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Unit-II/Part-C

Anti-hypertensive Agent

PRESENTED BY;-

MR. SAMARPAN MISHRA (ASSISTANT PROFESSOR)

SPECIALIZATION:- PHARMACEUTICAL CHEMISTRY

Hypertension ?

1. Hypertension, also known as high blood pressure, is a condition where the force of your blood against your artery walls is consistently too high.
2. This can lead to serious health problems like heart disease, stroke, and kidney failure if left untreated.
3. People with high blood pressure may not feel symptoms. The only way to know is to get your blood pressure checked.
4. Things that increase the risk of having high blood pressure include:
 - a. older age
 - b. genetics
 - c. being overweight or obese
 - d. not being physically active
 - e. high-salt diet
 - f. drinking too much alcohol

Healthy and unhealthy blood pressure ranges for all ages:

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)	and/or	DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
<u>HYPERTENSIVE CRISIS</u> (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Antihypertensive agents

- ▶ Antihypertensive agents are classified into several categories based on their mechanisms of action, which are often related to their chemical structures.
- ▶ Common classes include; diuretics, ACE inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers, beta-blockers, and others.
- ▶ These drugs work by targeting different pathways involved in blood pressure regulation, such as the renin-angiotensin system, the sympathetic nervous system, or by affecting blood vessel or heart function directly.

Classification of Antihypertensive agents with MOA

1. Diuretics:

These drugs increase the excretion of sodium and water by the kidneys, reducing blood volume and thus blood pressure.

- a. **Thiazide diuretics:** (e.g., hydrochlorothiazide, chlorthalidone) are commonly used as first-line treatment.
- b. **Loop diuretics:** (e.g., furosemide, bumetanide) are more potent but often reserved for specific situations.
- c. **Potassium-sparing diuretics:** (e.g., spironolactone, amiloride) are often used in combination with other diuretics or for specific conditions.

2. Renin-Angiotensin System (RAS) Inhibitors:

These drugs interfere with the renin-angiotensin system, which plays a crucial role in regulating blood pressure.

- a. **ACE inhibitors:** (e.g., lisinopril, enalapril) block the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor.
- b. **Angiotensin II receptor blockers (ARBs):** (e.g., losartan, valsartan) block the action of angiotensin II at its receptor sites.
- c. **Direct renin inhibitors:** (e.g., aliskiren) directly inhibit the enzyme renin, which initiates the RAS cascade.

Classification of Antihypertensive agents With MOA



3. Calcium Channel Blockers (CCBs):

These drugs block calcium channels in heart muscle and blood vessel walls, leading to vasodilation and reduced heart contractility.

- a. Dihydropyridines: (e.g., amlodipine, nifedipine) primarily affect blood vessels, causing vasodilation.
- b. Non-dihydropyridines: (e.g., verapamil, diltiazem) affect both heart and blood vessels.

4. Beta-blockers:

These drugs block the effects of epinephrine and norepinephrine on beta-adrenergic receptors, leading to reduced heart rate and contractility, and thus lower blood pressure.

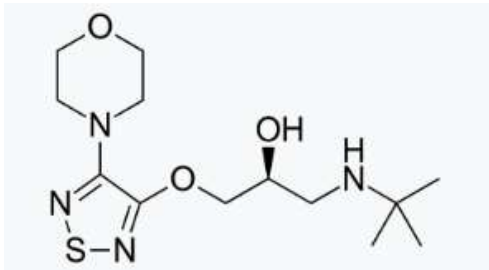
- a. Cardioselective beta-blockers: (e.g., atenolol, metoprolol) primarily affect the heart.
- b. Non-selective beta-blockers: (e.g., propranolol) affect both the heart and other organs.

5. Other Antihypertensive Agents:

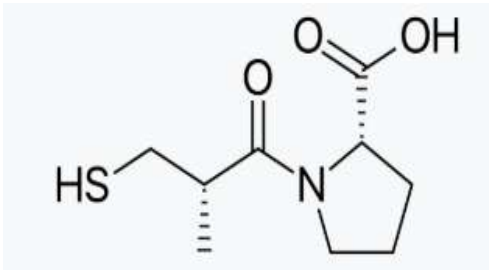
- a. Alpha-blockers: (e.g., prazosin, terazosin) block alpha-adrenergic receptors, causing vasodilation.
- b. Centrally acting agents: (e.g., clonidine, methyldopa) reduce sympathetic outflow from the brain, leading to vasodilation.
- c. Direct vasodilators: (e.g., hydralazine, minoxidil) directly relax blood vessel smooth muscle.

Table showing the Mechanism of Action (MOA) and Uses of the Individual drugs:

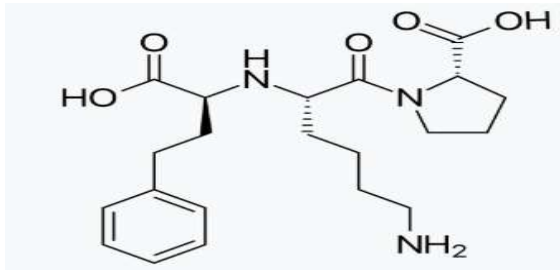
Drug Name	Mechanism of Action (MOA)	Uses
Timolol	Non-selective β -blocker; decreases aqueous humor production	Glaucoma, Hypertension
Captopril	ACE inhibitor; inhibits conversion of angiotensin I to II	Hypertension, Heart failure, Diabetic nephropathy
Lisinopril	ACE inhibitor; inhibits angiotensin II formation	Hypertension, Heart failure, Post-MI
Enalapril	ACE inhibitor; prevents formation of angiotensin II	Hypertension, Heart failure
Benazepril hydrochloride	ACE inhibitor; blocks angiotensin II formation	Hypertension
Quinapril hydrochloride	ACE inhibitor; inhibits angiotensin II production	Hypertension, Heart failure
Methyldopate hydrochloride*	Centrally acting α_2 -adrenergic agonist; decreases sympathetic outflow	Hypertension (especially during pregnancy)
Clonidine hydrochloride	Centrally acting α_2 -adrenergic agonist; decreases sympathetic tone	Hypertension, ADHD, Withdrawal symptoms
Guanethidine monosulphate	Inhibits norepinephrine release from sympathetic nerve terminals	Severe Hypertension (rarely used now)
Guanabenz acetate	Centrally acting α_2 -adrenergic agonist	Hypertension
Sodium nitroprusside	Releases nitric oxide, causes direct vasodilation of arteries and veins	Hypertensive emergencies, Acute heart failure
Diazoxide	Opens K^+ channels in smooth muscle, causes vasodilation	Hypertensive emergencies, Hypoglycemia (insulinoma)
Minoxidil	K^+ channel opener, causes arteriolar smooth muscle relaxation	Severe Hypertension, Hair growth (topical)
Reserpine	Depletes catecholamines and serotonin from nerve terminals	Hypertension (rarely used now)
Hydralazine hydrochloride	Direct arteriolar vasodilator	Hypertension, Heart failure



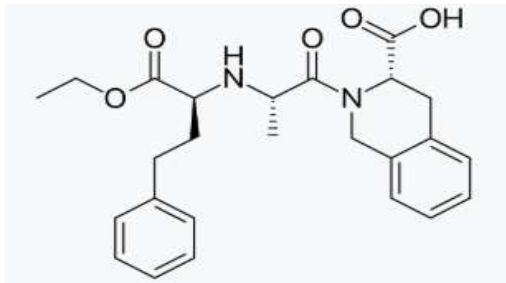
Timolol



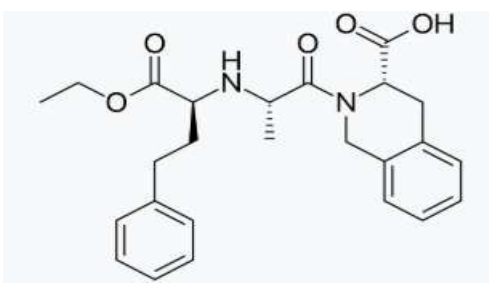
Captopril



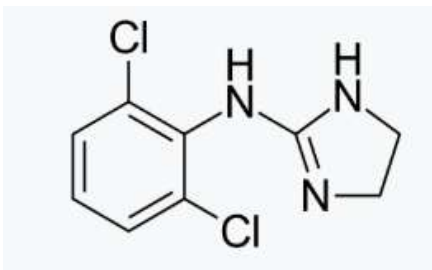
Lisinopril



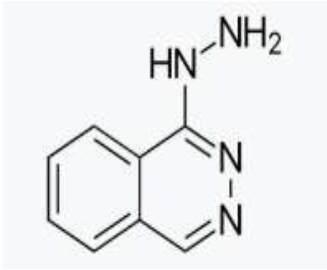
Quinapril.HCl



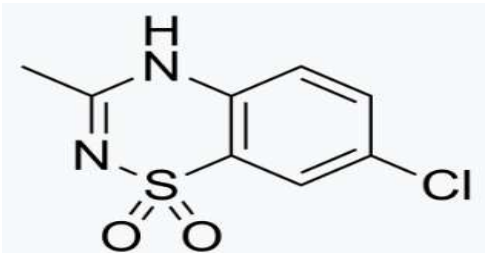
Quinapril.HCl



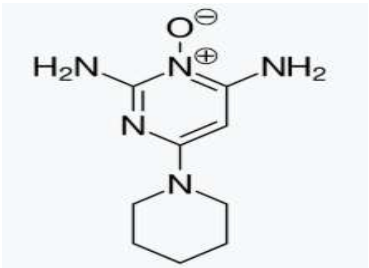
Clonidine.HCl



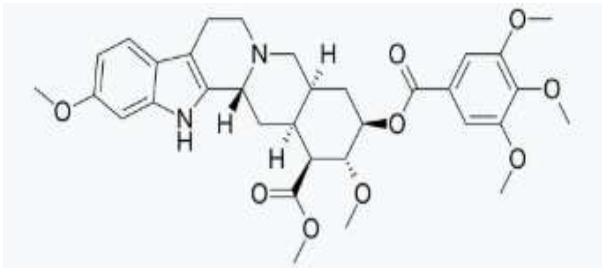
Hydralazine.HCl



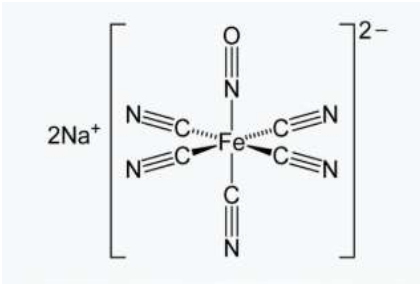
Diazoxide



Minoxidil

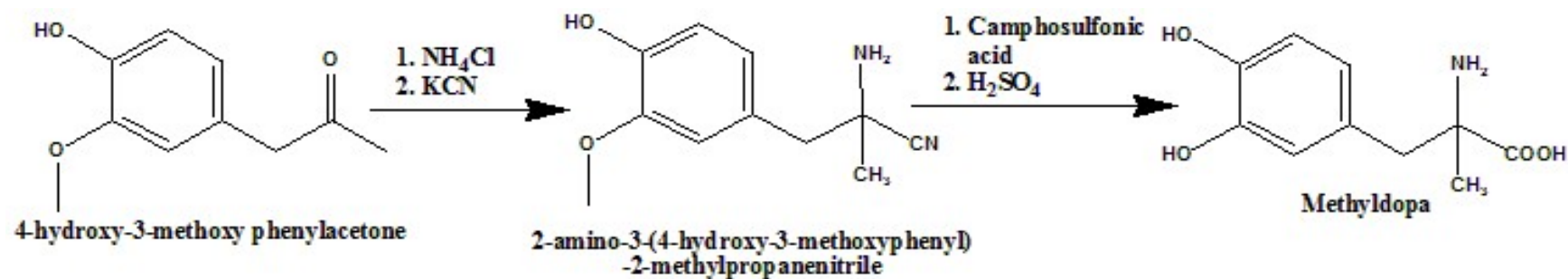


Reserpine



Sodium nitroprusside

Synthesis of Methyldopa



1. 4-hydroxy-3-methoxy phenylacetone is taken as starting material.
2. It undergoes reaction with ammonium chloride followed by reaction with potassium cyanide to α -amino nitrile compound.
3. L-isomer is separated out by reaction with camphosulfonic acid.
4. On reacting with sulfuric acid, we get methyldopa as final product.



THANK YOU