

Antihypertensive drugs have

4 main categories

- 1 Diuretics .
- 2 Sympathoplegics .
- 3 Vasodilators
- 4 Renin antagonists - angiotensin .

Diuretics

.Diuretics: Increase urine volume. Natriuretics: Increase urinary excretion of sodium

Diuretics are drugs that increase the volume of urine and are called diuretics, diuretics and diuretics. Most of these drugs, because they cause natriuresis and cause sodium excretion, are also considered natriuretics. In terms of mechanism, we must increase the osmotic pressure in the renal tubules to draw water into the tubules and increase the volume of urine

Disrupts ion reabsorption Increased osmotic pressure □ Water is drawn into tubules □ Urine volume increases

Different groups of diuretics

- 1) **Diuretics affecting complex tubules** carbonic anhydrase inhibitors or CAI such as acetazolamide
- 2) **Diuretics affecting the Henle arc** □ Like furosemide and ethacrynic acid
- 3) **Diuretics affecting complex round tubes** Thiazides such as hydrochlorothiazide and metolazone
- 4) **Diuretics affecting the collecting tube** □ Potassium sparing or K^+ sparing - such as spironolactone
amiloride - triamterene - applerone
- 5) **Osmotic diuretics** □ Like Mannitol
- 6) **ADH antagonists**
- 7) **Sodium glucose inhibitors**
- 8) Another drug that affects proximal tubules is Canagliflozin .which inhibits sodium-chlorine co-transmission ,

1. Carbonic anhydrase inhibitors

Its oral form **produces acetazolamide** by inhibiting the enzyme carbonic anhydrase in the proximal tubule of .diuresis

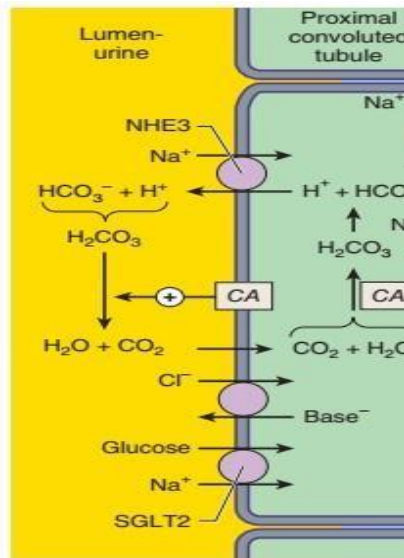


Image of the site of the carbonic anhydrase effect, ie the proximal part of the nephron

Application of carbonic anhydrase inhibitors

Treatment of glaucoma □ ,Carbonic anhydrase is involved in the production of fluid. In the long run

acetazolamide in the form of tablets and dorzolamide in the form of eye drops reduce the production of fluid and reduce the IOP) Does not cause tolerance and is consumed for a long time (.

Alkalinization of urine Because bicarbonate is excreted, it is used in poisoning, for example with aspirin which is acidic

Metabolic alkalosis □ Acetazolamide causes metabolic acidosis

Prevention of acute mountain sickness □

Acute mountain sickness When climbing a mountain, the intracranial pressure rises, and climbers consume it before climbing to a height to prevent an increase in intracranial pressure

Menstrual epilepsy □ **Catamenial epilepsy** Acetazolamide because it excretes bicarbonate, causes metabolic acidosis in the body and we know that in acidosis, neuronal irritability decreases and as a result, the seizure threshold rises and the person recovers . They are not used as regular anticonvulsants because they provide tolerance and are only used for short periods of menstruation

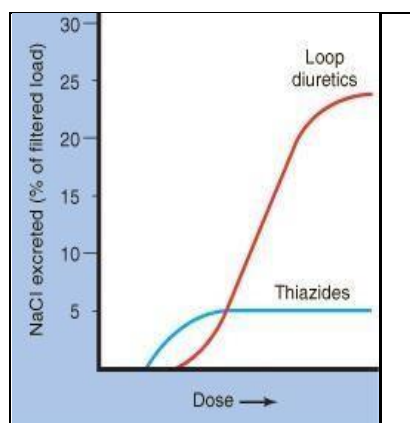
In these drugs, we do not see a decrease in blood pressure, although it is a diuretic, because these drugs upset the acid-base balance, and many of its effects are tolerated and lose its effectiveness



:Side effects of acetazolamide include

1. **Metabolic acidosis**
2. **Hypokalemia** □ Because these drugs increase potassium excretion
3. **Hypophosphatemia**
4. **Allergy** and cross-reaction of sulfonamides, drowsiness, paresthesia
5. **Encephalopathy** in patients with liver failure □ in cirrhosis of the liver is contraindicated
💡 Because alkalinity of urine worsens the condition **of hepatic encephalopathy** and in these cases it is contraindicated
6. **Kidney** and urinary stones Calcium phosphate in long-term use of high doses of the drug

2. Drugs affecting the Henle arch or loop diuretics



Comparison of efficacy between thiazides and diuretic loops

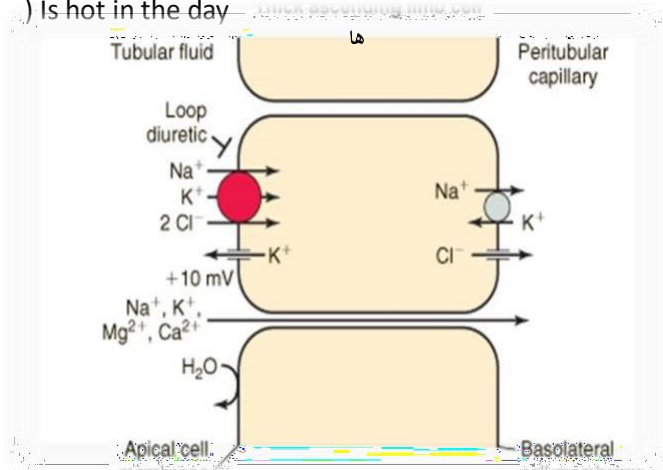
Drugs such as **Furosemide(Furosemide)** with the brand name of Lasix and Ethacrynic **Acid(Ethacrynic acid)** belong to this family

🌈 They have the highest efficacy among diuretics and are considered the strongest diuretics and can increase the volume of urine by 15 to 22 .ml

🌈 These drugs are rapidly absorbed orally and have a bioavailability of 65 to 122 so their effect is rapidly ,% . manifested and secreted by transporters into the renal tubules

Bumetanide and Torsemide are also not available in Iran ! You say what we have Torsemide in terms of , potency 4 Equivalent to furosemide) range of use of furosemide --0-00 mg per day and torsemide 5-00 mg

) Is hot in the day



4)**Treatment of acute pulmonary edema** (especially injection)

5 **Treatment of severe hypercalcemia**) Because they increase urinary excretion of calcium in contrast to thiazides, in symptomatic treatment they inject the ampoule of ferrosamide into a saline solution and infuse it. They control !) hypercalcemia (without administering fluid, it aggravates hypercalcemia in the patient

6)Treatment of heart failure or ascites

7 Sometimes they can be used to **treat high blood pressure** , although we prefer thiazide drugs such as)
. hydrochlorothiazide . Even in emergencies, furosemide ampoules can be used to lower blood pressure quickly

Side effects of loop diuretics



- 1) Decreased potassium \square which can cause muscle weakness and tremors
- 2) Magnesium Depletion \square In long-term use, severe magnesium depletion occurs, in which case a magnesium sac should be used to replenish the lost .magnesium, which is poured on the tongue
- 3) Metabolic alkalosis
- 4) Hyperuricemia or increased blood uric acid \square such as thiazides
- 5 Auditory toxicity or) \square Ototoxicity among antibiotics, aminoglycosides such as gentamicin, etc. also cause this complication and should not be used together

with these two drugs, but separately do not have much effect

Drug Interaction Loop Diuretics

. on hearing toxicity

- 6) Allergy due to the structure of sulfonamides (except atacrynic acid)

💡 + interfere with \square Li reduces the clearance of lithium and causes lithium . toxicity

💡 Increase the renal toxicity of other nephrotoxic drugs such as .cephalosporins

💡 Effects of auditory toxicity or ototoxicity They increase aminoglycoside .antibiotics such as gentamicin

💡 NSAIDs . reduce the effectiveness of these drugs

3 Thiazide diuretics .

most famous of them is **hydrochlorothiazide** . It is very high consumption and is available in doses of 05 and 50 mg in the .market. Another drug in this category is metolazone

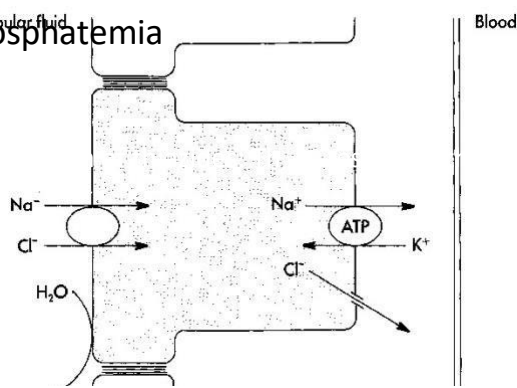
Combination of hydrochlorothiazide with triamterene and losartan as triamterene H. Triamterene: Diuretic (💡) And your loser)H your loser: Antihypertensive, angiotensin (2 receptor antagonist . Used)

Losartan in as LosartanH + Losartan

Hydrochlorothiazide **Parsian: Metolazone** is the most potent thiazide diuretic (used to treat each with its own side effect) and, unlike the rest, prevents hyperkalemia and hypokalemia in advanced . renal failure, respectively

It has applications. Its unique complication is

.hyperphosphatemia



- in this part Also transitional Na^+ & Cl Thiazides inhibit this transition as a result of impaired reabsorption of sodium and chlorine and pressure
The osmotic fluid of the filter rises and draws water into the tubule, increasing the volume of urine. Thiazide drugs increase the excretion of sodium and chlorine. In addition, the excretion of potassium also increases
Because the sodium in the filter is high, it can secrete aldosterone, which reabsorbs sodium and excretes potassium

.They also increase calcium reabsorption

Excretion Water and bicarbonate

Effects of thiazides on the body

- 1)Increased urinary excretion of sodium, potassium, chlorine, water and to some extent bicarbonate
- 2)Lower blood pressure
- 3) GFR reduction

Clinical application

- 1) **Elimination of swelling or edema** in mild to moderate cases of CHF (heart failure)
- 2) **Treatment of hypertension** □ Used in mild to moderate hypertension alone and in more severe cases in combination with other drugs.) Main application
- 3 **Control of hyperuricemia and binge drinking (polyuria and polydipsia) in diabetes insipidus**)□ These drugs increase the volume of urine in a normal person, but in people with diabetes insipidus, with a paradoxical effect they control binge drinking and hyperuricemia

October55 :We have two types of tasteless diabetes :

Central) a Which is due to ;ADH deficiency And the drug is ADH

b Nephrogenic: where the kidneys respond to)ADH Disrupted

□ . Diuretics are used in this case

💡 In diabetes mellitus Polydipsia And Polyuria we have. In normal people, thiazides are diuretics, but in tasteless diabetes, they paradoxically reduce the volume of urine and are effective in treating it

- 4 **Control of hypercalciuria (excretion of high amounts of calcium in urine)**)Thiazide drugs in the distal region increase calcium reabsorption, which in turn reduces urinary excretion of calcium
- 5) **Prevent the formation of calcium kidney stones** This effect occurs following a decrease in the amount of calcium in the urine

Drug interaction of thiazides



- 1) **Interaction with Digoxin** Digoxin is used in heart failure. Thiazides, and in general all hypokalemic drugs, increase digoxin toxicity. Occur . October 55)
- 2) **Interaction with other drugs that cause hypokalemia** □ Development of more severe hypokalemia
- 3 **Interference with)Li (Lithium)** Thiazides reduce urinary excretion of Li and (if taken at the same time as lithium itself, for example in the treatment of bipolar disorder), they increase its blood concentration and cause intoxication.

4 **Interference with)NSAIDs** □ **NSAIDs** (including diclofenac, ibuprofen, piroxicam, etc.) reduce the effectiveness of thiazides and their diuretic effect. Part of the diuretic effect of these drugs is due to prostaglandins and NSAIDs .inhibit the enzyme cyclooxygenase and thus produce Reduce prostaglandins

Toxicity and side effects of thiazides

- 1) **Severe diuresis with early progressive hyponatremia** is .a dangerous complication but has a low prevalence
- 2) **Hypokalemia** followed by tremor (and tremor)and .chronic weakness
- 3) **Hyperuricemia** □ **Hyperuricemia raises** blood uric acid levels and exacerbates gout. (It is relatively .contraindicated in gout, which means that if thiazide is a better medicine, we will not use thiazides
- 4) **Hyperglycemia** □ **Hyperglycemia** is believed to be due in part to reduced insulin secretion and serum potassium .concentrations
(Insulin secretion decreases when hypokalemia occurs) Of course, diabetics can use these drugs, but their blood .sugar must be controlled
- 5) **Increased lipids in plasma**
- 6) **Hypercalcemia**
- 7) **Development of sulfonamide allergies**
- 8) They cause a little impotence in men .

POTASSIUM SPARING DIURETICS Potassium preserving diuretics.4-

Carbonic anhydrase inhibitors, thiazides, and loop diuretics have been shown to reduce potassium. If these diuretics .retain potassium and even cause hyperkalemia. These drugs are classified into two groups



- 1 **Aldosterone antagonists** : Spironolactone and eplerenone)have a steroidal structure and are aldosterone antagonists. However, spironolactone also has anti-androgenic properties. And this property for the treatment of acne and hair(hirsutism)) . is used in women
- 2 **Sodium channel blockers**: include)amiloride and triamterene, ,which act on collecting tubes increasing sodium excretion and decreasing potassium and hydrogen excretion. Acidosis



Clinical application

1)Treatment of hypertension

October55 ,Unlike spironolactone :
triamterene and amiloride do not have a
steroidal structure and therefore have
.different mechanisms

**Eplerenone has only one difference with
spironolactone, which is the lack of anti-
androgenic properties**

Spironolactone has 72% of gastrointestinal %
absorption and has an active metabolite called
.canneron

- 2) Fix edema or swelling
- 3) Spironolactone and eplerenone for the treatment
of heart disease
- 4) Spironolactone and eplerenone in the treatment of
primary aldosteronism
- 5) Spironolactone in the treatment of acne and
hirsutism (anti-androgenic properties)
- 6) Triamterene and amiloride in the treatment of
heart disease and hypertension
- 7) Treatment of potassium loss caused by other diuretics) is
added to thiazide diuretics. For example, triamtereneH)

Toxicity and side effects

- 1) **Hyperkalemia** □ The use of these drugs in patients with renal insufficiency that are high in potassium and
in combination with drugs that cause hyperkalemia such as ACE inhibitors and losartan should be controlled. (The
most important complication
- 2) **Hyperkalemic metabolic acidosis**
- 3) **Gynecomastia in men** Due to the anti-androgenic properties of spironolactone
- 4) **Gastrointestinal disorders** for all four drugs

OSMOTIC DIURETICS Osmotic diuretics.5

In this category are **mannitol** , **urea** , **glycerin and isosorbide** , the most important of
which is **mannitol** . Mannitol is filtered and secreted in the renal tubules but is not
reabsorbed, so it increases the osmotic pressure and subsequently the inflow of water

Clinical application

.to establish osmotic balance. As a result, the volume of urine increases

Mannitol is a drug that if taken orally; Due to lack of absorption, it causes osmotic
.diarrhea. Therefore, as an **injectable** diuretic must be used

- 1 Reducing intraocular and cranial pressure and treating cerebral edema)□ ,Therefore
in glaucoma surgeries, mannitol is used to reduce CSF and ocular pressure .
- 2 Prevention of myoglobin and hemoglobin deposition)□ In patients with **favism** , for example, extensive
hemolysis may cause large amounts of hemoglobin to enter the renal tubules, which, if given the chance, may
precipitate and cause renal failure. The same is true for myoglobin in **rhabdomyolysis** . Mannitol prevents the
.deposition of these substances by creating pressure and diuresis

Side effects and toxicity

- 1)Increased extracellular fluid volume and hyponatremia due to water leakage from the cell
- 2)Human lung

3)Dehydration and hypernatremia if overdosed

5)Headache, nausea and vomiting

6 Hypersensitivity reactions) 4

6. ADH ANTAGONISTS ADH antagonists

ADH .is an anti-urinary hormone. So its antagonists have diuretic properties



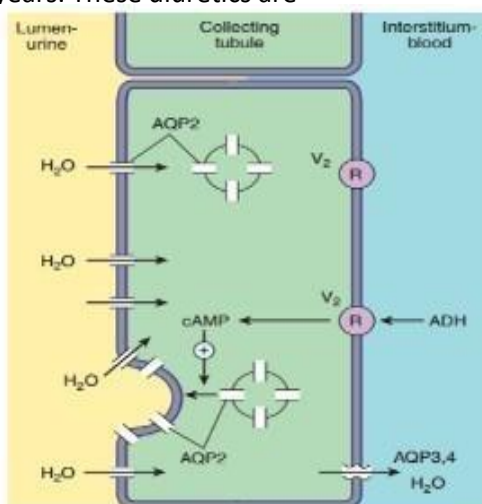
ADH antagonists They are known as **Vaptans** Such as **democyclycine** (banned for under .8) years) And **Connie Waptan** V_1 and V_2 (V) antagonists (And **toluaptan** V_2 antagonist. (Of these drugs in treatment **1** Hyponatremia and **2** .CHF control (heart failure) is .used **3** They are also used in .SIADH (ADH . (Syndrome

ADH agonists (such as desmopressin) reduce the volume and ,concentration of urine and are used for central diabetes insipidus and their side effects are hyponatremia and HTN .(hypertension)

Li is also an ADH antagonist but is never used to treat high blood .pressure

7. SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITORS Sodium and glucose transporter inhibitors

These diuretics have been introduced in recent years. These diuretics are



ADH Two types of V_1 receptors And V_2 has it. Type V_1 Has two types of V_{1a} And V_{1b} .Is V_1 receptors Most are found in arteries and CNS and V_2 receptors, mainly in the kidneys and renal tubules. When ADH binds to its receptor in the kidney, it stimulates adenyl cyclase and increases cAMP . cAMP increases .membrane aquaporin levels and water reabsorption ADH .antagonists block this effect and increase urine volume

sodium-glucose or SGLT2 inhibitors Drugs such as .Dapagliflozin and Canagliflozin

They are available and used as **third-line drugs to treat diabetes** . These drugs stop both sodium and glucose reuptake and glucose reabsorption in the **proximal tubules** due to inhibition of both sodium - glucose transfer and .increase urinary glucose excretion

🍷 Due to the entry of glucose into the urine, these drugs increase the risk of fungal .and urinary tract infections in women



Conclusion

Carbonic anhydrase inhibitors and SGLT2 blockers are effective in the proximal part of the tubule. Diuretic loop drugs also affect the thick part of the ascending branch of the Henle arch. Thiazides act on the beginning of the distal tubule and are one of the most widely used drugs in the treatment of hypertension.

		The amount of			Type
body pH	K ⁺	NaHCO ₃	NaCl		
Acidosis	□	□□□	□		Carbonic anhydrase inhibitor
Alkalosis	□	-	□□□□		Henle arc diuretics
Alkalosis	□	□ And -	□□		Thiazides
Acidosis	□	-	□		Potassium-sparing diuretics

