

DIURETICS

8.1 INTRODUCTION OF DIURETIC

- Diuretics (natriuretics) are drugs which cause a net loss of Na^+ and water in urine.
- Diuretics **increase the rate of urine** flow and sodium excretion, and are used to adjust the volume or composition of body fluids in a variety of clinical situations, including hypertension, heart failure, renal failure, nephritic syndrome, and cirrhosis. The normal fluid filtration in human body is **180 litres**, and about **1.5 litres** of urine is formed in 24 hrs.

8.2 CLASSIFICATION OF DIURETICS

CLASS	EXAMPLES
Thiazide diuretics	Chlorthalidone, Benzthiazide, Hydrochlorothiazide,
Thiazide-like diuretics	Metolazone, Xipamide
Loop diuretics	Furosemide, Bumetanide
Carbonic anhydrase inhibitors	Acetazolamide
Potassium sparing diuretics	Spirolactone
Osmotic diuretics	Mannitol, Glycerine

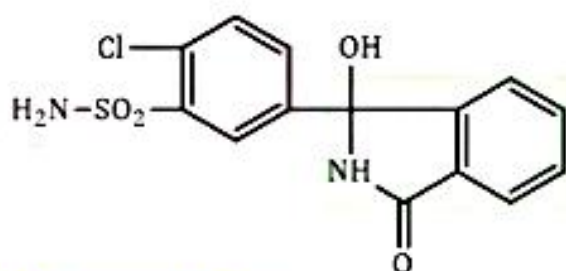
8.3 THIAZIDE DIURETICS

❑ CHLORTHALIDONE

- Chlorthalidone is thiazide like diuretics whereas other agents in this group are thiazides. These drugs act by inhibiting $\text{Na}^+\text{-Cl}^-$ symporter at the luminal membrane of early DT.

❖ **Chemical Formula** - $\text{C}_{14}\text{H}_{11}\text{ClN}_2\text{O}_4\text{S}$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-Chloro-5-(1-hydroxy-3-oxo-2,3-dihydro-1H-isoindol-1-yl)benzene-1-sulfonamide

❖ **Physicochemical Properties**

- It is a white to yellowish white crystalline powder.
- It is insoluble in water, ether and chloroform. But it is slightly soluble in alcohol and soluble in methanol.
- It is also soluble in alkali hydroxide solution

❖ **Pharmaceutical Formulation**

- It is available in the market in the form of tablets

❖ **Stability and storage**

- It is stored in airtight containers protected from light.

❖ **Popular Brand Names**

- Thalidon
- Hygroton
- Hythalton

❖ **Dose**

- 50-100 mg once a day in the morning;

❖ **Medicinal Uses**

- It is used for the treatment of oedema associated with congestive heart failure.

BENZTHIAZIDE

- Benzthiazide belongs to thiazide group of diuretics. It is more potent than chlorothiazide.

❖ **Chemical Formula** - $C_{15}H_{14}ClN_3O_4S_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 6-chloro-1,1-dioxo-3-(phenylmethylsulfanylmethyl)-4H-benzo[e][1,2,4]thiadiazine-7-sulfonamide

❖ **Physiochemical Properties**

- It is a white crystalline powder with a characteristic odour and taste.
- Benzthiazide is soluble in water, alcohol, chloroform or ether, and in alkaline solutions.

❖ **Pharmaceutical Formulation**

- It is available in the market in the form of tablets. It is administered by mouth.

❖ **Stability and storage**

- It is stored in airtight containers protected from light.

❖ **Popular Brand Names**

- Aquatag
- Ditide
- Diucen
- Edemax

❖ **Dose**

- Usually as diuretic initial dose is 50 to 200 mg per day.

❖ **Medicinal Uses**

- It is used to treat chronic oedema associated with congestive heart failure.

8.4 THIAZIDE-LIKE DIURETICS

❑ METOLAZONE

- It is a quinazoline derived non-thiazide diuretic, exerts its diuretic effect in the PT and in the cortical segment of the ascending limb of henle or distal convoluted tubule.
- Patients with non-oedematous, stable chronic renal failure, and high dosage of Metolazone increases urine flow significantly.

❖ **Chemical Formula** - $C_{16}H_{16}ClN_3O_3S$

❖ Structure



❖ IUPAC Nomenclature

- 7-chloro-2-methyl-4-oxo-3-o-tolyl-1,2,3,4-tetrahydroquinazoline-6-sulfonamide

❖ Physiochemical Properties

- Metolazone is a colourless, odourless, tasteless, crystalline powder, sparingly soluble in water or alcohol, but soluble in organic solvents.

❖ Pharmaceutical Formulation

- It is available in the market in the form of tablets. It is administered by mouth.

❖ Stability and storage

- It is stored in airtight containers protected from light.

❖ Popular Brand Names

- Zytanix
- Metoz
- Zaroxolyn

❖ Dose

- Usually as diuretic initial dose is 5–20 mg once a day in the morning.

❖ Medicinal Uses

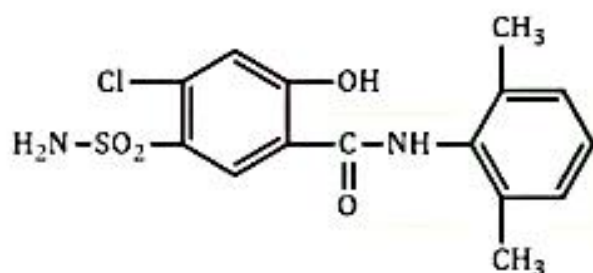
- It is used for hypertension and edema accompanying congestive heart failure.

❑ **XIPAMIDE**

- Xipamide resembles in chemical structure with Chlorthalidone. It has diuretic, hypotensive and toxic effects similar to thiazides. It is prepared synthetically.
- It is a sulfonamide diuretic drug. It is structurally related to Indapamide and exerts its diuretic effect at the distal section of the nephron.

❖ **Chemical Formula** - $C_{15}H_{15}ClN_2O_4S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-chloro-N-(2,6-dimethylphenyl)-2-hydroxy-5-sulfamoylbenzamide

❖ **Physiochemical Properties**

- It is a yellowish white, odourless, crystalline powder.
- It is soluble in water and alcohol and freely soluble in solutions of alkali hydroxides.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet.

❖ **Stability and storage**

- It is stored in airtight containers protected from light.

❖ **Popular Brand Names**

- Aquaphor
- Aquaphoril

❖ **Dose**

- Usually as diuretic initial dose is 20–40 mg once a day in the morning.

❖ **Medicinal Uses**

- It is used for the treatment of edema and hypertension.

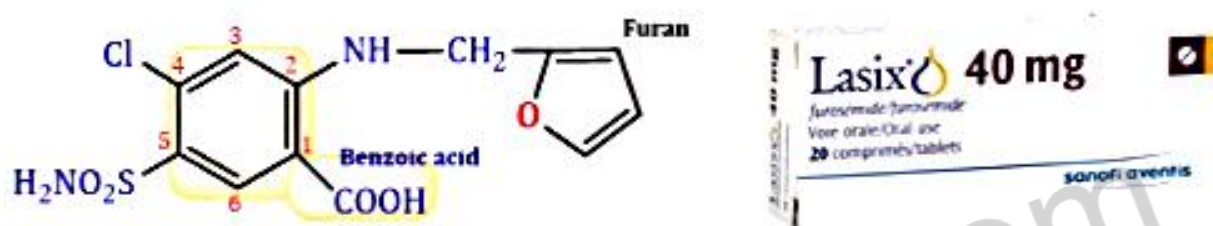
8.5 LOOP DIURETICS

❑ FRUSEMIDE

- Frusemide is related to sulfonamide but is a more powerful (potent) diuretic.
- Chemically it is a derivative of sulfa compound with a 2-Methyl Furan attached to the amino nitrogen. It is a white crystalline powder insoluble in water. But its sodium salt may be given as an injection.
- It has an immediate and shorter duration of action.

❖ **Chemical Formula** $C_{12}H_{11}ClN_2O_5S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-Chloro-2-[[furan-2-ylmethyl]amino]-5-sulfamoylbenzoic acid

❖ **Physiochemical Properties**

- It occurs as white crystalline powder and insoluble in water.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet and injection.

❖ **Stability and storage**

- It should be stored in well-closed airtight containers and protected from light.

❖ **Popular Brand Names**

- Lasix
- Furoscix

❖ **Dose**

- Usually 20–80 mg once daily in the morning. In renal insufficiency, upto 200 mg 6 hourly given by I.M. / I.V. route.

❖ **Medicinal Uses**

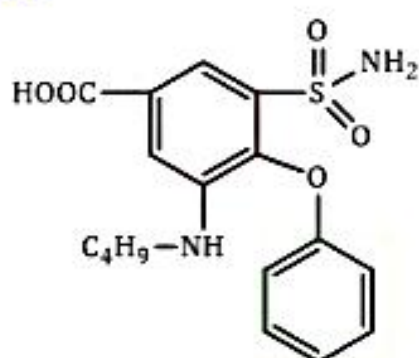
- As a diuretic.
- It is widely used to treat hypertension and edema.

❑ **BUMETANIDE**

- Bumetanide is a high ceiling (loop) diuretic. It is prepared synthetically. It occurs as white crystalline powder.
- It is odourless. It is sparingly soluble in water. It is a potent diuretic with short duration of action.
- It is 40 times more potent than furosemide. It is also known as loop diuretic because the principal site of action is the thick ascending segment of loop of henle.

❖ **Chemical Formula** - $C_{17}H_{20}N_2O_5S$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-butylamino-4-phenoxy-5-sulfamoyl-benzoic acid

❖ **Physiochemical Properties**

- It is a white crystalline powder and insoluble in water.
- It is soluble in alkaline solution. It works by blocking the active reabsorption of chloride and sodium ion in the ascending loop of Henle.

❖ **Pharmaceutical Formulation**

- It is available in the market in the form of tablets and injection.

❖ **Stability and storage**

- It is stored in airtight containers protected from light.

❖ **Popular Brand Names**

- Burinex
- Bumet

❖ **Dose**

- 1-5 mg oral once daily in the morning, 2-4 mg I.V. / I.M.

❖ Medicinal Uses

- It is used for the treatment of edema associated with congestive heart failure, hepatic and renal diseases.
- It is also used for the treatment of hypertension.

8.6 CARBONIC ANHYDRASE INHIBITORS

❑ ACETAZOLAMIDE

- Acetazolamide is a sulphonamide derivative with a Thiadiazole ring.
- Acetazolamide is a diuretic of carbonic anhydrase inhibitor class.

❖ Chemical Formula - $C_4H_6N_4O_3S_2$

❖ Structure



❖ IUPAC Nomenclature

- N-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl) acetamide

❖ Physiochemical Properties

- It occurs as white to faintly yellowish white crystalline powder and odourless. It is weakly acidic and slightly soluble in water.

❖ Pharmaceutical Formulation

- It is formulated form of intravenous injection and tablet and capsule.

❖ Stability and storage

- It should be stored in well-closed airtight containers and protected from light.

❖ Popular Brand Names

- Diamox
- Synomax
- IOPAR-SR

❖ Dose

- The usual dose is 250 mg OD/BD.

❖ Medicinal Uses

- As a diuretic
- In Glaucoma
- In Peptic ulcer and
- In Epilepsy etc.

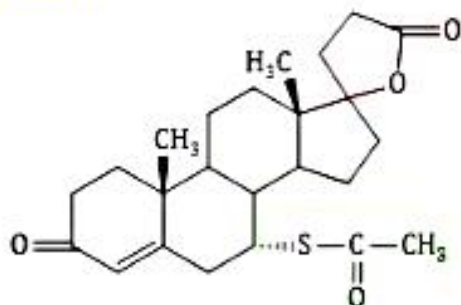
8.7 POTASSIUM SPARING DIURETICS

❑ SPIRONOLACTONE

- It is a potassium sparing diuretic and act as an aldosterone receptor antagonist.

❖ Chemical Formula - $C_{24}H_{32}O_4S$

❖ Structure



❖ IUPAC Nomenclature

- 7 α - acetylthio-17 α -hydroxy-3-oxopregn-4-ene-21-carboxylic acid γ -lactone

❖ Physicochemical Properties

- It occurs as light cream coloured crystalline powder with mercaptan like odour.
- It is insoluble in water, slightly soluble in methanol, soluble in ethyl acetate and ethanol.

❖ Pharmaceutical Formulation

- It is formulated form of tablet and solution form.

❖ Stability and storage

- It is stable in air.
- It is stored in a tight and light resistant container.

❖ Popular Brand Names

- Aldactone
- CaroSpir