

Diuretics

- Drugs that block specific transport functions of the renal tubules are valuable clinical tools in the treatment of these disorders.
- Although various agents that increase urine volume (diuretics)
- have been described since antiquity, it was not until 1937 that carbonic anhydrase inhibitors were first described and not until 1957 that a much more useful and powerful diuretic agent (chlorothiazide) became available.



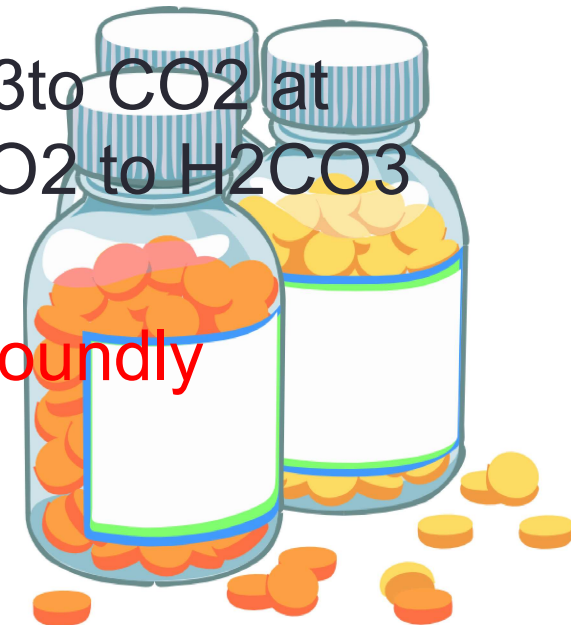
Diuretics Categories

- CARBONIC ANHYDRASE INHIBITORS
- SODIUM GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITORS
- LOOP DIURETICS
- THIAZIDES
- POTASSIUM-SPARING DIURETICS
- OSMOTIC DIURETICS
- ANTIDIURETIC HORMONE (ADH, VASOPRESSIN) AGONISTS



CARBONIC ANHYDRASE INHIBITORS

- They were discovered in 1937 when it was found that bacteriostatic sulfonamides caused an alkaline diuresis and hyperchloremic metabolic acidosis.
- Carbonic anhydrase is present in many nephron sites, but the predominant location of this enzyme is the epithelial cells of the PCT
- where it catalyzes the dehydration of H_2CO_3 to CO_2 at the luminal membrane and rehydration of CO_2 to H_2CO_3 in the cytoplasm
- inhibition of carbonic anhydrase activity profoundly depresses HCO_3^- reabsorption in the PCT.



CARBONIC ANHYDRASE INHIBITORS DRUGS

- Acetazolamide
 - Dichlorophenamide
 - Methazolamide
 - Brinzolamide
 - Dorzolamide
- Orally
- Topical for glaucoma



Clinical Indications

1. **Glaucoma** (**dorzolamide, brinzolamide**) The reduction of aqueous humor formation by carbonic anhydrase inhibitors decreases the intraocular pressure.
2. **Urinary Alkalinization** Uric acid and cystine are relatively insoluble and may form stones in acidic urine. Therefore, in cystinuria, a disorder of cystine reabsorption, solubility of cystine can be enhanced by increasing urinary pH to 7–7.5 with carbonic anhydrase inhibitors.
3. **Metabolic Alkalosis**



Clinical Indications

- Acute Mountain Sickness** Weakness, dizziness, insomnia, headache, and nausea can occur in mountain travelers who rapidly ascend above 3000 m. The symptoms are usually mild and last for a few days. In more serious cases, rapidly progressing pulmonary or cerebral edema can be life-threatening. By decreasing CSF formation and by decreasing the pH of the CSF and brain, acetazolamide can increase ventilation and diminish symptoms of mountain sickness. This mild metabolic central and CSF acidosis is also useful in the treatment of sleep apnea.
- Other Uses** in the treatment of epilepsy and in some forms of hypokalemic periodic paralysis. They are also useful in treating patients with CSF leakage.

