Thiazides

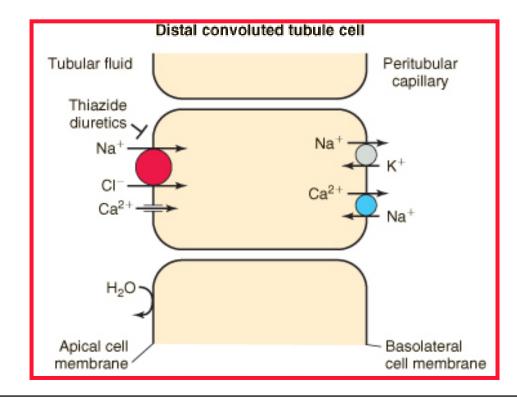
Chlorthiazide

MOA

As a diuretic, chlorothiazide inhibits active chloride reabsorption at the early distal tubule via the Na-Cl cotransporter, resulting in an increase in the excretion of sodium, chloride, and water.

This results in an increase in potassium excretion via the sodium-potassium exchange mechanism in the collecting duct.

It causes Hypokalemia.



Uses: Chlorothiazide is indicated as adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and estrogen therapy. It is also indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effectiveness of other antihypertensive drugs.

Hydrochlorothiazide

$$\begin{array}{c} 4 \\ CI & 5 \\ N & 3 \\ H_2NO_2S & 7 & 8 & 0 & 1 \end{array}$$

MOA: Similar to chlorthiazide

Uses: Similar to chlorthiazide

Hydroflumethiazide

MOA: Similar to chlorthiazide

Uses: Similar to chlorthiazide

Cyclothiazide

MOA: Similar to chlorthiazide

Uses: Similar to chlorthiazide

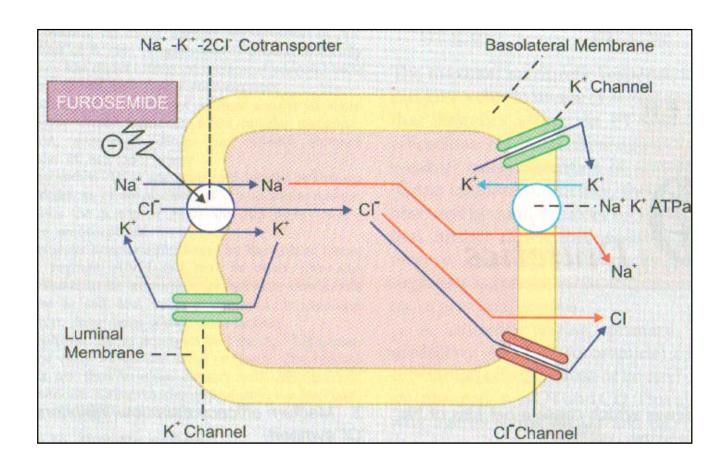
Loop Diuretics/High ceiling diuretic

Furosemide

MOA

o It enter proximal tubule via organic acid transporter and inhibits Na-K-2Cl transporter in thick ascending loop of henle. It competes with Cl- binding site.

 \circ This inhibition results in increased excretion K+ and H+ excretion in CCD. It also leads to excretion of water along with sodium, chloride, magnesium and calcium ions.



Synthesis

CI CISO₃H CI-SO₂ COOH NH₃ H₂N-SO₂ COOH + H₂NH₂C O HCI HCI HCI H₂N-SO₂
$$\frac{5}{6}$$
 COOH HCI HCI H₂N-SO₂ $\frac{5}{6}$ $\frac{1}{2}$ COOH NH₃ H₂N-SO₂ $\frac{5}{6}$ $\frac{1}{2}$ COOH NH₃ H₂N-SO₂ $\frac{5}{6}$ $\frac{1}{2}$ COOH NH₃ H₂N-SO₂ $\frac{5}{6}$ $\frac{1}{2}$ COOH NH₂N-SO₂ $\frac{5}{2}$ $\frac{6}{2}$ $\frac{1}{2}$ NHCH₂ $\frac{1}{2$

Uses: It is indicated as adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and estrogen therapy. It is also indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effectiveness of other antihypertensive drugs.

Ethacrynic acid

$$\begin{array}{c} O & 5 & 6 \\ H_2C = C - C & 4 & 1 \\ C_2H_5 & CI & 3 & 2 & CI \end{array}$$

MOA: Similar to Furosemide

Uses: Similar to Furosemide

Bumetanide

MOA: Similar to Furosemide

Uses: Similar to Furosemide

K⁺ sparing diuretics

Spironolactone

MOA

- o It is a competitive antagonist of mineralocorticoid receptor.
- o It prevents aldosterone stimulated increases in Na+transporter expression.

Uses: Spironolactone is indicated for the treatment of heart failure, management of edema in cirrhotic adults not responsive to fluid and sodium restrictions.

Triamterene

MOA: It is secreted into lumen by proximal tubule cells and Inhibits epithelial Na+ channel.

Uses: Triamterene is indicated for the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and the nephrotic syndrome; also in steroid-induced edema, idiopathic edema, and edema due to secondary hyperaldosteronism.

Amiloride

$$\begin{array}{c|ccccc}
1 & O & NH \\
C & C & C \\
6 & 2 & N \\
H_2N & 5 & N & 3 & NH_2 \\
4 & & & & & & & \\
\end{array}$$

MOA: It is secreted into lumen by proximal tubule cells and Inhibits epithelial Na+ channel.

Uses: It is indicated for the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and the nephrotic syndrome; also in steroid-induced edema, idiopathic edema, and edema due to secondary hyperaldosteronism.

