# Diuretics

= compouns used for ↑ of urine excretion in order to ↓ the excessive volume of extraceallular liquid or for other therapeutical purposes

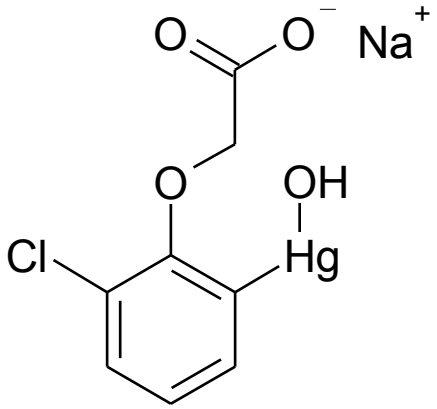
## History

Mercury compounds

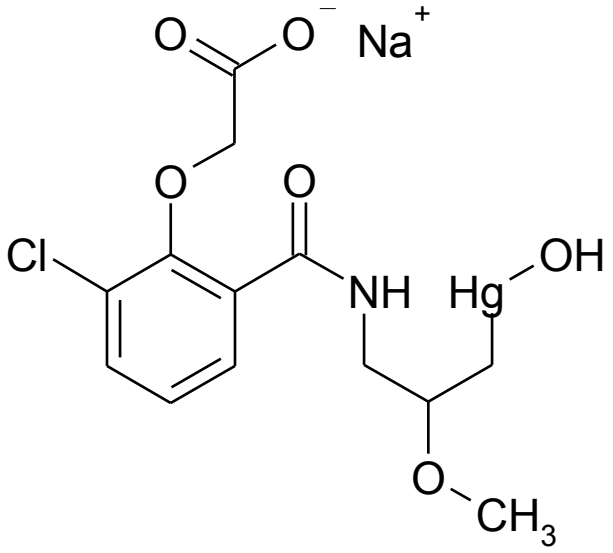
16th century – *Paracelsus* – red HgO (?)

19th century – $Hg_2Cl_2$ „calomel“

beginning of the 20th century – less toxic organic compounds with covalently bound Hg




Novasurol




**mersalyl**
Salyrgan®

**Classification of actually used diuretics**

1. Saluretics

1.1. Sulfonamides

1.1.1 Sulfonamides with acyclic -$SO_2NH_2$ group

1.1.2 Thiazide diuretics

2. „Potassium conserving“ diuretics

3. „Loop“ diuretics (= diuretics acting in the loop of Henle)

3.1. Sulfonamides – amino(hetero)arenesulfonamide derivatives

3.2. Phenoxyacetic acid derivatives

4. Osmotic diuretics

(5. Purine alcaloida – xanthine derivatives)

# 1. Saluretics

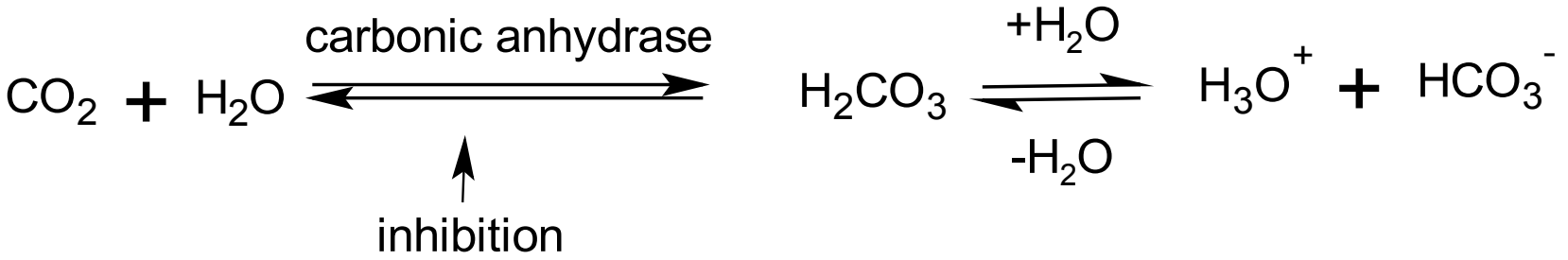
•inhibit reabsorption (back resorption) of $Na^+$ and $Cl^-$ in more distal part of the nephrone, ions bind water, which is then excreted

•they cause decrease of $K^+$ in organism (exchange for $Na^+$ and active secretion in distal tubule)

## 1.1. Sulfonamides

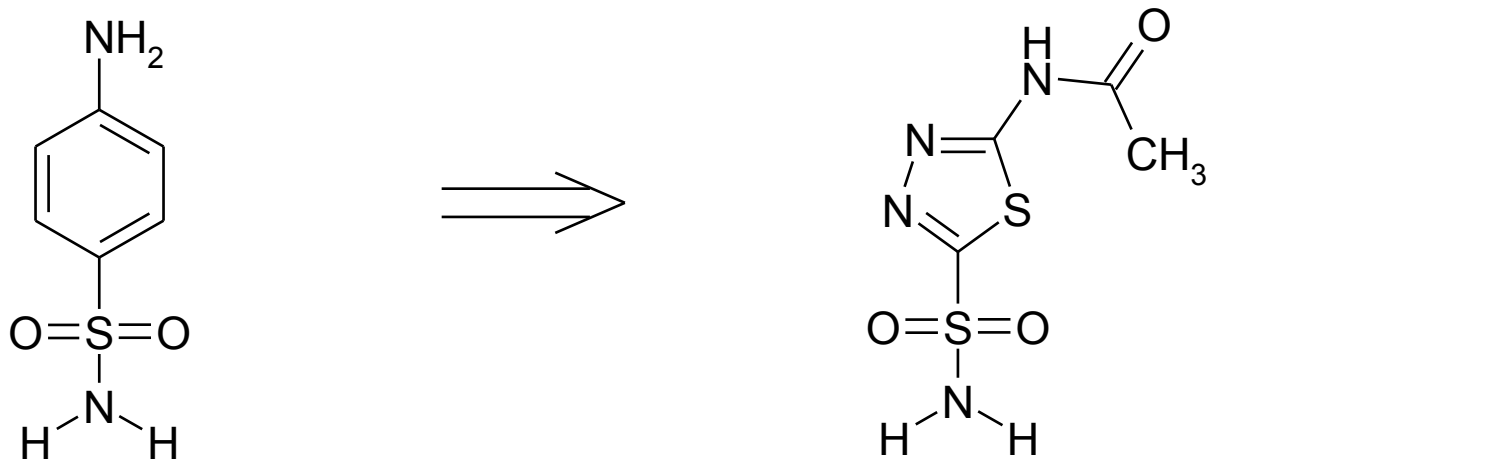
•diuretic activity of antibacterial sulfonamides observed as a side effect before 1940

•1949 Schwartz: carbonic anhydrase inhibtion




• the enzyme is inhibited $\Rightarrow \downarrow H_2CO_3 \Rightarrow \downarrow H_3O^+$ , which normally exchanges for $Na^+$, in glomerular filtrate $\Rightarrow Na^+$ remains in the renal tubule together with $HCO_3^-$, they bind osmotic equivalent of water $\Rightarrow$ excretion of a large quantity of urine

# 1.1.1. Sulfonamides with acyclic -$SO_2NH_2$ group

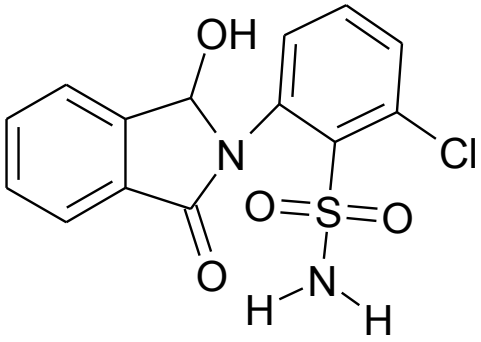


N-(5-sulfamoyl-[1,3,4]thiadiazol-2-yl)-acetamide

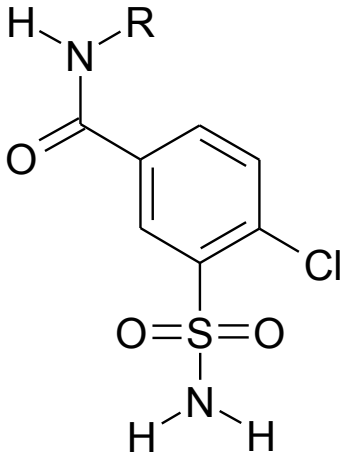
**sulfanilamide**
(lead compound of antibacterial sulfonamides)

**acetazolamide**
one of the firsr sulfonamide diuretics
Diluran® - today treatment of glaucom

## 1.1.1. Sulfonamides with acyclic -$SO_2NH_2$ group - continued




**chlorthalidone**
~~Urandil~~®
•hypertension, edema in heart insufficiency

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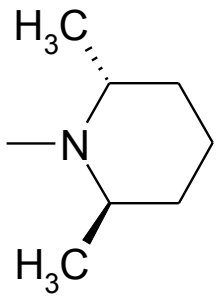
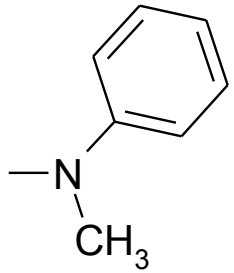
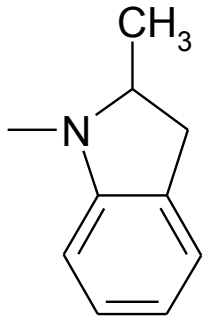



**clopamide**
~~Crystepin~~®
(+ reserpin, dihydroergocristin)




**metipamide**
Hypotylin®

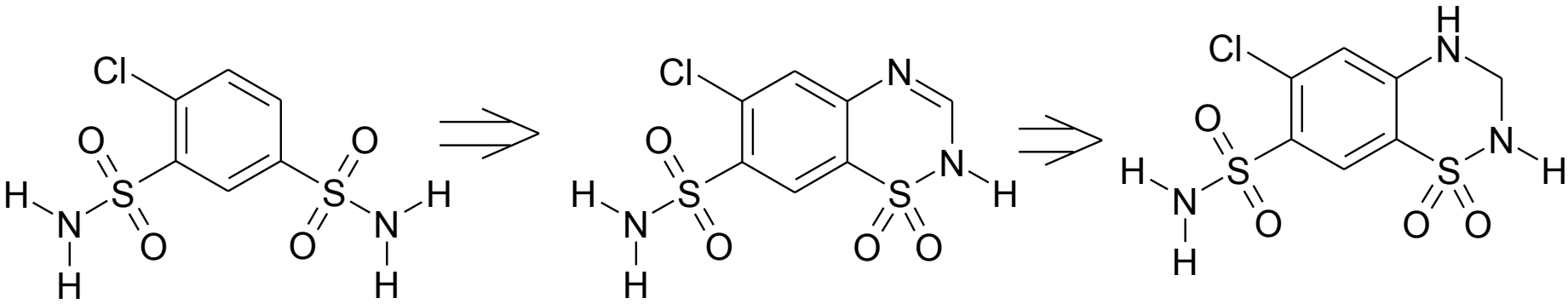



**indapamide**
•also antioxidant efffect
Indap®
Noliprel®(+ perindopril)
Prenewel ® ...

## 1.1.2 Thiazide diuretics

= sulfonamides with $–SO_2NH-$ group in a cycle

Elicitation of their structure




**clofenamide**
diuretic sulfonamide with acyclic $–SO_2NH_2$ groups; today obsolete

**chlorothiazide**
1st „thiazide“ diuretic; today obsolete

**hydrochlorothiazide**
most frequently combined with amiloride (Moduretic®, Rhefluin®) or with quinapril (Accuzide ®) for treatment of hypertension

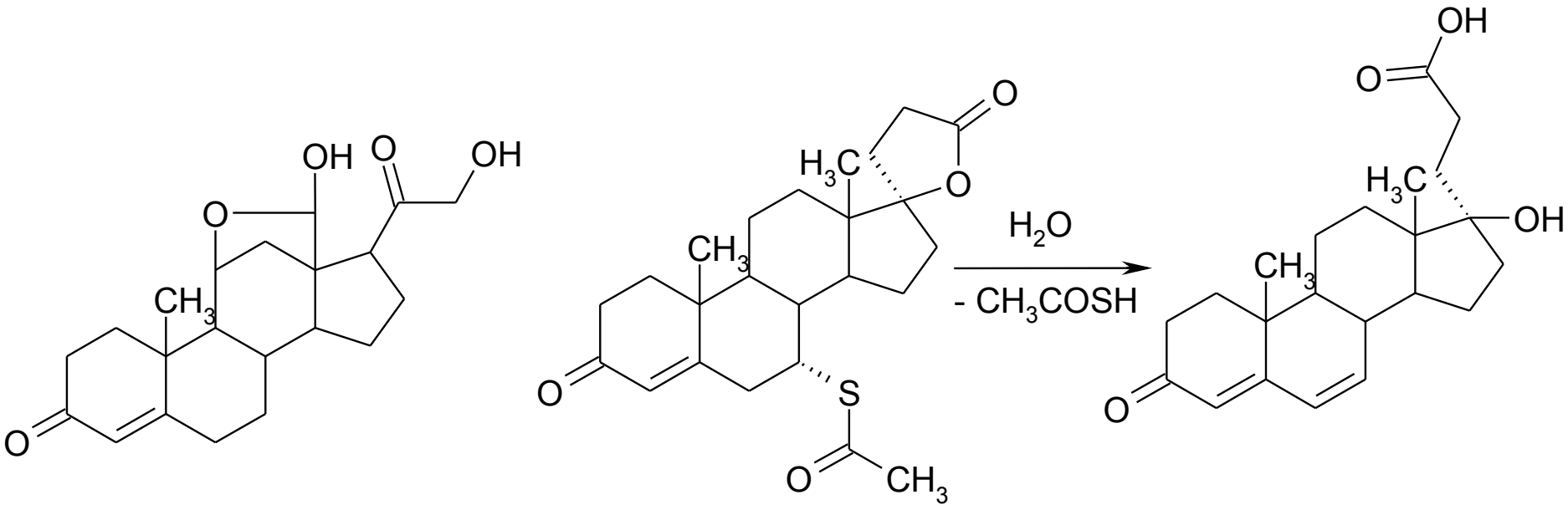
Activity

**1 : 20**

## 2. „Potassium conserving“ diuretics

•inhibit reabsorption of $Na^+$ v distal tubule; retention of $K^+$ occurs simultaneously

Aldosterone antagonists



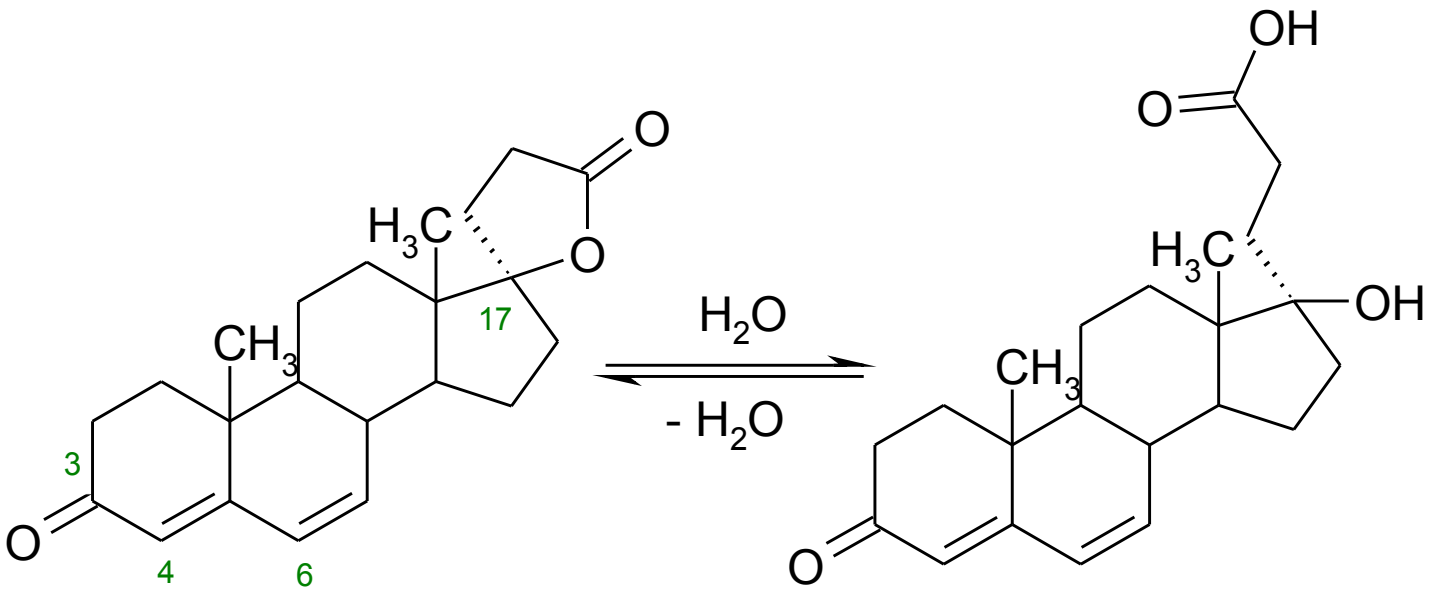

aldosterone

**spironolactone**
•prodrug of canrenoic acid
•hyperaldosteronemia
Verospiron® tbl.

**canrenoic acid**
•active compound
Aldactone® inj. – $K^+$ salt for parenteral application *(kalii canrenoas)*

Canrenon and canrenoic acid

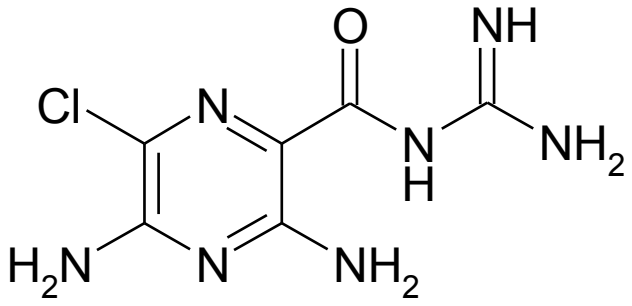
- both forms are in an equilibrium




canrenone
(lactone)

canrenoic acid
(a hydroxy acid)

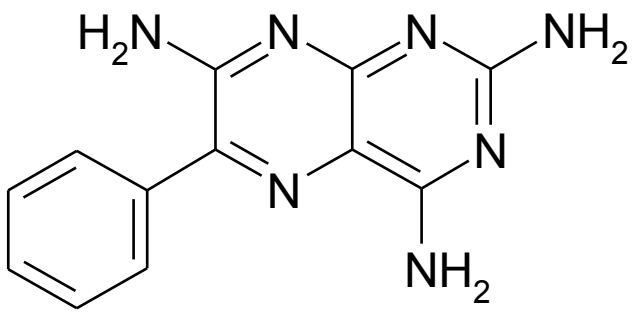
## 2. „Potassium conserving“ diuretics - continued




N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-guanidine

**amiloride**

Amicloton®, Moduretic®, Loradur® (+ hydrochlorothiazide) …




2,4,7-triamino-6-phenylpteridine

**triamterene**

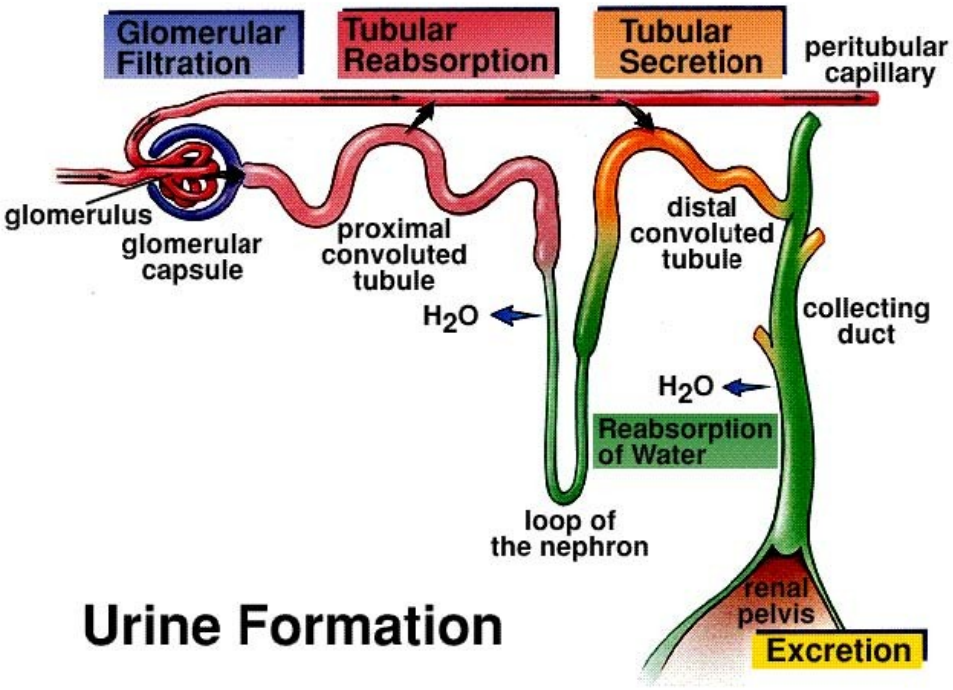
~~Dytac® tbl.~~

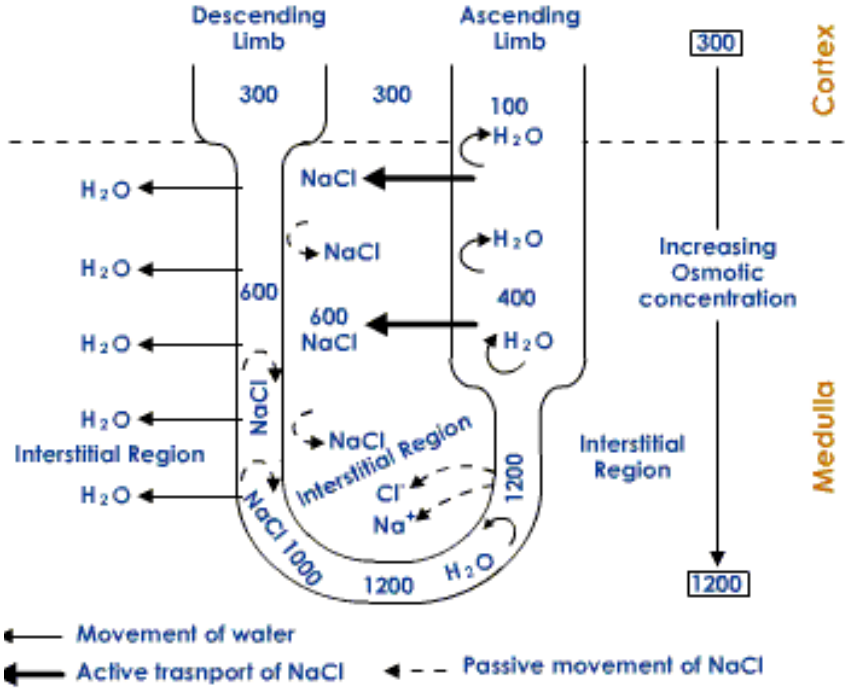
# 3. „Loop“ diuretics

•inhibit absorption of elektrolytes ($Na^+$, $K^+$, $H^+$ a $Cl^-$) in the ascending limb of Henle loop

(⇒ hyponatraemia, hypokalaemia, hypochloraemia and alkalosis possible)

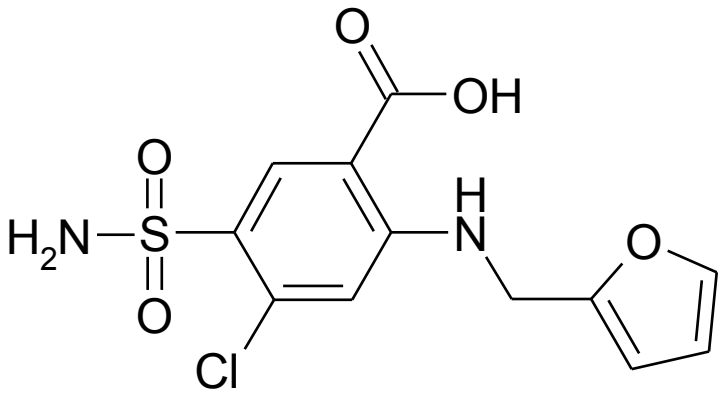
•efficient also in ↓ function of kidneys



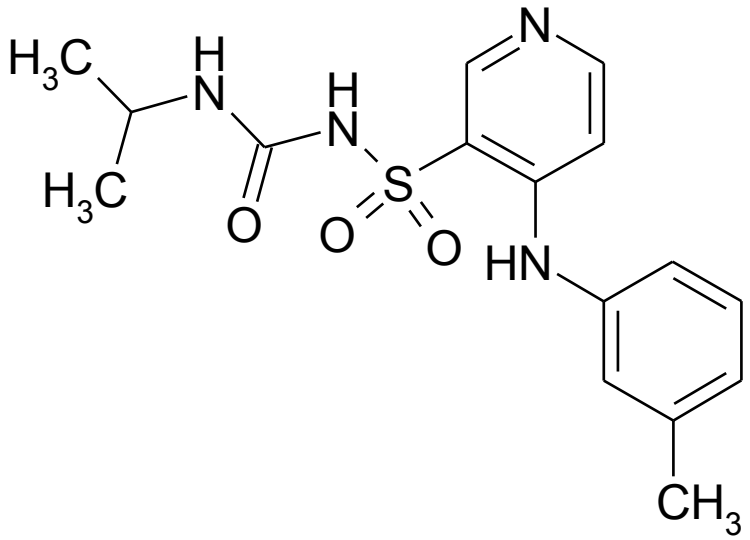



## 3. „Loop“ diuretics

### 3.1. Sulfonamides – amino(hetero)arenesulfonamide derivatives



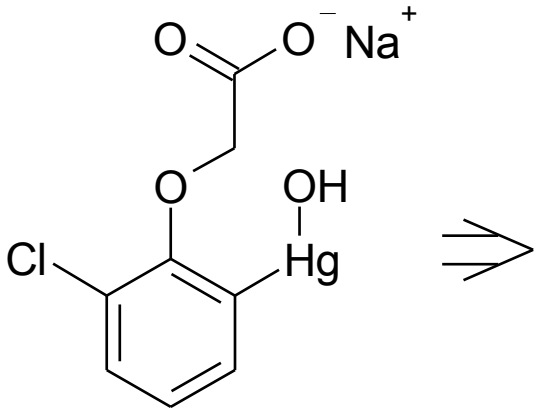

**furosemide**
Furon® tbl.
•oedema, chron. renal insufficiency

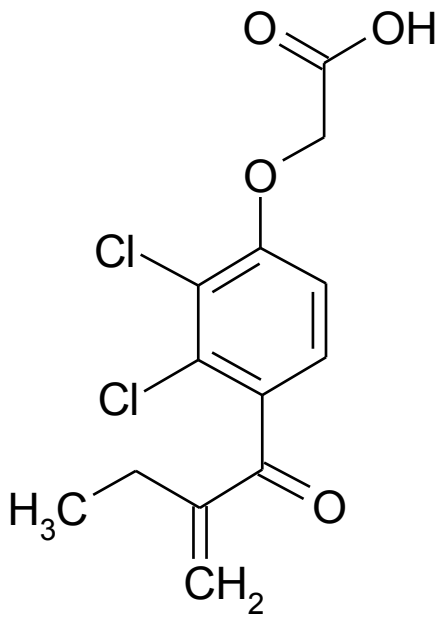


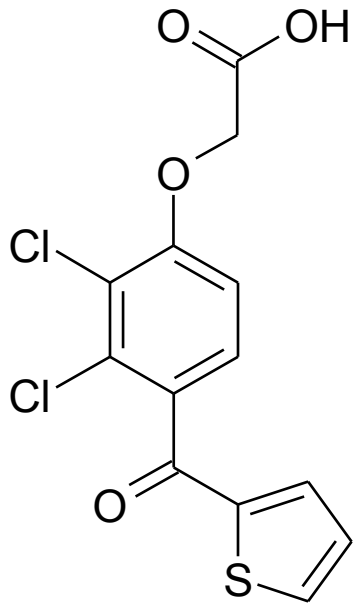

**torasemide**
**syn. torsemide** [USAN]
Trifas® tbl.

## 3.2. Phenoxyacetic acid derivatives

Derivation of the structure: directly from mercury diuretics




Novasurol

**ethacrynic acid**
Uregyt® tbl.

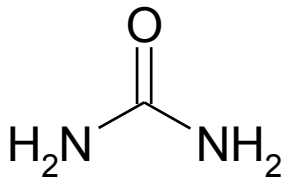
**tienilic acid**
(syn. **ticrynafen** [USAN])

## 4. Osmotic diuretics

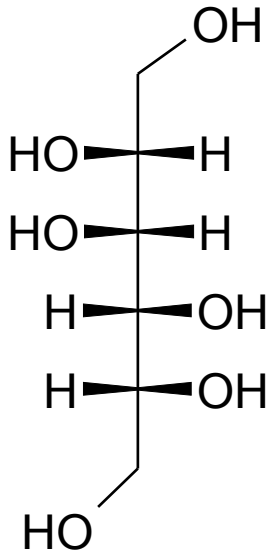
•osmotically active compounds, ↑ osmotic pressure of the glomerulal ultrafiltrate ⇒ ↓ its glomerular reabsorption

•administered only intravenously

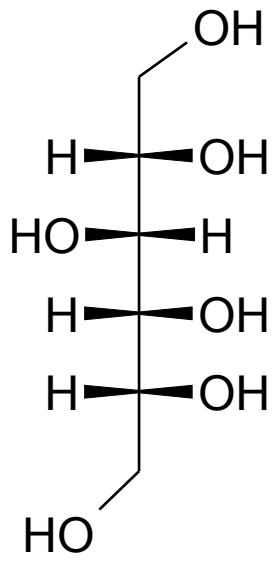
•removal of intracranial hypertension in patients with brain oedema, treatment of acute renal failure, forced diuresis in intoxications




**urea**
Urea VUAB® inf. sic.




**D-mannitol**
Osmofundin 15% N® inf.




**D-sorbitol**
syn. **D-glucitol**
Infusio sorbitoli® inf. sol.