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Diploma in Pharmacy 1<sup>st</sup> Year  
Pharmaceutical Chemistry  
Chapter 8 : DIURETICS

Topics

Page No

**DIURETICS**

3

- Acetazolamide
- Furosemide \*
- Bumetanide
- Benzthiazide
- Xipamide
- Chlorthalidone
- Metolazone
- Spironolactone



- Drugs promoting urine output are known as diuretic drugs, which refer only to those agents that act directly on the kidneys.
- These drugs primarily increase the excretion of water and ions like sodium ( $\text{Na}^+$ ), chloride ( $\text{Cl}^-$ ), or bicarbonates ( $\text{HCO}_3^-$ ) from the body.
- Glomerular filtration, tubular reabsorption, and tubular secretion in kidneys determine the excretion of substances.
- It is also employed in the treatment of various disorders like diabetes insipidus, nephrotic syndrome, hypertension, nutritional oedema, oedema of pregnancy, and liver cirrhosis.
- They also decrease the intracellular and cerebrospinal fluid pressure.

## Examples

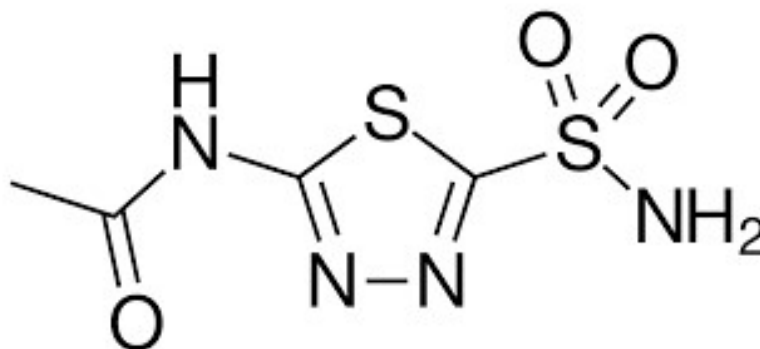
Examples of diuretics are given below:

- Acetazolamide
- Furosemide
- Bumetanide
- Benzthiazide
- Xipamide
- Chlorthalidone
- Metolazone
- Spironolactone

# Acetazolamide

- Acetazolamide is the prototype carbonic anhydrase inhibitor.
- This type of diuretics inhibit carbonic anhydrase enzyme in the membrane and cytoplasm of epithelial cell.

## Chemical Structure



## Mechanism of Action

- Acetazolamide is a carbonic anhydrase inhibitor. That means this drug works to cause an accumulation of carbonic acid by preventing its breakdown. The result is lower blood pH (i.e., more acidic), given the increased carbonic acid, which has a reversible reaction into bicarbonate and a hydrogen ion.

## Uses

- Acetazolamide is self-limiting in nature.
- It produces adverse effects like acidosis and hypokalaemia.
- Thus, it is not used as a diuretic anymore; instead, it is currently being employed in the treatment of
  - ◆ Glaucoma
  - ◆ Alkalinising Urine
  - ◆ Epilepsy
  - ◆ Acute Mountain Sickness

## Stability and Storage Conditions

- It can be stored up to 48 months.
- It should not be stored above 25°C.
- It should be stored in the original pack in order to protect from light and moisture.

## Types of Formulations

1. Capsules
2. Tablets

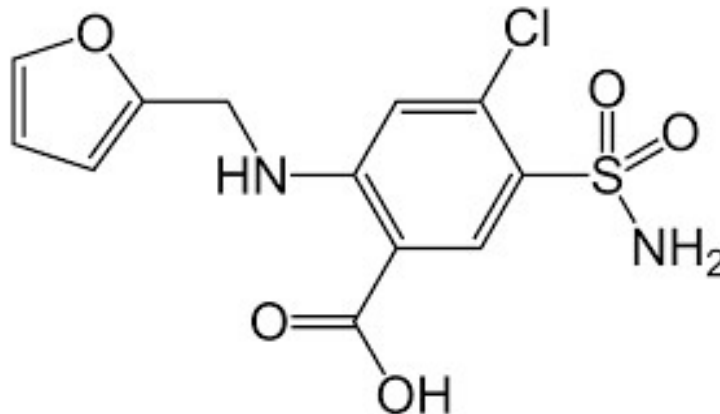
## Popular Brand Names

- ◆ Diamox
- ◆ Diamox Sequels

## Furosemide \*

→ Furosemide is a benzoic-sulfonamide-furan with fast onset and short duration of action. It is used for treating oedema and chronic renal insufficiency.

### Chemical Structure



### Mechanism of Action

- Furosemide, an anthranilic acid derivative, is a rapid acting, highly efficacious diuretic Rankin (2002). Its mechanism of action is inhibition of the sodium-potassium-2 chloride (Na<sup>+</sup>-K<sup>+</sup>-2 Cl<sup>-</sup>) co-transporter (symporter) located in the thick ascending limb of the loop of Henle in the renal tubule Jackson (1996).

### Uses

- It is used for the treatment of oedema related to congestive heart failure, liver cirrhosis, and renal disease.
- It is also used either alone or with other antihypertensive agents for the management of hypertension.

### Stability and Storage Conditions

- It should be kept at room temperature from 59°F (15°C) and 86°F (30°C).
- This drug should be kept away from light.
- This medication should not be stored in moist or damp areas like bathrooms.

### Types of Formulations

1. Tablet
2. Solution

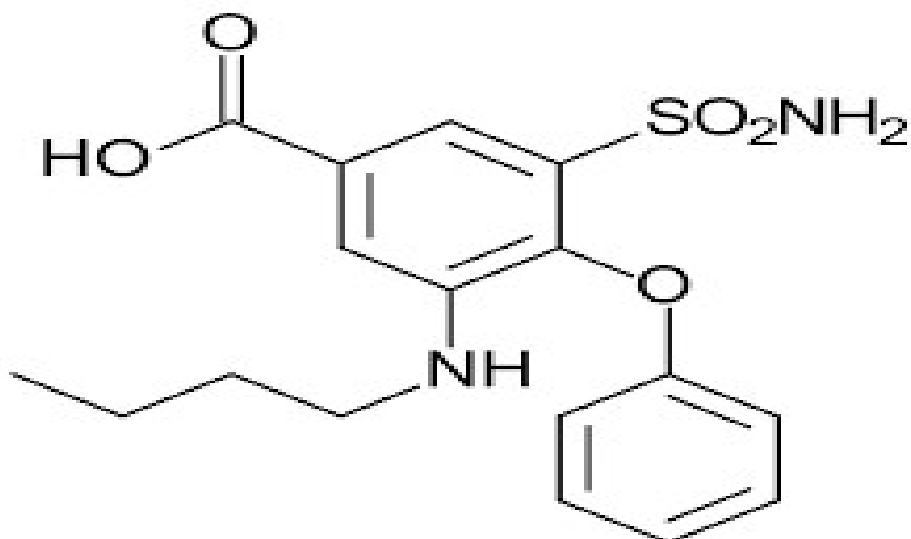
### Popular Brand Names

- ◆ Lasix,
- ◆ Diaqua-2,
- ◆ Lo-Aqua

## Bumetanide

- Bumetanide is a loop diuretic of sulfamyl category.
- It is used for treating heart failure.
- It is used by the people who are not responding to high doses of furosemide or other diuretics.

### Chemical Structure



### Mechanism of Action

- The mechanism of action and effects of bumetanide are similar to those of furosemide. The drug increases urinary excretion of water, sodium, and chloride by inhibiting reabsorption of sodium and chloride through interference with the chloride-binding cotransport system in the ascending loop of Henle.

### Uses

- It is used for treating oedema related to congestive heart failure, hepatic and renal disease including nephrotic syndrome.

### Stability and Storage Conditions

- It should be stored at room temperature between 68°F and 77°F (20°C and 25°C), and should be kept away from light.

### Type of Formulation

1. Tablets

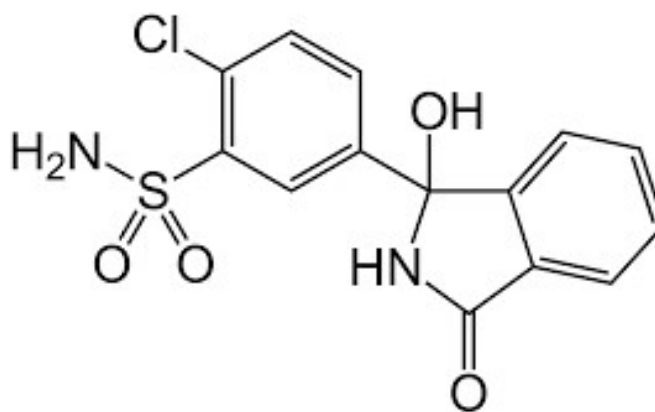
### Popular Brand Names

- ◆ Bumex,
- ◆ Burinex

# Chlorthalidone

→ Chlorthalidone is a diuretic which is used in the treatment of hypertension or edema caused by heart failure, renal failure, hepatic cirrhosis, estrogen therapy, and other conditions.

## Chemical Structure



## Mechanism of Action

- Chlorthalidone inhibits sodium reabsorption at the level of the distal convoluted tubule and thus chloride via inhibition of the Na/Cl symporter. By removing sodium reabsorption at this location, the distal convoluted tubule of the nephron retains a higher sodium content.

## Uses

- Chlorthalidone is used alone or together with other medicines to treat high blood pressure (hypertension).

## Stability and Storage Conditions

- It should be dispensed in a tight, light-resistant container as defined in USP using a child-resistant closure.
- This medication should be kept away from reach of children.

## Type of Formulation

1. Tablets

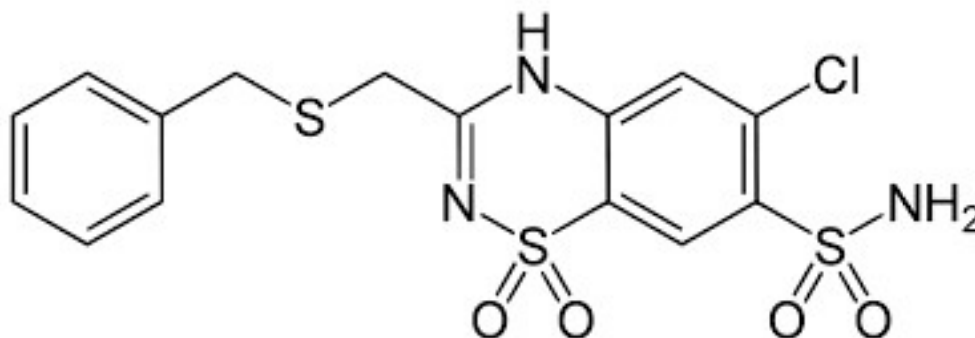
## Popular Brand Names

- ◆ Hygroton
- ◆ Thalitone
- ◆ Chlorthalid

## Benzthiazide

→ Benzthiazide is a class of thiazide diuretics which has an intermediate acting agent. Benzthiazide is also known as benzothiazide.

### Chemical Structure



### Mechanism of Action

- Benzthiazide is used to treat hypertension and edema. Like other thiazides, benzthiazide promotes water loss from the body (diuretics). They inhibit Na<sup>+</sup>/Cl<sup>-</sup> reabsorption from the distal convoluted tubules in the kidneys. Thiazides also cause loss of potassium and an increase in serum uric acid.

### Uses

- It is used in the treatment of High blood pressure (hypertension).
- The build-up of fluid in your body oedema.

### Stability and Storage Conditions

- It should be stored at room temperature in a well closed container and should be protected from light.

### Type of Formulation

1. Tablets

### Popular Brand Names

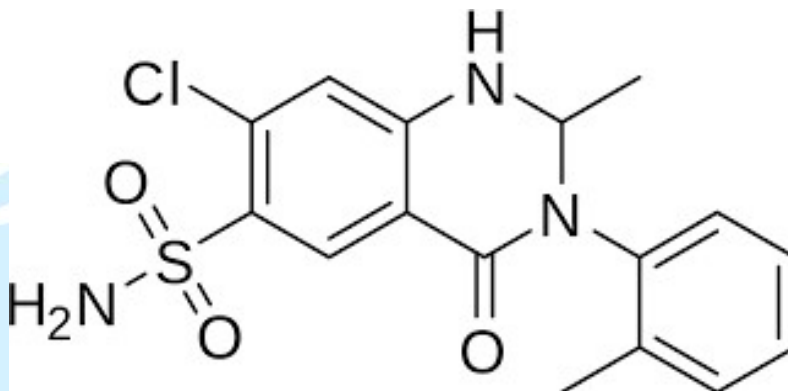
- ◆ Exna



# Metolazone

→ Metolazone is a thiazide like diuretic which is used in the treatment of hypertension.

## Chemical Structure



## Mechanism of Action

- Metolazone works by inhibiting sodium transport across the epithelium of the renal tubules (mostly in the distal tubules), decreasing sodium reabsorption, and increasing sodium, chloride, and water excretion.

## Uses

- Prevent body from absorbing too much salt that can cause fluid retention.
- Treat fluid retention (edema) in people with congestive heart failure, or a kidney disorder such as nephrotic syndrome.

## Stability and Storage Conditions

- It should be stored at room temperature (77°F or 25°C) away from light and moisture.

## Type of Formulation

1. Tablets

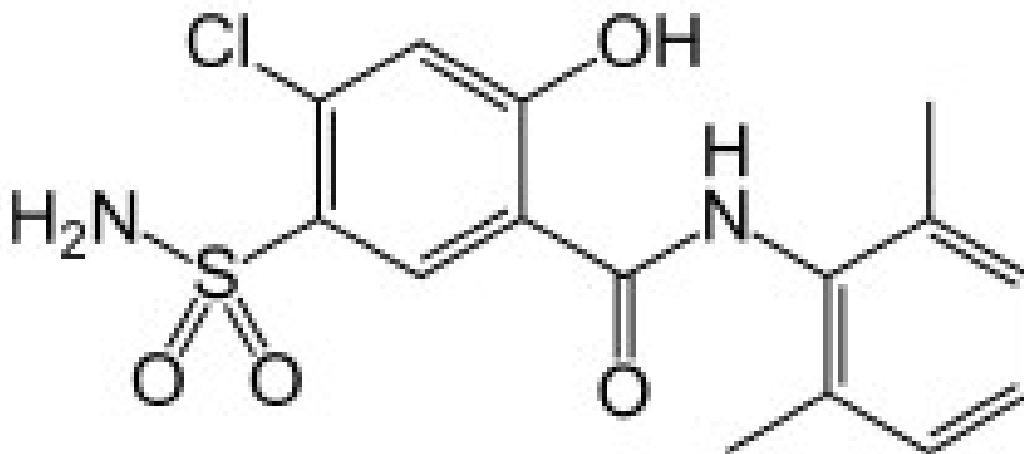
## Popular Brand Names

- ◆ Zaroxolyn
- ◆ MykrOx

# Xipamide

→ Xipamide is a diuretic which is used for the treatment of oedema.

## Chemical Structure



## Mechanism of Action

- Xipamide leads to an increase of K<sup>+</sup> and Mg<sup>2+</sup> excretion, but to a decrease of Ca<sup>2+</sup> excretion in urine, a characteristic feature of the thiazide-like diuretics.

## Uses

- Xipamide is used for:
- Treating hypertension (high blood pressure)
- Treating oedema

## Stability and Storage Conditions

- It should be stored in cool and dry place and should be kept away from direct heat and light.

## Type of Formulation

1. Tablets

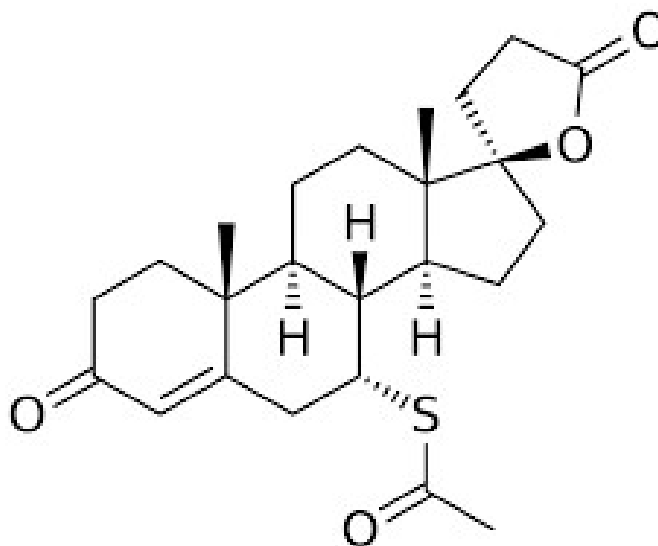
## Popular Brand Names

- ◆ Aquaphoril
- ◆ Aquaphor

# Spirolactone

→ Spirolactone is a potassium sparing diuretic which acts by antagonising aldosterone in the distal renal tubules.

## Chemical Structure



## Mechanism of Action

- Aldactone (spironolactone) is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule.

## Uses

- It is used for treating refractory oedema in patients having failure, nephrotic syndrome, or hepatic cirrhosis.
- It is also used for treating hypokalaemia, Conn's syndrome, and low-renin hypertension.

## Stability and Storage Conditions

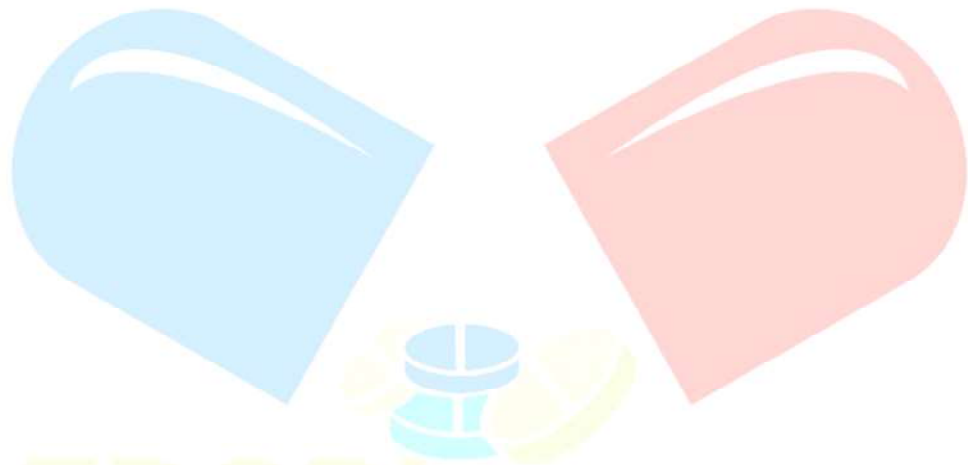
- Spirolactone should be kept at room temperature between 68°F and 77°F (20°C and 25°C).
- It should be kept away from light and high temperature.

## Types of Formulations

1. Tablet
2. Capsule

## Popular Brand Names

- ◆ Aldactazide
- ◆ Aldactone
- ◆ Carospir



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