Name of Unit	Antihistaminic Agents, Gastric Proton Pump Inhibitors & Anti-Neoplastic Agents
Subject /Course	Medicinal Chemistry-II
Subject/Course ID	BP 501T
Class: B.Pharm. Semester	5th
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Learning Outcome of Module 02

LO	Learning Outcome	Course Outcome Code
LO1	To understand the classification, uses & mechanism of action of antianginal agents.	BP501.1
LO2	To understand the chemical synthesis of selected drugs.	BP501.2
LO3	To understand the Structural Activity Relationship of different class of drugs.	BP501.4

Content Table

Topic
Anti-Anginal Vasodilators: Amyl nitrite, Nitroglycerin*, Pentaerythritol tetranitrate, Isosorbide dinitrite*, Dipyridamole. Calcium Channel Blockers: Verapamil, Bepridil hydrochloride, Diltiazem hydrochloride, Nifedipine, Amlodipine, Felodipine, Nicardipine, Nimodipine. **Diuretics** Carbonic anhydrase inhibitors: Acetazolamide*, Methazolamide, Dichlorphenamide. Thiazides: Chlorthiazide*, Hydrochlorothiazide, Hydroflumethiazide, Cyclothiazide. Loop diuretics: Furosemide*, Bumetanide, Ethacrynic acid. Potassium sparing Diuretics: Spironolactone, Triamterene, Amiloride. Osmotic Diuretics: Mannitol. **Anti-Hypertensive Agents** Timolol, Captopril, Lisinopril, Enalapril, Benazepril hydrochloride, Quinapril hydrochloride, Methyldopate hydrochloride,* Clonidine hydrochloride, Guanethidine monosulphate, Guanabenz acetate, Sodium nitroprusside, Diazoxide, Minoxidil, Reserpine, Hydralazine hydrochloride.

ANTI-ANGINAL

Angina pectoris, usually referred to as **angina**, denotes severe chest pain which may be caused by **ischemia** (lack of blood, and hence lack of oxygen supply) of heart muscle. This ischemia is the result of **obstruction** or **spasm of coronary artery** (vessels supplying blood to heart). Thus, the main cause of angina is coronary artery disease which results from atherosclerosis of the cardiac arteries.

Unstable angina (usually grouped with similar conditions as the acute coronary syndrome) may have symptoms like:

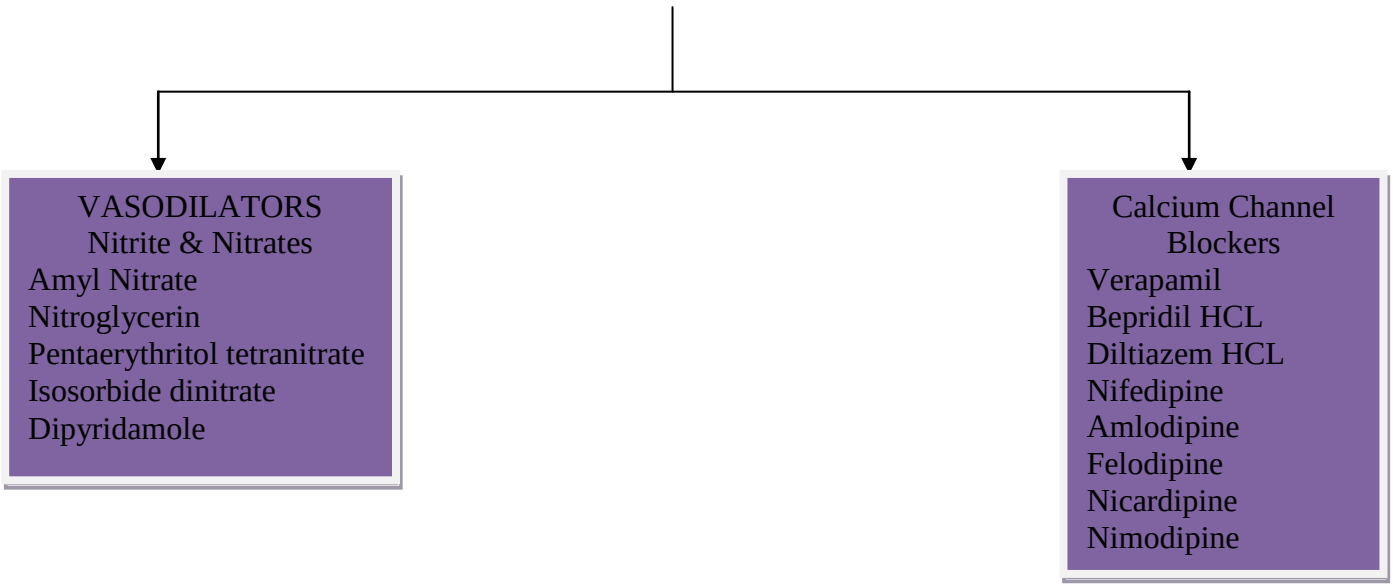
1) Worsening ("crescendo") of angina attacks,

2) Sudden onset of angina at rest, and

3) Angina lasting more than 15 minutes.

CLASSIFICATION

ANTI ANGINAL DRUGS



VASODILATORS

Organic nitrates and nitrites are simple nitric and nitrous acid esters of glycerol having different volatilities (**e.g.,** isosorbide dinitrate and isosorbide mononitrateare so lids at room temperature , nitro glycerine is moderately volatile, and amyl nitrite is highly volatile). These compounds are used in angina pectoris. They rapidly reduce the myocardial oxygen demand, followed by rapid relief of symptoms. They are effective in classic as well as in variant angina pectoris. Organic nitrates cause arterial and venous vasodilation by directly acting on the arterial and vascular

smooth muscle s. Nitroglycerine and isosorbide dinitrate decrease the oxygen consumption and restore the balance between oxygen supply. and oxygen demand by decreasing the preload and afterload. Coronary blood flow remains unchanged . Reduction in mean blood pressure activates the sympathetic nervous system. The decrease in oxygen consumption due to arterial and venous vasodilation is partly reversed by the increase in heart rate and contractility. Organic nitrates inhibit or reverse coronary artery spasm in variant angina patients.

Mechanism of Action

Nitrates principally act by direct non -specific relaxation of smooth muscles. The principle of action for all organic nitrates is the same; they only differ in their duration of action.

The mechanism can be explained as follows:

1) Enzymatic de -nitration of organic nitrates occurs rapidly in the smooth muscle cells, which releases the reactive free radical nitric oxide (NO).

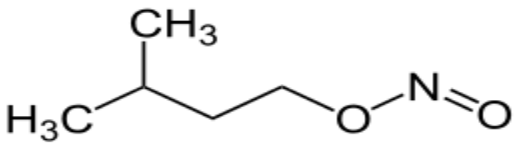
2) This radical activates the cytosolic guanylyl cyclase , which in turn increasescGMP. This dephosphorylates Myosin Light Chain Kinase (MLCK) via cGMP dependent protein kinase

3) Thus, the availability of pho sphorylated (active) MLCK is decreased, which in turn interrupts myosin activation.

4) It does not interact with actin and thus does not cause contraction. Hence, relaxation occurs.

5) Concentration of cGMP within the cells is also increased which may decrease the entry of Ca2+ ions, contributing to relaxation.

1. **Amyl Nitrite**



Mechanism of Action

The anti-anginal activity of amyl nitrite is due to the reduction in systemic and pulmonary arterial pressure (after load) and decreased the cardiac output due to peripheral vasodilation (and not coronary artery dilation). Amyl nitrite is a source of nitric acid that is responsible for the above mentioned mechanism. Amyl nitrite when used as an antidote to cyanide poisoning

stimulate the formation of met hemoglobin that combines with cyanide to form cyanmethemoglob (non-toxic).

Uses

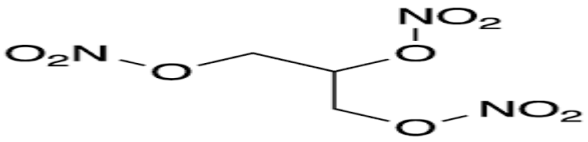
1) It is used in the treatment of heart diseases and angina.

2) Sometimes, it is used as an antidote to cyanide poisoning. To aid the formation of met hemoglobin, amyl nitrite acts as an oxidant. The formed met hemoglobin in turn sequesters Cyanide as cyanomethemoglobin.

3) It used as a cleaning agent and solvent in industrial and household applications. It replaced Dichlorodifluoromethane, an industrial chemical used as a printed circuit board cleaner thatwas banned in 1996 due to the damage to ozone layer.

4) It is added in some perfumes in a very small quantity.

2. Nitroglycerine



Mechanism of Action

Nitroglycerine acts by dilating the blood vessels, thus affecting the vascular smooth muscles. It decreases the cardiac oxygen demand in case of stable angina, and increases the oxygen supply in variant angina.

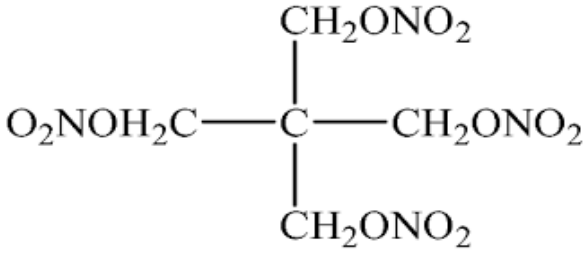
Uses

1) It is administered sublingually for treating angina and left ventricular failure.

2) Its intravenous administration helps in controlling hypertension during heart surgery, and in Congestive heart failure (unresponsiveness to general treatments).

3) As a result of improved left ventricular function and reduced pulmonary arterial pressure, it Provides sudden relief of paroxysmal nocturnal dyspnoea.

3. Pentaerythritol Tetranitrate



Mechanism of Action

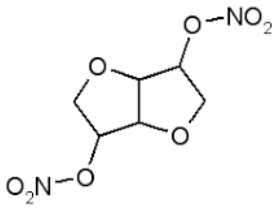
Pentaerythritol tetranitrate is a lipid -soluble polyolester of nitric acid of nitro vasodilators class. After the de -nitration reaction, pentaerythritol tetranitrate releases free nitric oxide (NO) that triggers NO -dependent signaling transduction that involves the soluble guanylate cyclase (sGC).

Uses

1) It is used as a vasodilator just like nitroglycerine (glyceryl dinitrate) and other nitrates for treating heart conditions.

2) It is used in the treatment of angina pectoris.

4. Isosorbide Dinitrate



Mechanism of Action

Isosorbide dinitrate is converted to nitric oxide (NO) just like the other nitrites and organic nitrates. Nitric oxide is an active intermediate that activates guanylate cyclase (atrial natriuresis peptide receptor A) enzyme, and stimulates the synthesis of cyclic guanosine 3',5'-monophosphate (cGMP).

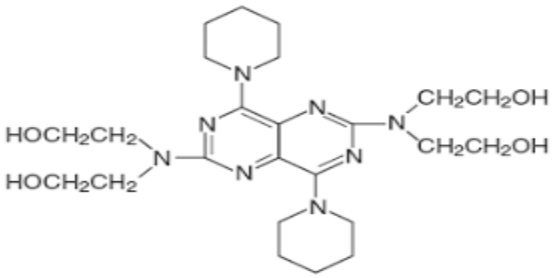
Uses

1) It is used for treating angina, congestive heart failure and oesophageal spasms.

2) It is also used for treating or preventing the angina attacks.

3) It dilates the blood vessels so that the blood flow easily through them and the heart also pumps blood easily.

5. Dipyridamole



Mechanism of Action

Dipyridamole inhibits adenosine deaminase and phosphodiesterase, thus prevents the degradation of cAMP (inhibitor of platelet function). This increase in cAMP concentration inhibits the release of arachidonic acid from membrane phospholipids and reduces the activity of thromboxane A2. Dipyridamole also stimulates the release of prostacycling that potentiates the activity of adenylate

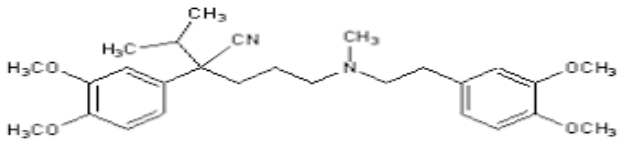
cyclase. Hence, the intra-platelet concentration of cAMP increases and platelet aggregation is blocked.

Uses

1) It is used as an adjunct to Coumarin anticoagulants for preventing post -operative thromboembolic Complications of cardiac valve replacement.

2) It also used for treating angina.

6. Verapamil



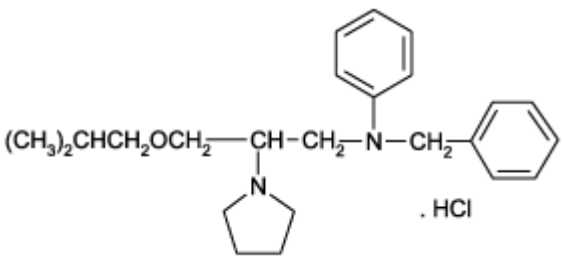
Mechanism of Action

Verapamil blocks the voltage-dependent calcium channels. Its effect on L –type calcium channels in the heart decreases ionotropy and chronotropy, thus lowering the heart rat e and blood pressure. The mode of action of Verapamil in cluster headache is linked to its calcium channel blocking activity; however, the channel sub-types involved is still unknown.

Uses

It is the first generation calcium channel blocker used for treating hyper tension, supraventricular tachyarrhythmias, cluster headache prophylaxis, and angina pectoris.

7. Bepridil Hydrochloride

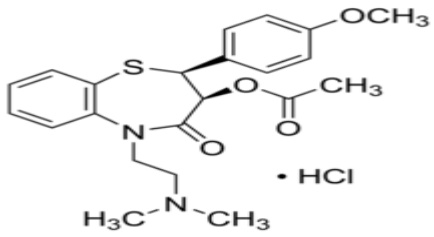


Mechanism of Action

Bepridil has inhibitory effects on slow calcium (L-type) as well as on fast sodium inward currents in myocardial and vascular smooth muscle s. It interrupts the binding of calcium to calmodulin, and inhibits voltage and receptor operated calcium channels. Bepridil blocks the transmembrane influx of calcium ions into cardiac and vascular smooth muscles. It lowers the heart rate and arterial pressure at rest and at a given level of exercise by causing peripheral arteriole dilation and reducing the total peripheral resistance (after load) against which the heart works.

Uses It is used for treating hypertension and chronic stable angina (classic effort -associated angina).

8. Diltiazem Hydrochloride



Mechanism of Action

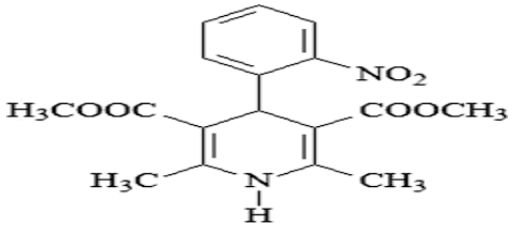
Diltiazem hydrochloride blocks the influx of extracellular calcium across the myocardial and vascular smooth muscle cell membranes. It does so by deforming the channel, blocking ion-control gating mechanisms, and/or inhibiting calcium release from sarcoplasmic reticulum. As a result, the contractile processes of the myocardial smooth muscle cells are inhibited, and this causes the dilation of coronary and systemic arteries, and enhances oxygen delivery to the myocardial tissue.

Uses

1) It is used for treating angina and hypertension.

2) It is used for treating supraventricular tachycardias (PSVT) as effectively as Verapamil.

9. Nifedipine



Mechanism of Action

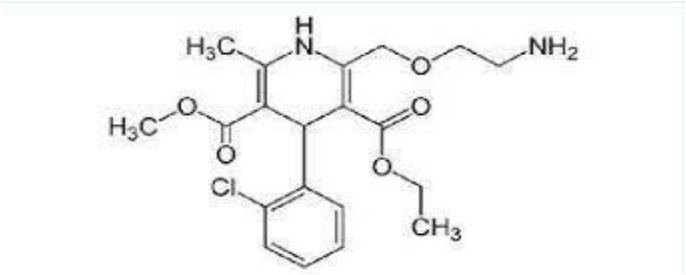
Nifedipine blocks the influx of extracellular calcium through the myocardial and vascular membrane pores by physically plugging the channel. The decrease in intracellular calcium blocks the con tactile processes of smooth muscle cells. This causes dilation of the coronary and systemic arteries, increases oxygen delivery to myocardial tissue s, decreases total peripheral resistance, decreases systemic blood pressure, and decreases after load.

Uses

1) It is used in the treatment of vasospastic angina, chronic stable angina, hypertension, and Reynaud's Phenomenon.

2) It is also used as a first line agent for left ventricular hypertrophy and for isolated systolic hypertension (long-acting agents).

10. Amlodipine



Mechanism of Action

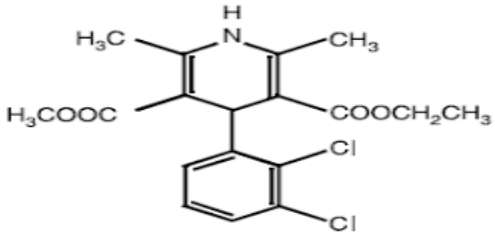
Amlodipine inhibits the influx of calcium ions through L -type calcium channels, thus reduces the contractility and vasoconstriction of arterial smooth muscle s. Calcium ions enter the cells through L-type calcium channels and bind to calmodulin. The resultant complex binds to and activates Myosin Light Chain Kinase (MLCK). Phosphorylation of the regulatory light chain subunit of myosin is catalysed by the activated MLCK; this is a key step in muscle contraction.

Uses

1) It is a long-acting calcium channel blocker used for treating mild to moderate essential hypertension and exertion-related angina (chronic stable angina).

2) It is used alone or with other antihypertensive and anti -anginal drugs for treating coronary artery disease, chronic stable angina , and vasospastic angina (Prinzmetal's or variant angina).

11. Felodipine



Mechanism of Action

It inhibits the influx of calcium ions through L-type calcium channel. It also act as an antagonist of mineralocorticoid receptor.

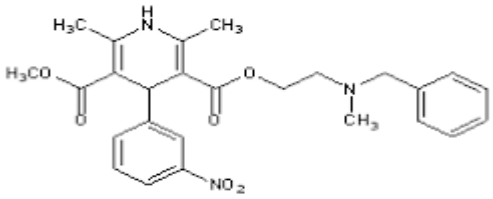
Uses

1) It is used for treating hypertension.

2) It lowers high blood pressure and prevents strokes, heart attacks, and kidney problems.

3) It is used for treating angina.

12. Nicardipine



Mechanism of Action

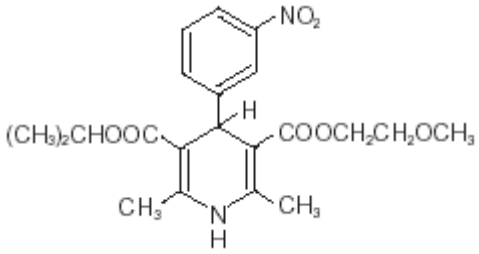
Nicardipine blocks the influx of extracellular calcium across the myocardial and vascular smooth muscle cell membranes. It does so by deforming t he channel, inhibiting ion -control gating mechanisms, and/or interrupting calcium release from the sarcoplasmic reticulum. As a result of reduced intracellular calcium, the contractile processes of myocardial smooth muscle cells are inhibited. This leads to the dilation of coronary and systemic arteries, increased oxygen delivery to myocardial tissues, decreased total peripheral resistance, decreased systemic blood pressure, and decreased after load.

Uses

1) It is used for treating chronic stable angina.

2) It is also used in the treatment of hypertension

13. Nimodipine



Mechanism of Action

Same as Nicardipine

Uses

It is used as an adjunct to improve neurologic outcome following Subarachnoid Hemorrhage (SAH) from ruptured intracranial berry aneurysms by decreasing the occurrence and severity of ischemic deficits.

DIURETICS

Diuretics are the chemical agents which increase the excretion of urine by kidneys. They lead to the secretion of excess water and salt that accumulate in tissues and urine, results in decrease in body fluids especially the extracellular fluid. So, diuretics are used in management of heart failure, edema or hypertension.

Classification

1. Carbonic anhydrase inhibitors: Acetazolamide, Methazolamide, Dichlorphenamide.
2. Thiazides: Chlorthiazide, Hydrochlorothiazide, Hydroflumethiazide, Cyclothiazide.
3. Loop diuretics: Furosemide, Bumetanide, Ethacrynic acid.
4. Potassium sparing Diuretics: Spironolactone, Triamterene, Amiloride.
5. Osmotic Diuretics: Mannitol.

1. CARBONIC ANHYDRSE INHIBITORS:-

Carbonic anhydrase is an enzyme which is involved in the conversion of CO2 and H2O into H and HCO3, H gets exchanged with sodium ions while the HCO, gets reabsorbed. Blockage of this enzyme decreases the exchange of H- Na ions and hence make the urine more alkaline and there is large excretion of Na' and HCO, ions .Inhibition of carbonic anhydrase inhibits reabsorption of HCO3 and there is accumulation of HCO3, in the tubular lumen. There is decrease in amount of H ions available for exchange with Na. So large amount of Na ions retained in the tubule and gets excreted by the kidney with an increased volume of water. There is also significant loss of K.The urine which is normally acidic becomes alkaline and systemic acidosis occurs. During acidosis, the carbonic anhydrase inhibitors are not effective till the ache base balance is restored.

2. THIAZIDES:-

Thiazides diuretics act mainly to block sodium and chloride reabsorption at the best portion of the distal tubules. Thiazides inhibit a Na Cl symport in the luminal membrane of the epithelial cells in the distal convoluted tubule. Thus, thiazides inhibit NaCl reabsorption in the distal convoluted tubule, and may have a small effect on the NaCl reabsorption in the proximal tubule. Thiazides enhance Ca reabsorption in the distal convoluted tubule by inhibiting Na entry and thus enhancing the activity of Na Ca exchanger in the basolateral membrane of epithelial cells.

They also have a mild anti carbonic anhydrase effect. The resulting diuretics are accompanied by increased excretion of potassium bicarbonates, chloride, and water

The anti-hypertensive action of the thiazide is attributable to two factors:

a) Depletion of sodium and subsequent reduction in plasma volume, and

b) A decrease in peripheral resistance.

3. LOOP DIURETICS:- Loop diuretic acts mainly at thick ascending limb of the loop of Henle. These diuretics produce peak diuresis which is much greater than other diuretics. Loop diuretics inhibit reabsorption of Na^+, CI^- and K^+ ions by inhibiting Na+/K+/2CI^- symport of the thick ascending limb of loop of Henle. By inhibiting Na/K/2CI^- symport, these agents also inhibit reabsorption of Ca++ and Mg++

Earlier it was investigated that organo mercurial diuretics acted by blocking renal enzyme possessing sulfhydryl (-SH) groups.

The high ceiling diuretics are effective in the treatment of acute pulmonary odema, hypertension, hypocalcaemia, Hyperkalemia, acute renal failure and in treatment of toxic ingestion of bromide, fluoride and iodide.

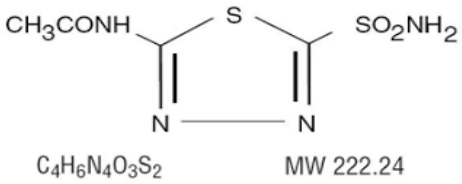
4. POTASSIUM SPARING DIURETICS:-Potassium sparing diuretics are mild diuretics that inhibit the sodium reabsorption in the late distal tubule and thus indirectly spare potassium excretion. They tend to cause bicarbonate loss, but not chloride.

5. OSMOTIC DIURETICS:-

Mechanism of action: Osmotic diuretics are filtered at the glomerulus and are not reabsorbed by the renal tubules Because of its osmotic action in the proximal tubules, these prevent the absorption of water and impair sodium reabsorption by lowering the concentration of sodium in the tubular fluid. In the loop of Henle, these reduce medullary hypertonicity by increasing medullary blood flow. In the collecting duct, these reduce sodium and water reabsorption because of papillary washout and high flow rate. The primary sites of action for osmotic diuretics are the Loop of Henle and the proximal tubule where the membrane is most permeable to water.

DRUGS

1. Acetazolamide:-



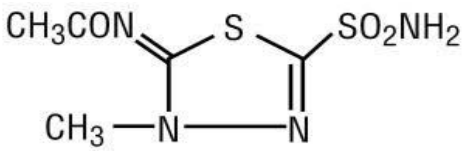
Uses

1 It is used in the treatment of glaucoma and drug induced edema.

2 It is also used as an anticonvulsant for treatment of epilepsy.

3 It has also been used in the treatment of Meniere's disease (disorder of inner ear), attitude sickness and neuromuscular disorders.

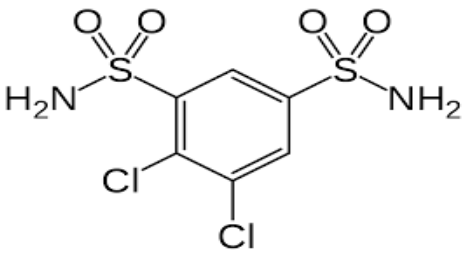
2) Methazolamide



USES

1. It is used as a diuretic.
2. It is used in the treatment of glaucoma.
3. It is also having antineoplastic activity.

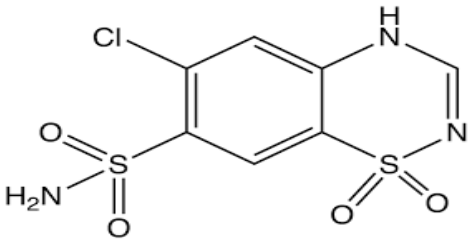
3) Dichlorphenamide



USES

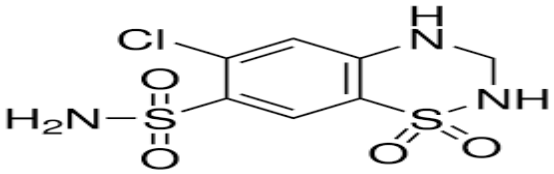
1. It is used in the treatment of glaucoma.
2. It is found effective in cases of therapy resistant epilepsy.
3. It is also used as diuretics.

4) Chlorothiazide



USES; It is used as diuretic & as an antihypertensive. It is also used to manage excess fluid associated with CHF.

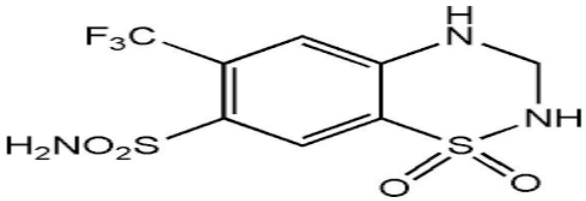
5) Hydrochlorothiazide



USES

It is used as a diuretic or as an antihypertensive drug. It is given with potassium supplements due to excessive loss of potassium ions in the routine treatment of hypertension.

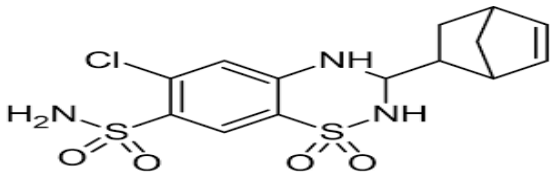
6) Hydroflumethiazide



USES

It is as an antihypertensive & diuretic.

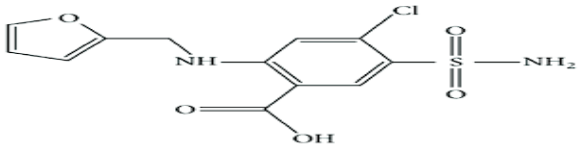
7) Cyclothiazide



USES

1. It is used as a diuretic.
2. It is given as adjunctive therapy in edema associated with CHF.
3. It is also used in the management of hypertension.

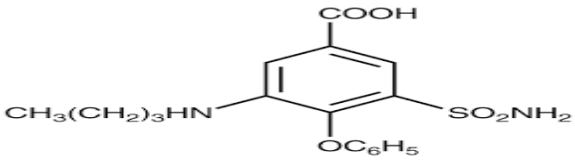
8) Furosemide



USES

It is used as a diuretic for the treatment of odema, antihypertension & CHF. It is having weak carbonic anhydrase inhibitor activity.

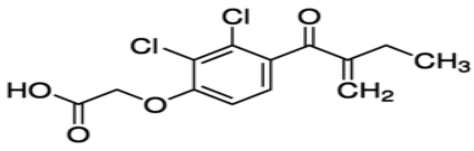
9) Bumetanide



USES

It is used for the treatment of odema & hypertension.

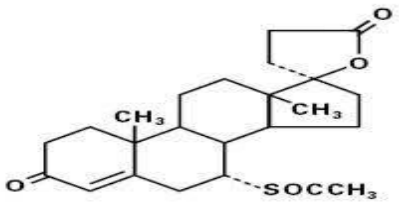
10) Ethacrynic acid



USES

It is used for the treatment of odema & hypertension.

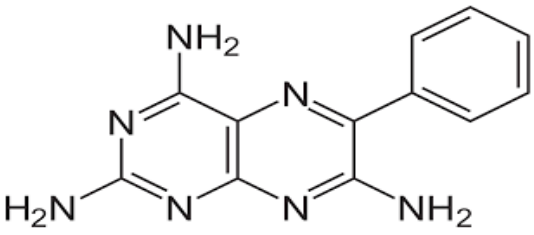
11) Spironolactone



USES

1. It is used in the treatment of refractory odema associated with nephritic syndrome, CHF & cirrhosis of liver.
2. It is used to spare the potassium ions with other diuretic agents.

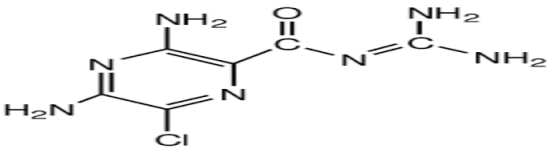
12) Triamterene



USES

It is used as diuretic in treatment of refractory odema.

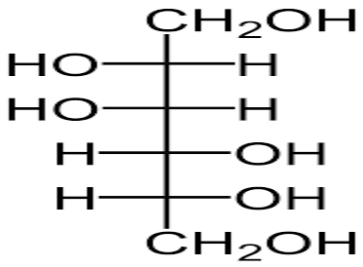
13) Amiloride



USES

In conjunction other diuretics it is used in the treatment of refractory odema associated with nephritic syndrome, cirrhosis of liver & CHF.

14) Mannitol



USES

1. Mannitol is used as diagnostic agent for kidney function.
2. It is often used in the management of cerebral odema.
3. It is used to increase urine volume in patient with acute renal failure.

HYPERTENSION

It is one of the common cardiovascular disorders and it is a state of the body in which the systolic blood pressure (BP) is 150 mm Hg or more and diastolic BP is 95 mm Hg or more. Hypertension may be classified into primary and secondary:

PRIMARY HYPERTENSION

It is otherwise known as essential hypertension. It is characterized by the following:

- Elevation of diastolic BP.
- Normal cardiac output.
- An increase in peripheral resistance.

SECONDARY HYPERTENSION

Factors causing secondary hypertension are as follows:

- Acute or chronic renal disease.
- Hyperaldosteronism.

- Cushing's syndrome.
- Oral contraceptives, steroids, estrogen, and sympathomimetics.

Antihypertensive drugs are defined as the drugs that are used to decrease the elevated blood pressure (hypertension).

CLASSIFICATION

1. Diuretics

2. Drugs acting on sympathetic system

a. **Centrally acting drugs:** - Clonidine, Methyldopate hydrochloride, Guanabenz acetate.

b. **Adrenergic blockers:-** Timolol,

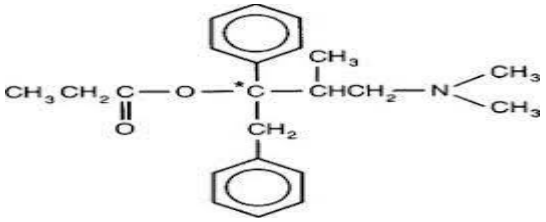
3. Adrenergic neuron blockers: - Guanethidine monosulphate & Reserpine.

4. Direct vasodilators:- Diazoxide, Minoxidil & Hydralazine hydrochloride.

5. Angiotensin Converting Enzymes Inhibitors (ACE):-Captopril, Lisinopril, Enalapril, Benazepril hydrochloride, Quinapril hydrochloride,

DRUGS

1. **Timolol**

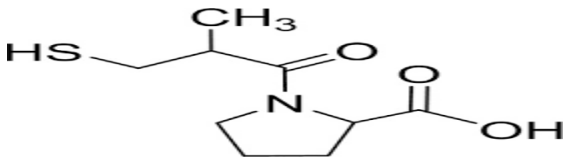


Mechanism of action:- The blockade of beta(2) receptors by timolol in the blood vessels leads to a decrease in peripheral vascular resistance, **reducing blood pressure**. The exact mechanism by which timolol reduces ocular pressure is unknown at this time, however, it likely decreases the secretion of aqueous humor in the eye.

USES:-

- This medication is used to treat high pressure inside the eye due to glaucoma (open angle-type) or other eye diseases (e.g., ocular hypertension). Lowering high pressure inside the eye helps to prevent blindness.
- This medication works by decreasing the amount of fluid within the eye.

2. Captopril

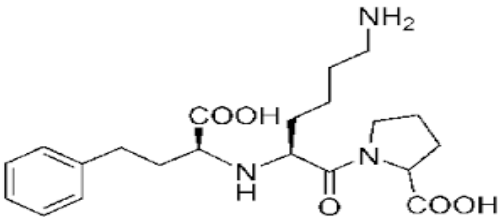


Mechanism of action:- Captopril blocks the conversion of angiotensin I to angiotensin II and prevents the degradation of vasodilatory prostaglandins, thereby inhibiting vasoconstriction and promoting systemic vasodilation.

USES:-

It is used for treatment of hypertension, heart failure, myocardial infarction & diabetic nephropathy.

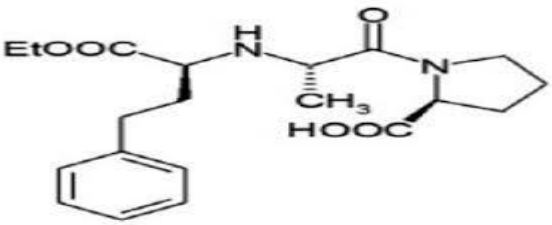
3. Lisinopril



Mechanism of action:-It acts by blocking the action of ACE.

USES:-It is used for the management of hypertension, heart failure and diabetic nephropathy & prophylactic after myocardial infaraction.

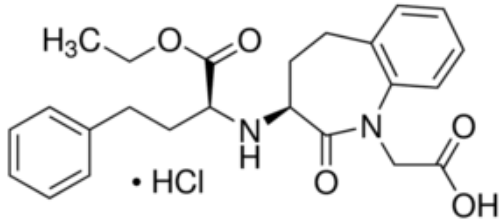
4. Enalapril



Mechanism of action:-It inhibits the ACE & block the conversion of Angiotensin I to Angiotensin II.

USES:-It is used for treatment of hypertension & heart failure.

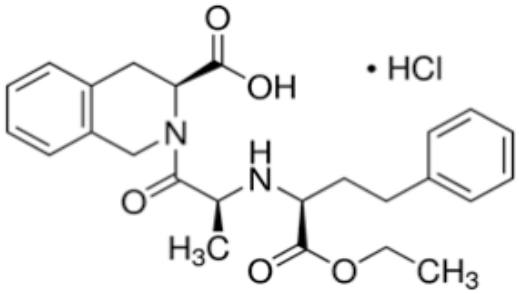
5. **Benazepril hydrochloride**



Mechanism of action:- Benazepril, after hydrolytic bioactivation to benazeprilat, inhibits angiotensin converting enzyme (ACE), a peptidyl dipeptidase catalysing the conversion of angiotensin I to the vasoconstrictor angiotensin II.

USES:-It is useful for hypertension, heart failure & diabetic kidney disease. It is also used in kidney & heart failure in dogs & cats.

6. **Quinapril hydrochloride**



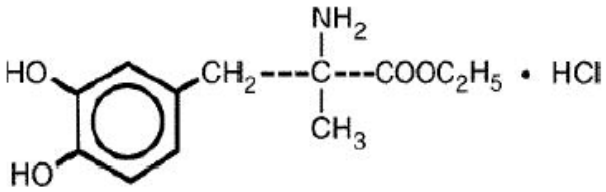
Mechanism of action:- Quinapril hydrochloride is deesterified to the principal metabolite, quinaprilat, which is an inhibitor of ACE activity in human subjects and animals. ACE is a peptidyl dipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor, angiotensin II.

USES:-

- Quinapril is used to treat high blood pressure. Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems.

- This medication is also used to treat heart failure. Quinapril belongs to a class of drugs known as ACE inhibitors.

7. Methyldopate hydrochloride

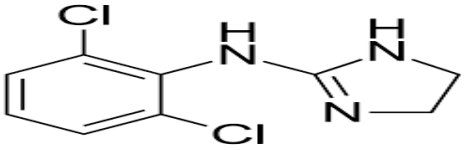


Mechanism of action:-It converts into α-methyl noradrenaline, which is potent α_2-adrenergic agonist.

USES:-

It is used as antihypertensive agents.

8. Clonidine hydrochloride

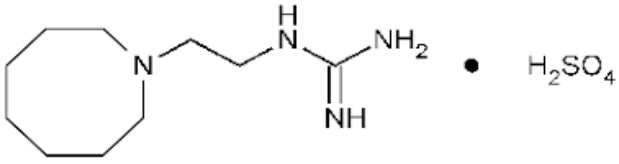


Mechanism of action:-It act by stimulating α_2 _adrenergic receptor in CNS which results in decrease in the sympathetic outflow from the CNS.

USES:-

- This medication is used alone or with other medications to treat high blood pressure (hypertension). Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems.
- Clonidine belongs to a class of drugs (central alpha agonists) that act in the brain to lower blood pressure.

9. Guanethidine monosulphate:-

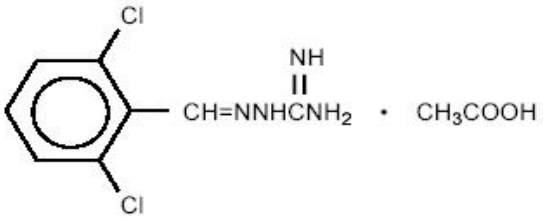


Mechanism of action:- Guanethidine works by decreasing the heart rate and relaxing the blood vessels so that blood can flow more easily through the body, thereby reducing these risks. It is a postganglionic sympathetic nerve terminal blocker that prevents the release of norepinephrine from nerve terminals.

USES:-

- It is used in treatment of hypertension.
- It is also used in the topical treatment of open angle glaucoma.
- It has been used to treat chronic pain caused by complex regional pain syndrome (pain of the body usually starts from limb, swelling & changes to skin and bones).

10. Guanabenz acetate

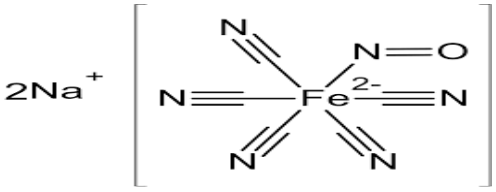


Mechanism of action:-

It acts by stimulating 0,-adrenergic receptors which results in a decreased sympathetic outflow to the heart, kidney and peripheral vasculature.

USES :-It is used to treat high blood pressure.

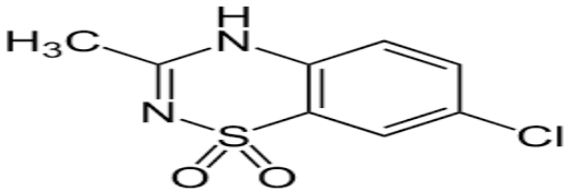
11. Sodium nitroprusside



Mechanism of action:- It is metabolised to nitric oxide which activates guanylate cyclase. This results in vasodilations of both arteries and veins.

USES:- It is used in severe hypertension as a short acting hypertensive agent with duration of action 1 to 10 minutes.

12. Diazoxide

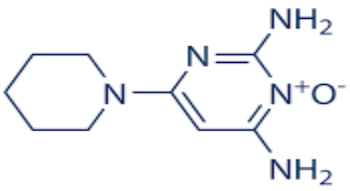


Mechanism of action:-It may act by action on the large conductance calcium activated potassium channel or action on carbonic anhydrase in smooth muscle.

USES :-

- It is used as vasodilator in the treatment of hypertension.
- It is used to counter hypoglycemia in disease state like insulinoma.

13. Minoxidil

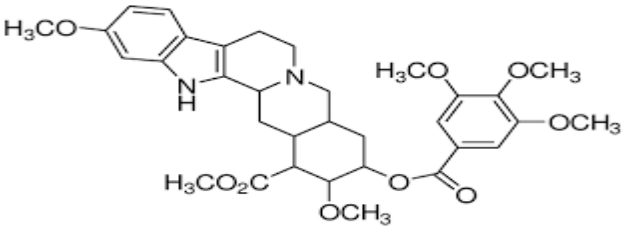


Mechanism of action:- It acts by opening ATP sensitive potassium channels in vascular smooth muscle cells.

USES :-

- Topically, it is widely used in treatment of hair loss.
- It is given by mouth for the treatment of severe hypertension unresponsive to standard therapy.

14. Reserpine



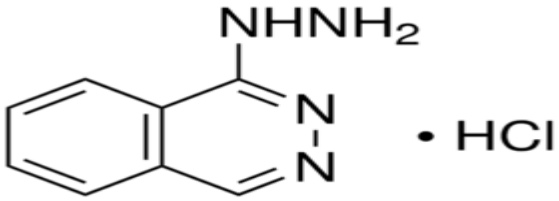
Mechanism of action:- It affects the norepinephrine storage site and decreases stored norepinephrine in peripheral sympathetic nerve terminals as well as decreases catecholamines

and serotonin stores in brain, heart and other organs. This leads to reduction in blood pressure CNS depression and bradycardia.

USES :-

- It is used to treat mild to moderate hypertension.
- It is also used in psychoses treatment.

15. Hydralazine hydrochloride



Mechanism of action:- It is assumed that hydralazine acts by direct relaxation of vascular smooth muscle. It also alters the cellular calcium metabolism and interferes with the calcium movement within the vascular smooth muscle that are responsible for contraction.

USES :-

- It is used to treat high blood pressure and heart failure.
- It is used in combination with isosorbide dinitrate for treatment of congestive heart failure.
- It is not a first line therapy for hypertension because it increases cardiac output and plasma renin concentration which results in fluid retention.

SHORT ANSWER QUESTION (5 Marks)

1. Write a short note on vasodilators.
2. Classify antianginal drugs. Explain any two drugs belongs to organic nitrates
3. Give mechanism of action of a) Vasodilators b) Calcium channel blockers
4. Write the structure and uses of a) Amlodipine b) Isosorbide dinitrate c) Diltiazem
5. Give the synthesis of Nitroglycerine and isosorbide dinifrate.
6. Give the classification and uses of diuretics.
7. Discuss the SAR of diuretics.
8. Write a short note on carbonic anhydrase inhibitors.
9. Discuss loop diuretics.

LONG ANSWER QUESTION (10 Marks)

1. What is an angina pectoris classify antianginal agent? Explain structure, properties, Mechanism of action and uses of Nitroglycerine, Dipyridamole
2. Comment on calcium channel blockers.
3. Discuss potassium sparing diuretics.
4. Give a detailed note on thiazides in detail.
5. What are diuretics? Give their classification, uses and SAR.