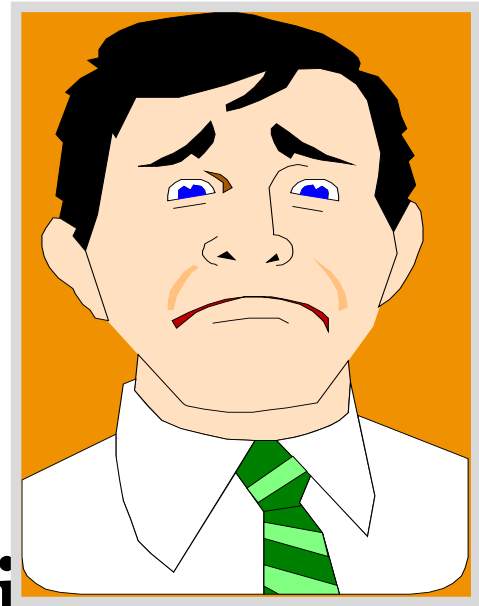


Renin-Angiotensin-Aldosterone System



Adverse Effects

- **Hyperkalaemia.**
- **Metabolic acidosis.**
- **Gynecomastia**
- **Impotence**
- **Menstrual irregularities**
- **GIT upset and peptic ulcer**



Contraindications:

○ Hyperkalaemia:

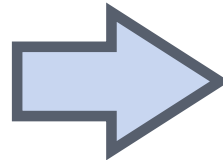
- chronic renal failure
- K⁺ supplement use
- β-blockers
- ACE inhibitors.

- **Liver disease** (dose adjustment is needed).



Drug -Drug Interactions

**ACE Inhibitors
Beta-Blockers
K Supplements
K-Sparing
Diuretics
Aliskiren**



**↑Hyperkalemia-
induced by
K-Sparing
diuretics**

Potassium-sparing diuretics

Na⁺ channels inhibitors

- **Amiloride**
- **Triamterene**



SODIUM CHANNEL INHIBITORS

Triamterene
Potency 0.1,
 $t^{1/2}$ 4.2 h,

Amiloride
Potency 1,
 $t^{1/2}$ 21h,

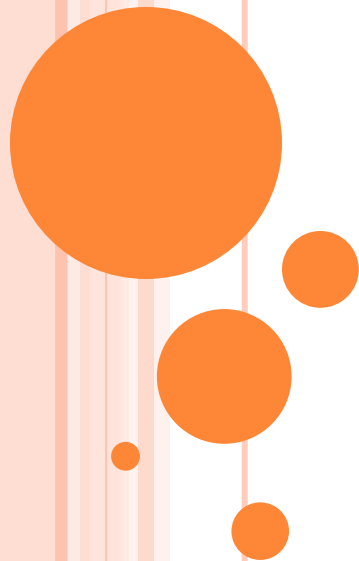
Mechanism of action

- Inhibition of Na influx through directly blockade of the epithelial sodium channel (ENaC) on the lumen side of the kidney collecting tubule (triamterene – amiloride).



USES OF SODIUM CHANNEL INHIBITORS

- Used in Combination with Loop & Thiazide Diuretics
- Treatment for lithium-Induced Diabetes Insipidus



ADVERSE EFFECTS OF SODIUM CHANNEL INHIBITORS

Triamterene

Hyperkalemia

Renal stones

Amloride

Hyperkalemia

CONTRAINDICATIONS OF SODIUM CHANNEL INHIBITORS

Triamterene & amiloride

The risk of developing **hyperkalemia** is increased in patients who are also on ACE inhibitors, angiotensin II receptor antagonists, other potassium-sparing diuretics, or any potassium-containing supplements.

Therapeutic applications of diuretics

Treatment of hypertension:

- o Thiazide diuretics
- o used alone or in combination with beta-blockers at low-dose (fewer side effects)
- o In presence of renal failure, loop diuretic is used.



Therapeutic applications of diuretics

Edema States

- Thiazide diuretic is used in mild edema with normal renal function
- Loop diuretics are used in cases with impaired renal function.



Congestive Heart failure

- Thiazides may be used in only mild cases with well-preserved renal function
- Loop diuretics are much preferred in severe cases especially when GF is lowered
- In life-threatening acute pulmonary edema, furosemide is given IV.



Renal failure

- Thiazides are used till $\text{GFR} \geq 40\text{-}50$ ml/min
- Loop diuretic are used below given values, with increasing the dose as GFR goes down.

Diabetes inspidus

Large volume (>10 L/day) of dilute urine
thiazide diuretics reduces urine volume

Hepatic cirrhosis with ascites

- Spironolactone is of choice.



Diuretics	Mechanism of action	Effects
CA inhibitors Acetohexamide Dorzolamide	Inhibition of NaHCO_3 reabsorption in PCT	\uparrow Urinary Na HCO_3 , K Urinary alkalosis Metabolic acidosis
Osmotic diuretic Mannitol	Osmotic effect in PCT	\uparrow Urine excretion \uparrow Little Na
Loop diuretics Furosemide	Na/K/2Cl transporter in TAL the most effective	\uparrow Urinary Na, K, Ca, Mg
Thiazide diuretics hydrochlorothiazide	Na and Cl cotransporter in DCT	\uparrow Urinary Na, K, Mg BUT \downarrow urinary Ca (hypercalcemia) Metabolic alkalosis
K-sparing diuretic Spironolactone.	competitive antagonist of aldosterone in CCT	\uparrow Urinary Na \downarrow K, H secretion Metabolic acidosis

Diuretics

Uses

CA inhibitors

Acetohexamide

Dorzolamide (topically) for
glaucoma

Glaucoma, epilepsy

Mountain sickness

Alkalosis

Phosphatemia

Osmotic diuretic

Mannitol

• Cerebral edema, glaucoma

• Acute renal failure, drug toxicities

Loop diuretics

Furosemide

Acute pulmonary edema (**Drug of
choice**)

Heart failure

Hyperkalemia, Hypercalcemia

Thiazide diuretics

hydrochlorothiazide

Commonly used

Hypertension, mild heart failure,
nephrolithiasis, diabetes inspidus

K-sparing diuretic

Spironolactone.

Hepatic cirrhosis

(Drug of choice)

Diuretics	Side effects
CA inhibitors Acetohexamide Dorzolamide	Metabolic acidosis , Urinary alkalosis Hypokalemia
Osmotic diuretic Mannitol	Extracellular water expansion Dehydration Hypernatremia
Loop diuretics Furosemide	Hypokalemia, hypovolemia, hyponatremia, hypomagnesemia, hypocalcemia Precipitate gout, alkalosis
Thiazide diuretics hydrochlorothiazide	Hypokalemia, hyponatremia, hypovolemia, hypomagnesemia, hypercalcemia Alkalosis, precipitate gout Hyperlipidemia, hyperglycemia
K-sparing diuretic Spironolactone.	Gynaecomastia Hyperkalaemia , Metabolic acidosis. GIT upset and peptic ulcer

