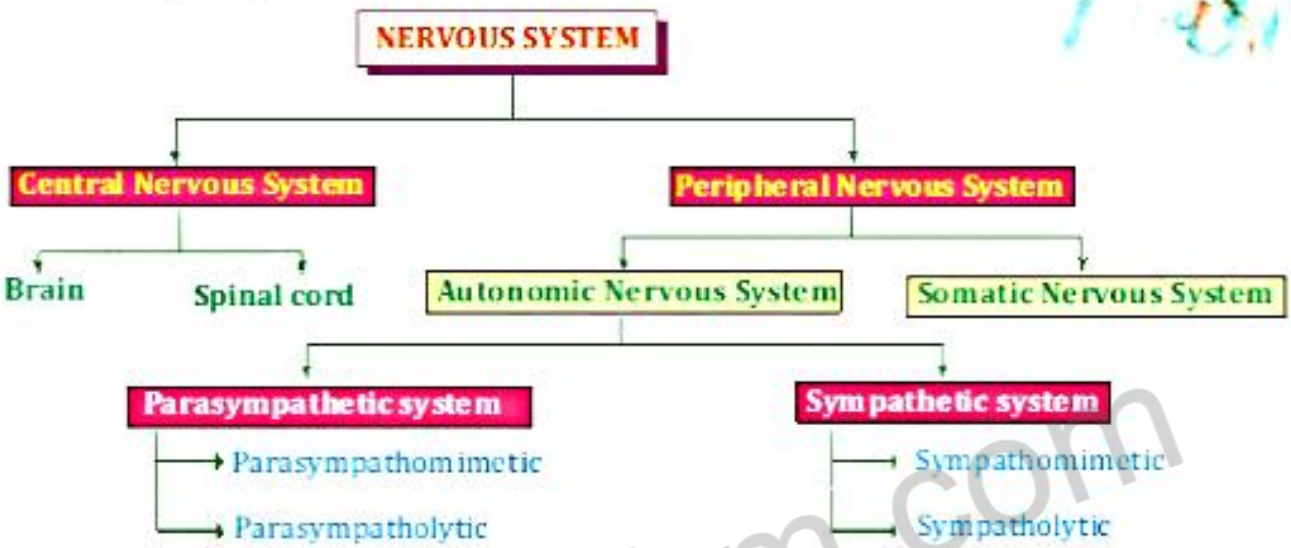
6.1 NERVOUS SYSTEM

- The nervous system has an important role to communicate information from outside the body; process it and to take corrective action based on received response.
- The nervous system can also be identified in two forms: central and peripheral.



6.2 AUTONOMIC NERVOUS SYSTEM

- Autonomic nervous system (ANS) represents the unconscious regulation and control the visceral functions of the body.
- It is involuntary in nature and activity of this system is maintained automatically and regulated by Hypothalamus.
- Autonomic nervous system has two division – Parasympathetic and Sympathetic.

6.2.1 Parasympathetic/ Cholinergic system

- ✓ The impulse transmission on neuroeffector junction is mediated by a neurotransmitter called Acetylcholine (Ach) and transmission is termed as cholinergic transmission.
- ✓ Acetylcholine (ACh) is the principal neurotransmitter, so it is called cholinergic system.
- ✓ Preganglionic neurons of parasympathetic system arise from III, VII, IX, and X cranial nerves and 2nd, 3rd, and 4th sacral portion of the vertebra, respectively, hence it is also termed as craniosacral outflow.
- ✓ In Parasympathetic system, preganglionic fibers are very long and postganglionic fibers are very short.

➢ **Receptors involved in Cholinergic system :-**

✓ Two types of cholinergic receptors: Muscarinic and Nicotinic receptor.

1. Nicotinic receptor (N)

✓ Receptor with intrinsic ion channel (**Ligand gated cation channel**). Activation of these receptor directly opens the ion channel and causes membrane depolarization.

✓ It is further divided into two types: - N_M receptor and N_N receptor.

✓ It is located at various parts of the body such as: Autonomic ganglia, skeletal muscle, and adrenal muscle.

✓ **Agonists:** eg. - Phenyltrimethyl ammonium (PTMA), Dimethyl Phenyl Piperazinium (DMPP).

✓ **Antagonist:** eg. - α-Bungarotoxin, Tubocurarine, Hexamethonium, Trimethaphan.

1. Muscarinic receptor (M)

✓ It is a type of G-Protein coupled receptor.

✓ It is located at: Heart, smooth muscle, exocrine gland and brain.

✓ **Stimulated (Agonist) by –** Oxotremorine (M_1), Methacholine (M_2), Bethanechol (M_3).

✓ **Blocked (Antagonist) by –** Atropine.

6.2.2 Sympathetic/Adrenergic System

- The impulse transmission on neuroeffector junction is mediated by a neurotransmitter called Adrenaline and transmission is termed as adrenergic transmission.
- The principal neurotransmitter is adrenaline, so it is called adrenergic system.
- Adrenergic transmission is related to sympathetic division of ANS, so it is called sympathetic system.
- Preganglionic nerves of the sympathetic system arise from the lateral gray horn of 12th thoracic segments and the first lumbar segments of spinal cord.
- In Sympathetic system, the preganglionic fibres are short and postganglionic fibres are long.
- It is located at Heart, eye, urethra, adipose tissue, smooth muscle of GIT, bronchial and urinary bladder, exocrine gland and brain.

❖ **Receptors involved in Adrenergic system:-**

- ✓ Two types of adrenergic receptors are present: α and β receptor.
- ✓ α receptors has following subtypes: α_1, α_2 whereas, β receptors has following subtypes: β_1, β_2 and β_3.
- ✓ α Agonists – Adrenaline, Dopamine, Ephedrine.
- ✓ α Antagonists – Prazosin, Yohimbine Rauwolscine
- ✓ β Agonists – Dobutamine Salbutamol, Terbutalin, Mirabegron
- ✓ β Antagonists – Metoprolol, Atenolol.

6.2.3 Neurotransmitters of Autonomic nervous system

ANS	Preganglionic	Postganglionic
Sympathetic	Acetylcholine	Epinephrine/Adrenaline
Para-sympathetic	Acetylcholine	Acetylcholine

6.2.4 Parasympathetic Vs Sympathetic Nervous System

DESCRIPTIONS	PARASYMPATHETIC	SYMPATHETIC
Origin	Cranio–sacral (III, VII, IX, X; S_2–S_4)	Dorso–lumbar (T_1 to L_2 or L_3)
Distribution	Limited to head, neck, trunk	Wide
Position of Ganglia	Away from effector organs	Close to effector organs
Neurotransmitter	Acetylcholine (Major) Nitric oxide (Minor)	Noradrenaline (Major) Acetylcholine (Minor)
Main function	Keep body cool and calm (Rest and Digest situation)	Prepare body for Fight and Flight situation

6.3 ADRENERGIC AGONITS

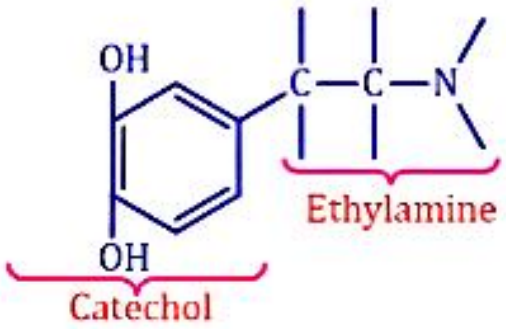
Adrenergic Agonist regulator of the activities of the vital organs, such as heart and peripheral vasculature, especially in response to stress. Adrenergic agents are divided into three classes.

6.2.5 Classification of Adrenergic Drugs

CLASS	DRUGS
Direct acting agents	Nor-epinephrine, Epinephrine, Phenylephrine, Dopamine, Methyldopa, Clonidine, Dobutamine, Isoproterenol, Terbutaline, Salbutamol, Bitolterol, Naphazoline, Oxymetazoline and Xylometazoline.
Indirect acting agents	Hydroxyamphetamine, Pseudoephedrine, Propylhexedrine
Agents with mixed mechanism	Ephedrine, Metaraminol.

6.2.6 General Classification of Adrenergic Agonists

- **Catecholamines** - Compounds with hydroxyl (–OH) substitution in the third and fourth position of the benzene ring are termed as Catecholamines.

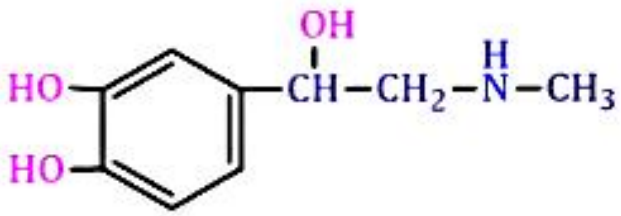


❑ EPINEPHRINE (ADRENALINE)

- Adrenaline is a hormone that regulates respiration and is used to treat medical conditions.

❖ **Chemical Formula** - $C_9H_{13}NO_3$

❖ **Structure**



❖ IUPAC Nomenclature

- 4-(1-Hydroxy-2-(methylamino)ethyl)benzene-1,2-diol

❖ Physiochemical Properties

- Adrenaline is a catecholamine and belongs to the family of biogenic amines. It is a white or creamy white, sphaero-crystalline powder.
- It dissolves in solutions of mineral acids, potassium hydroxide, and of sodium hydroxide, but sparingly soluble in water, insoluble in ethanol and ether. It is used as a sympathomimetic, Broncho lytic, and antiasthmatic.

❖ Pharmaceutical Formulation

- It is commonly injected in Intravenous, Endotracheal, Intraosseous (active bone marrow), and Intramuscular.

❖ Stability and storage

- It should be stored in between 20°C to 25°C.
- Protect from light, do not freeze.
- Do not use the solution if it's coloured, cloudy, or particulate matter.

❖ Popular Brand Names

- Vasocon
- Epibbas

❖ Dose

- Its usual dose is 0.3 to 0.5 mg subcutaneously or IM, may be repeated if necessary every 5 to 10 minutes.

❖ Medicinal Uses

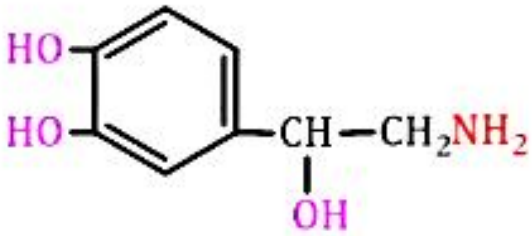
- It is used to treat several conditions including allergic reaction anaphylaxis, cardiac arrest, and superficial bleeding.

❑ NOR-EPINEPHRINE (Noradrenaline, NA, NE)

- This substance is used to increase blood pressure in cases of low blood pressure and as a vasoconstrictor in certain dental Anaesthetics.

❖ **Chemical Formula -** $C_8H_{11}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-(2-amino-1-hydroxyethyl)benzene-1,2-dio

❖ **Physiochemical Properties**

- It is a white or brownish-white, crystalline powder, slightly soluble in ethanol and soluble in water. It differs from adrenaline only by lacking the methyl substitution on the amino ethanol. L-isomer is pharmacologically active.
- Noradrenaline is a potent agonist for α_1 receptors and has relative actions on β_2 receptors.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of intravenous Injections.

❖ **Stability and storage**

- Store at room temperature and Protected from light

❖ **Popular Brand Names**

- Adrenor
- Cnorin
- Veraline

❖ **Dose**

- Initial dose 8 to 12 mcg/min continuous IV infusion.

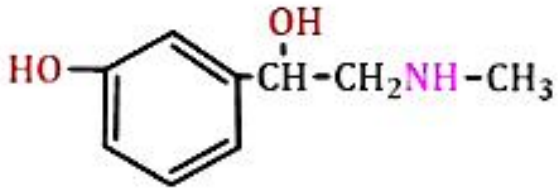
❖ **Medicinal Uses**

- Treatment of critically low blood pressure (hypotension).
- It is used as a vasoconstrictor in some local Anaesthetics.

❑ PHENYLEPHRINE

❖ **Chemical Formula -** $C_9H_{13}NO_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-[-1-Hydroxy-2-(methylamino)ethyl]phenol

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder, freely soluble in ethanol and water.

❖ **Stability And Storage**

- It is stored in tightly closed light-resistant containers.

❖ **Pharmaceutical formulation**

- The patient has reported using various methods of administration, such as oral, nasal, topical, intravenous, and intramuscular.

❖ **Popular Brand Names**

- Neo-synephrine
- Nostril
- Pretz-d

❖ **Dose**

- Phenylephrine injection may be administered subcutaneously or intramuscularly in a dosage of 2 to 5 mg with further doses of 1 to 10 mg if necessary according to response, or in a dose of 100-500 micrograms by slow intravenous injection as a 0.1% solution.

❖ **Medicinal Uses**

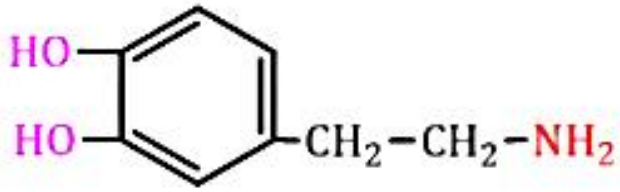
- It is mainly used to treat nasal congestion, hypotension, and Shock.

❑ DOPAMINE

- Dopamine exerts the CVS effects by interacting with D_1 dopaminergic receptors, especially in the renal, mesenteric, and coronary beds.

❖ **Chemical Formula** - $C_8H_{11}NO_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-(2-Aminoethyl)benzene-1,2-diol

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder, soluble in alcohol, sparingly soluble in acetone and methylene chloride, but freely soluble in water

❖ **Stability And Storage**

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

❖ **Pharmaceutical formulation**

- This drug is formulated in the form of intravenous Injections.

❖ **Popular brand names**

- Flagtropin
- Dopacan
- Dopastat

❖ **Dose**

- The usual dose is 0.2–1.0 mg/min I.V. infusion.

❖ **Medicinal Uses**

- It mainly treats acute renal failure, heart failure, and shock.

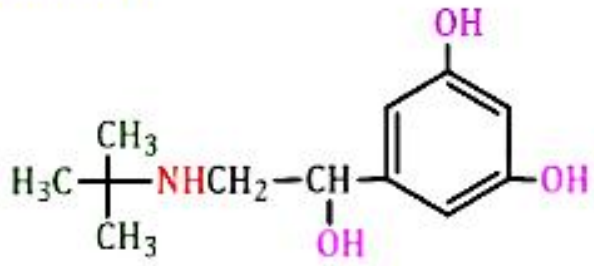
➢ **Noncatecholamines** - Those compounds that lack the hydroxyl at third and fourth position of the benzene ring are noncatecholamines. They release noradrenaline or dopamine from the sympathetic neurons.

❑ TERBUTALINE

- It is used only as a bronchodilator and in the treatment of asthma.
- It possesses strong β-agonistic activity.

❖ **Chemical Formula** $C_{12}H_{19}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 5-[2-(tert-Butylamino)-1-hydroxyethyl]benzene-1,3-diol

❖ **Physiochemical Properties**

- It exists as a gray-white crystalline powder, odourless and with a bitter taste, soluble in water and alcohol.
- The drug exhibits the properties of a direct-acting sympathomimetic agent, having predominantly β_2 adrenergic activity, and has a selective action on the β_2 receptors.

❖ **Stability And Storage**

- Store at room temperature and protected from light.

❖ **Pharmaceutical Formulation**

- It is formulated form of Oral (tablets, oral solution), inhalational (Dry powder inhaler, nebulizer solution), and Subcutaneous injection.

❖ **Popular Brand Names**

- Bricanyl
- Brethine
- Asmaril

❖ **Dose**

- For Respiratory disorder - 5 mg oral, 0.25 mg subcutaneous route and 250 µg by inhalation.

❖ **Medicinal Uses**

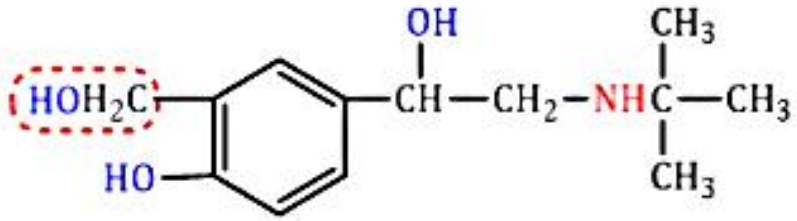
- Terbutaline is used to treat wheezing and shortness of breath from lung problems such as asthma, chronic obstructive pulmonary disease, bronchitis and emphysema.

❑ SALBUTAMOL (ALBUTEROL)

- It has strong β_2 adrenergic activity.

❖ **Chemical Formula** - $C_{13}H_{21}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-4-[2-(tert-Butylamino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder, sparingly soluble in water, but freely soluble in ethanol. It has strong β_2 adrenergic activity.
- It is useful in the treatment of acute myocardial infarction, severe left ventricular failure.

❖ **Stability And Storage**

- It is light sensitive and hence it is stored in a well-closed light-resistant container.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, inhaler, capsule syrup and injection.

❖ **Popular Brand Names**

- Biomydrine
- Asthalin
- Ventolin

❖ **Dose**

- 2–4 mg oral, 0.25–0.5 mg I.M./subcutaneous.

❖ **Medicinal Uses**

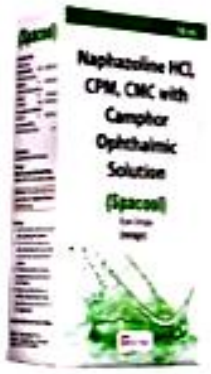
- It is used in bronchial asthma, nasal congestion, and bronchial asthma.
- It is also used in the prevention of premature labour.

❑ NAPHAZOLINE

- It is a directly acting sympathomimetic drug, which is mostly used as a local vasoconstrictor for the relief of nasal congestion due to allergic or infarction manifestations.

❖ **Chemical Formula** $C_{14}H_{14}N_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-(naphthalen-1-ylmethyl)-4,5-dihydro-1H-imidazole

❖ **Physiochemical properties**

- It is a white crystalline, odourless, and bitter compound. The salt is soluble in water and in alcohol.
- They essentially exist in an ionized form at physiological pH because of the very basic nature of the imidazoline ring (pK_a 9 to 10).

❖ **Stability And Storage**

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light.

❖ **Pharmaceutical Formulation**

- It is formulated form of nasal drop and eye drops.

❖ **Popular Brand Names**

- Clear eyes
- Spacool
- Naphcon-a

❖ **Dose**

- For nasal mucosa, 2 drops of 0.05% solution.
- For conjunctivity, 1 to 2 drops of a 0.1% solution after every 3 to 4 h.

❖ **Medicinal Uses**

- It is used for nasal congestion and to relieve redness due to minor eye irritations.

❑ TETRAHYDROZOLINE

- Tetrahydrozoline is an alpha agonist for the alpha-1 receptor. This action relieves the redness of the eye caused by minor ocular irritants.

❖ **Chemical Formula** - $C_{13}H_{16}N_2$

❖ **Structure**

❖ **IUPAC Nomenclature**

- 2-(1,2,3,4-tetrahydronaphthalen-1-yl)-4,5-dihydro-1H-imidazole

❖ **Physiochemical Properties**

- Tetrahydrozoline is colourless, odourless, and tasteless crystal powder.
- Very soluble in water and ethanol, slightly soluble in chloroform and insoluble in diethyl ether.
- Tetrahydrozoline is a derivative of imidazoline with central and peripheral alpha-adrenergic properties.

❖ **Stability And Storage**

- It is stored in tightly closed light-resistant containers.

❖ **Pharmaceutical Formulation**

- It is formulated form of eye drop and nasal Decongestants

❖ **Popular Brand Names**

- Visine
- Rohto arctic

❖ **Dose**

- 1-2 drops to affected eye every 6-12 hours.

❖ **Medicinal Uses**

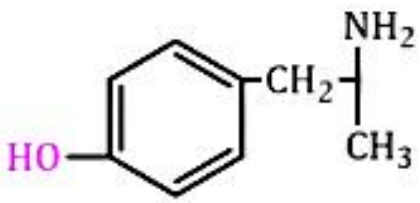
- Reducing swelling and congestion of the eye.

❑ HYDROXY AMPHETAMINE

- It is used medically in eye drops to dilate the pupil (a process called mydriasis) so that the back of the eye can be examined.

❖ **Chemical Formula** $C_9H_{13}NO$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 4-(2-aminopropyl)phenol

❖ **Physiochemical Properties**

- It is the racemic free base and naturally occurring trace amine.
- It is more soluble in water and slightly soluble in methanol.

❖ **Stability And Storage**

- It should be stored below 30°C
- Protect from light, do not freeze.

❖ **Pharmaceutical Formulation**

- It is formulated form of eye drop.

❖ **Popular Brand Names**

- Paremyd

❖ **Dose**

- Instill 1 to 2 drops in the conjunctival sac(s) once.

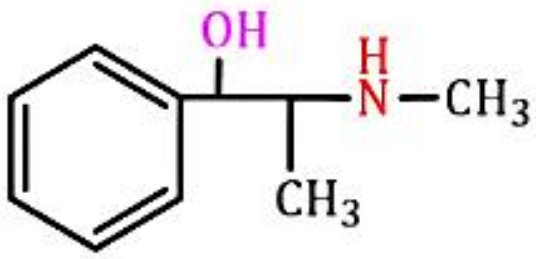
❖ **Medicinal Uses**

- Hydroxyamphetamine used ophthalmic by relaxing in eye muscles and widens the pupil.
- Hydroxyamphetamine ophthalmic solution is used to dilate (widen) the pupil in an inflammatory condition or in post-surgery situations.

❑ PSEUDOEPHEDRINE

❖ **Chemical Formula** - $C_{10}H_{15}NO$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (S,S)-2-methylamino-1-phenylpropan-1-ol

❖ **Physiochemical Properties**

- It is white, odourless crystals or powder with bitter in taste along with the slight aromatic odour.
- It acidic in nature and completely soluble in water, methanol and partially soluble in chloroform.

❖ **Stability And Storage**

- It should be stored at room temperature.

❖ **Pharmaceutical Formulation**

- It is formulated form of Tablet, capsule, syrup, cream, gel, ointment, liquid or injection.

❖ **Popular Brand Names**

- Sudafed
- Afrinol
- Sinutab

❖ **Dose**

- Usual Immediate release adult dose is 30 to 60 mg orally every 4 to 6 hours and pediatric is 15 mg orally every 4 to 6 hours as needed.

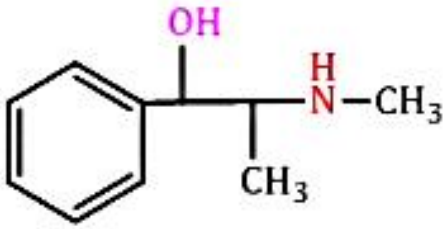
❖ **Medicinal Uses**

- It relieves nasal congestion caused by allergies, colds, and hay fever, as well as sinus congestion and pressure.

❑ EPHEDRINE

❖ **Chemical Formula** $C_{10}H_{15}NO$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-(methylamino)-1-phenylpropan-1-ol

❖ **Physiochemical Properties**

- Ephedrine occurs as fine, white, odourless crystals and darkens on exposure to light.

❖ **Stability And Storage**

- It should be stored in between 15˚ C to 25˚C.Store away from heat, moisture, and light.

❖ **Pharmaceutical Formulation**

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

❖ **Popular Brand Names**

- Alkovaz
- Epherincare
- Ephever

❖ **Dose**

- The usual dose is 10 to 25 mg every 3 to 4 hours.

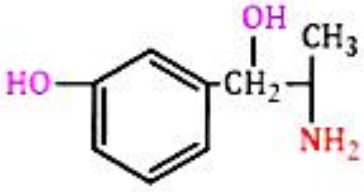
❖ **Medicinal Uses**

- It is used to prevent low blood pressure during anaesthesia.
- It has also been used for asthma, narcolepsy, and obesity but is not the preferred treatment.

❑ METARAMINOL

❖ **Chemical Formula** $C_9H_{13}NO_2$

❖ **Structure**



❖ IUPAC Nomenclature

- (1R,2S)-3-[-2-amino-1-hydroxy-propyl]phenol

❖ Physiochemical Properties

- It is a white crystalline powder, insoluble in ether, slightly soluble in ethanol, and freely soluble in water.
- It is structurally similar to phenylephrine.

❖ Stability And Storage

- Stable between 2-8°C for 24-48 hours.

❖ Pharmaceutical Formulation

- It is formulated form of injection.

❖ Popular Brand Names

- Aramine
- Metaramin
- Pressonex

❖ Dose

- Its usual dose is 0.5 to 5 mg I.V. in an emergency.

❖ Medicinal Uses

- Used in the prevention and treatment of hypotension, particularly as a complication of anaesthesia.

6.3 ADRENERGIC ANTAGONIST

- An adrenergic antagonist is a drug that inhibits the function of adrenergic receptors.
- There are five adrenergic receptors, which are divided into two groups.
- The first group of receptors are the beta (β) adrenergic receptors.
- There are β_1, β_2, and β_3 receptors.
- The second group contains the alpha (α) adreno-receptors.
- There are only α_1 and α_2 receptors.
- Adrenergic receptors are located near the heart, kidneys, lungs, and gastrointestinal tract.

6.3.1 Classification of Adrenergic Antagonist

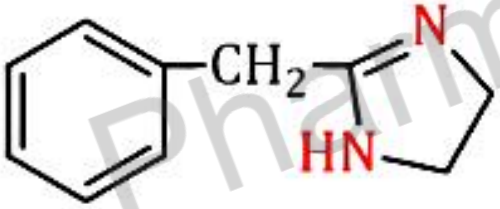
CLASS	RECEPTOR	DRUG
α - blocker	Non-selective	Tolazoline Phentolamine Phenoxybenzamine
	α_1 – blocker	Prazosin
β- blocker	Non-selective	Propranolol
	β_1– blocker	Atenolol
	α and β Blocker	Carvedilol

❑ TOLAZOLINE

- Tolazoline is a non-selective competitive α-adrenergic receptor antagonist. It is a vasodilator that is used to treat spasms of peripheral blood vessels.

❖ **Chemical Formula** $C_{10}H_{12}N_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-Benzyl-4,5-dihydro-1H-imidazole

❖ **Physiochemical Properties**

- It is a white, bitter taste, crystalline compound with a slight aromatic odour, soluble in water, alcohol, and chloroform but sparingly soluble in ether.
- It is an imidazolidine derivative.

❖ **Stability And Storage**

- It is stored in a tight container protected from light.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablets, eye drops and intravenous injections.

❖ **Popular Brand Names**

- Tolazine
- Tolazoline

❖ **Dose**

- For adults 25 mg slowly injected, then increased upto 50 to 75 mg twice/day to 2 or 3 times/week.

❖ **Medicinal Uses**

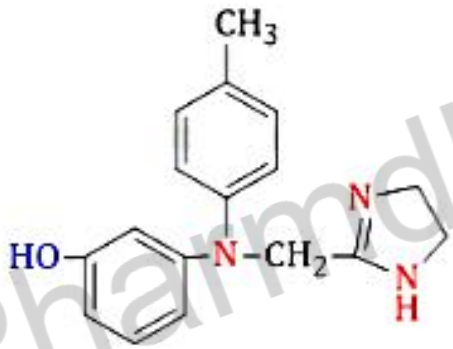
- It is used to treat peripheral vascular disorders.
- In Raynaud's disease
- It also stimulates gastric secretion.
- In treatment of iritis (eye drops).

❑ **PHENTOLAMINE**

- Its primary action is vasodilation due to the α1 blocker.

❖ **Chemical Formula** $C_{17}H_{19}N_3O$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-[(4,5-Dihydro-1H-imidazol-2-ylmethyl)(4-methylphenyl)amino]phenol

❖ **Physiochemical Properties**

- It is solid white crystalline powder with bitter taste.
- Phentolamine is a synthetic imidazoline derivative. It is fully soluble in water and alcohol, sparingly soluble in chloroform, practically insoluble in acetone, ethyl acetate.

❖ **Stability And Storage**

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

❖ **Pharmaceutical Formulation**

- It is formulated form of Injection, Tablet, Capsule, Syrup, Cream, Gel, and Ointment.

❖ **Popular Brand Names**

- Fentanor
- Phentosol
- Regitine

❖ **Dose**

- Its usual dose is 5 mg I.V. injection, repeated as required.

❖ **Medicinal Uses**

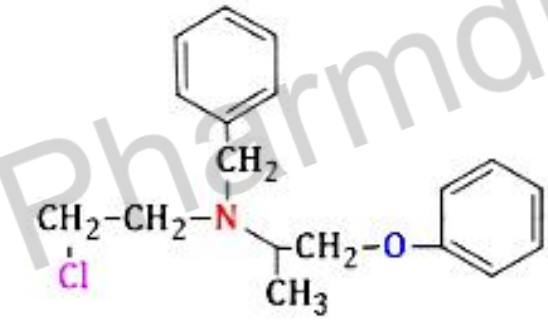
- It is used to control hypertension produced by Pheochromocytoma.
- It also has usefulness in the treatment of cocaine-induced cardiovascular complications.

❑ **PHENOXYBENZAMINE**

- It is a non-selective, irreversible alpha-blocker.
- It has a slower onset and a longer-lasting effect compared with other alpha blockers.

❖ **Chemical Formula** $C_{18}H_{22}ClNO$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-N-Benzyl-N-(2-chloroethyl)-1-phenoxypropan-2-amine

❖ **Physiochemical Properties**

- Colourless, crystalline compound soluble in alcohol, water, and chloroform.

❖ **Stability And Storage**

- Store at room temperature 20°C to 25°C.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of capsules and intravenous injections.

❖ Popular Brand Names

- Dibenzyline
- Fenoxene
- Biophenox

❖ Dose

- The usual dose initially 10 mg/day, increased gradually to 60 mg/day in divided doses.

❖ Medicinal Uses

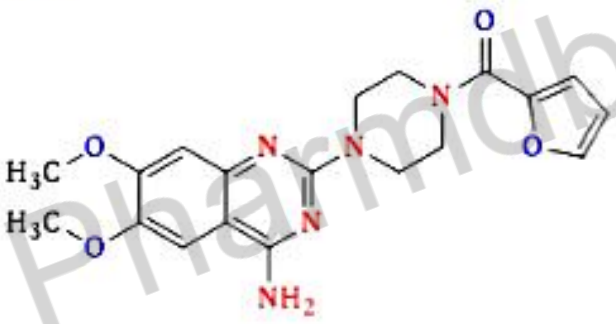
- It is used in the treatment of hypertension, specifically that caused by Pheochromocytoma.

❑ PRAZOSIN

- Prazosin was the first alpha antagonist (α_1 – blocker) used for benign prostatic hypertrophy.

❖ Chemical Formula $C_{19}H_{21}N_5O_4$

❖ Structure



❖ IUPAC Nomenclature

- [4-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl](2-furyl)methanone

❖ Physiochemical Properties

- It is a white crystalline powder, soluble in water and alcohol.

❖ Stability And Storage

- It is stored in well-closed, light-resistant containers at 15°C - 30 °C.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of Capsules.

❖ Popular Brand Names

- Minipress
- Prazocin – 5
- Prazopil xl

❖ **Dose**

- Usual Dose 1–4 Mg two times a day/three times a day.

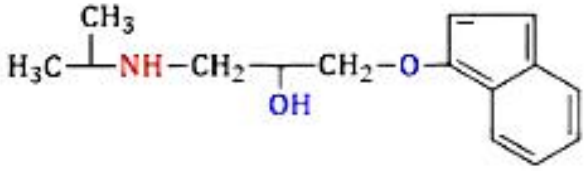
❖ **Medicinal Uses**

- Prazosin is a medication used to manage and treat hypertension, post-traumatic stress disorder (PTSD), and Raynaud disease.

❑ PROPRANOLOL

❖ **Chemical Formula** $C_{16}H_{21}NO_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-1-(1-methylethylamino)-3-(1-naphthyloxy)propan-2-ol

❖ **Physiochemical Properties**

- It is a white or almost white powder, soluble in water and in ethanol.

❖ **Stability And Storage**

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

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

❖ **Popular Brand Names**

- Inderal
- P-nolol
- Proplace

❖ **Dose**

- The oral adult dose for arrhythmias is 10 to 30 mg 3 to 4 times/day.

❖ **Medicinal Uses**

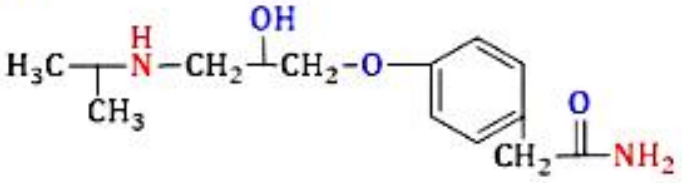
- It is used to treat high blood pressure, irregular heartbeats, shaking (tremors), and other conditions.
- It is also used to prevent migraine headaches and chest pain (angina).

❑ ATENOLOL

- Atenolol is a β1– 1-blocker that affects the heart and circulation (blood flow through arteries and veins).

❖ **Chemical Formula** $C_{14}H_{22}N_2O_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-2-{4-[2-Hydroxy-3-(propan-2-ylamino)propoxy]phenyl}acetamide

❖ **Physiochemical Properties**

- It is a white or almost white powder, sparingly soluble in water, but soluble in ethanol.
- It is a β1 selective drug with low lipid solubility.

❖ **Stability And Storage**

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet, injection and oral solution.

❖ **Popular Brand Names**

- Tenolol-50
- Atenolol- Stada
- Hipres – 50

❖ **Dose**

- The usual dose is 50 mg/day once daily.

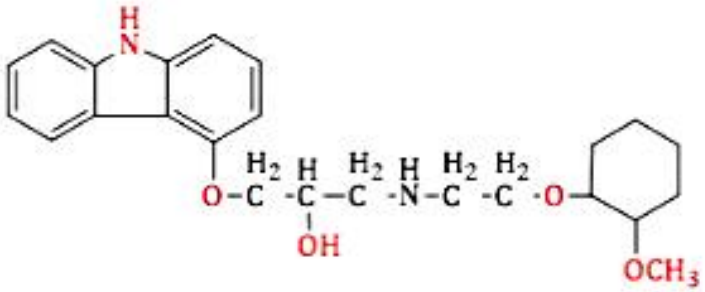
❖ **Medicinal Uses**

- Atenolol is used to treat angina (chest pain), hypertension (high blood pressure) and cardiac arrhythmias.

❑ CARVEDILOL

❖ **Chemical Formula** $C_{24}H_{26}N_2O_4$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 1-((9H-carbazol-4-yl)oxy)-3-((2-((2-methoxycyclohexyl)oxy)ethyl)amino)propan-2-ol

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder, insoluble in water and dilute acids, but soluble in alcohol.

❖ **Stability And Storage**

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet.

❖ **Popular Brand Names**

- Carvenlol – 25
- Coreg
- Carvedrol – 3.125

❖ **Dose**

- Start with 3.125 mg twice a day for 2 weeks or maximum 25 mg twice a day.

❖ **Medicinal Uses**

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

6.4 CHOLINERGIC DRUGS RELATED AGENTS

- Cholinergic drugs or agents are also known as the parasymapatho-mimetics or parasympathetic drugs. Cholinergic agents are those agents that can reproduce the action of the acetylcholine by directly interacting with the receptors or by stimulating parasympathetic nervous system by inhibiting anticholinesterase enzyme.

6.4.1 Classification of Cholinergic Drugs

DIRECTLY ACTING	INDIRECTLY ACTING
Acetylcholine	Neostigmine
Carbachol	Edrophonium
Pilocarpine	Tacrine
	Pralidoxime
	Echothiopate

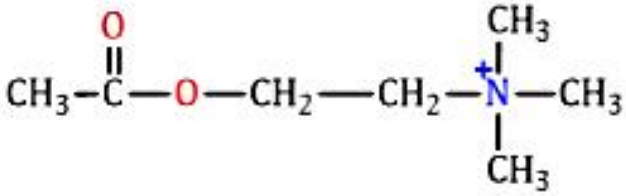
6.4.2 Classification of cholinergic direct acting drugs

❑ ACETYLCHOLINE

- Acetylcholine is the chief neurotransmitter of the parasympathetic nervous system, the part of the autonomic nervous system that contracts smooth muscles, dilates blood vessels, increases bodily secretions, and slows heart rate.

❖ **Chemical Formula** $C_7H_{16}NO_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-Acetoxy-N,N,N-trimethylethanaminium

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder or colourless crystals, very hygroscopic in nature, slightly soluble in methylene chloride, soluble in water and alcohol.

❖ **Stability And Storage**

- It should be stored in well closed ampoules and protected from light

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of Powder for injection, Syrup, Gel, Lozenges, and Strips.

❖ **Popular Brand Names**

- Miochol E
- N-acetylcysteine,
- Mucomyst

❖ **Dose**

- Its usual dose is 10mg/ml intraocular.

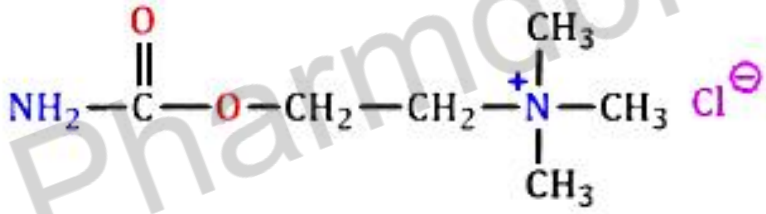
❖ **Medicinal Uses**

- Used as natural neurotransmitter support for mental processing.

❑ **CARBACHOL**

❖ **Chemical Formula** $C_6H_{15}ClN_2O_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-[(Aminocarbonyl)oxy]-N,N,N-trimethylethanaminium chloride

❖ **Physiochemical Properties**

- Carbachol is prismatic crystal of an ammonium salt and a carbamate ester.
- It is soluble in ethanol, methanol and Dimethyl sulfoxide (DMSO) and insoluble in acetone, chloroform, and ether.

❖ **Stability And Storage**

- Store in the refrigerator (4°C). Stock solutions are stable for up to 6 months at 4°C.

❖ **Pharmaceutical Formulation**

- It is formulated form of Topical ophthalmic solution, drops and ointments.

❖ Popular Brand Names

- Isopto Carbachol
- Miostat
- Carbacare

❖ Dose

- Topically 0.1 ml of 0.75 to 3% solution.

❖ Medicinal Uses

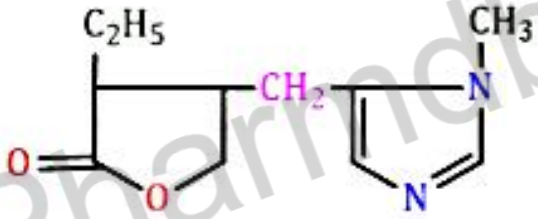
- It is used for its miotic actions in the treatment of glaucoma to reduce intraocular pressure.

❑ PILOCARPINE

- Pilocarpine is obtained from the leaves of pilocarpus microphyllus.
- It stimulates the smooth muscles and gland cells that are innervated by cholinergic nerves.

❖ Chemical Formula $C_{11}H_{16}N_2O_2$

❖ Structure



❖ IUPAC Nomenclature

- (3S,4R)-3-Ethyl-4-((1-methyl-1H-imidazol-5-yl)methyl)dihydrofuran-2(3H)-one

❖ Physiochemical Properties

- It is a white or almost white crystalline powder or colourless crystals, hygroscopic, very soluble in water and in alcohol.

❖ Stability And Storage

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

❖ Pharmaceutical Formulation

- This drug is formulated in the form of tablets, and eye drops.

❖ **Popular Brand Names**

- Pilocar
- Carpine
- Salagen

❖ **Dose**

- Topically 0.1 ml of 0.5 to 6% solution into the conjunctival sac 1 to 5 times/day.

❖ **Medicinal Uses**

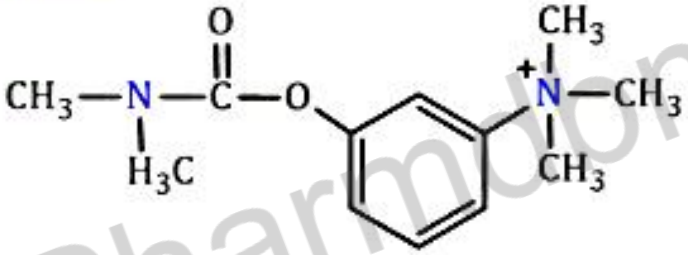
- It is used for glaucoma (to reduce intra-ocular tension in the eye).

❑ NEOSTIGMINE

- The compound is very hygroscopic and is always used in injection. Its aqueous solutions are neutral to litmus.

❖ **Chemical Formula** $C_{12}H_{19}N_2O_2^+$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-{[(Dimethylamino)carbonyl]oxy}-N,N,N-trimethylbenzenaminium

❖ **Physiochemical Properties**

- It exists as white, odourless, crystalline powder with a bitter taste, freely soluble in water, alcohol, and insoluble in ether.

❖ **Stability And Storage**

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

❖ **Pharmaceutical Formulation**

- It is formulated form of tablet and injection.

❖ **Popular Brand Names**

- Bloxiverz
- Prostigmin
- Vagostigmin

❖ **Dose**

- Its usual dose is 15–30 mg oral, 0.5–2.5 mg S.C. / I.M.

❖ **Medicinal Uses**

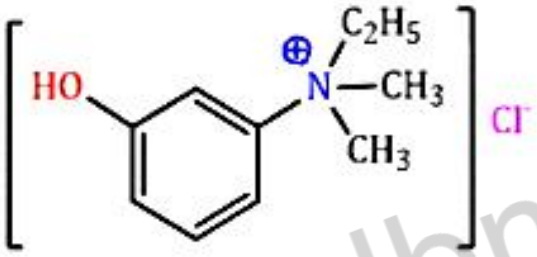
- Used in myasthenia gravis.
- Antidote for atropine and curare poisoning and in atony of intestine.

❑ **EDROPHONIUM CHLORIDE**

- It is a readily reversible acetylcholinesterase inhibitor.
- It prevents the breakdown of the neurotransmitter acetylcholine and acts by competitively inhibiting the enzyme acetylcholinesterase, mainly at the neuromuscular junction.

❖ **Chemical Formula** $C_{10}H_{16}NO^+$

❖ **Structure**



❖ **IUPAC Nomenclature**

- N-Ethyl-3-hydroxy-N,N-dimethylbenzenaminium

❖ **Physiochemical Properties**

- It exists as a white crystalline powder, soluble in water and alcohol, insoluble in methylene chloride.

❖ **Stability And Storage**

- It is stored in a tight container protected from light.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of Intramuscular and intravenous injection.

❖ **Popular Brand Names**

- Tensilon
- Enlon-plus

❖ **Dose**

- By I.V. 2 to 10 mg usually 2 mg is injected initially and if no adverse reaction takes place within 30 sec, the remaining 8 mg may be injected.

❖ **Medicinal Uses**

- Diagnosis of Myasthenia Gravis
- Reversal of Neuromuscular Block
- Pregnancy Considerations

❑ **TACRINE HYDROCHLORIDE**

❖ **Chemical Formula** $C_{13}H_{15}ClN_2$

❖ **Structure**

❖ **IUPAC Nomenclature**

- 1,2,3,4-Tetrahydroacridin-9-amine

❖ **Physiochemical Properties**

- Tacrine hydrochloride is a white solid crystal. It is freely soluble in distilled water.

❖ **Stability And Storage**

- Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of a Tablet, capsule.

❖ **Popular Brand Names**

- Cognex
- Donecept-5

❖ **Dose**

- 40 mg/day (10 mg QID).

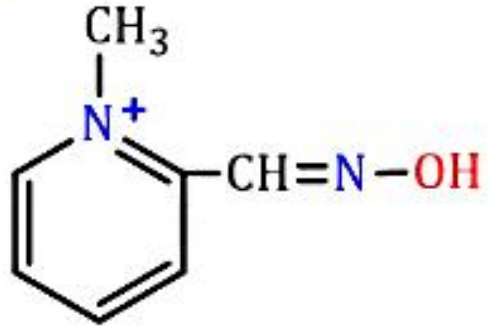
❖ **Medicinal Uses**

- It is used as a respiratory stimulant.
- Also used in the treatment of Alzheimer's disease and other central nervous system disorders.

❑ PRALIDOXIME CHLORIDE

❖ **Chemical Formula** $C_7H_9N_2O^+$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-[(hydroxyimino)methyl]-1-methylpyridin-1-ium

❖ **Physiochemical Properties**

- It exists as a white to pale yellow crystalline powder, odourless, soluble in water.
- Pralidoxime chloride, a quaternary ammonium compound.

❖ **Stability And Storage**

- It is stored in a tight container protected from light.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of tablet and injection.

❖ **Popular Brand Names**

- Protopam
- Pralidoxime auto injector
- Neopam

❖ **Dose**

- Three 600 mg intramuscular doses (3 doses of 2 mL each) in rapid succession.

❖ **Medicinal Uses**

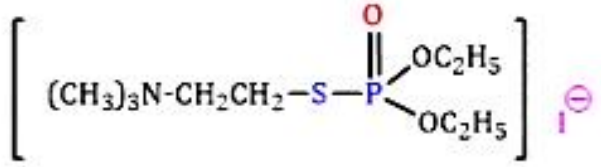
- It is typically used in cases of organophosphate poisoning.

❑ ECHOTHIOPATE IODIDE

- Echothiopate (Phospholine) is an irreversible acetylcholinesterase inhibitor.

❖ **Chemical Formula** $C_9H_{23}INO_3PS$

❖ **Structure**



❖ IUPAC Nomenclature

- 2-(Diethoxyphosphorylsulfanyl)ethyl-N,N,N-trimethylazanium iodide

❖ Physiochemical Properties

- It occurs as a white, crystalline, hygroscopic solid.
- It is a quaternary salt, soluble in water (1:1) and dehydrated alcohol (1:25) aqueous solutions have a pH of about 4.

❖ Stability And Storage

- Store the unmixed product in the refrigerator at 2-8°C, keep away from light and moisture.
- It is stable at room temperature for about 1 month.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of Eye drops and ointment.

❖ Popular Brand Names

- Phospholine Iodide

❖ Dose

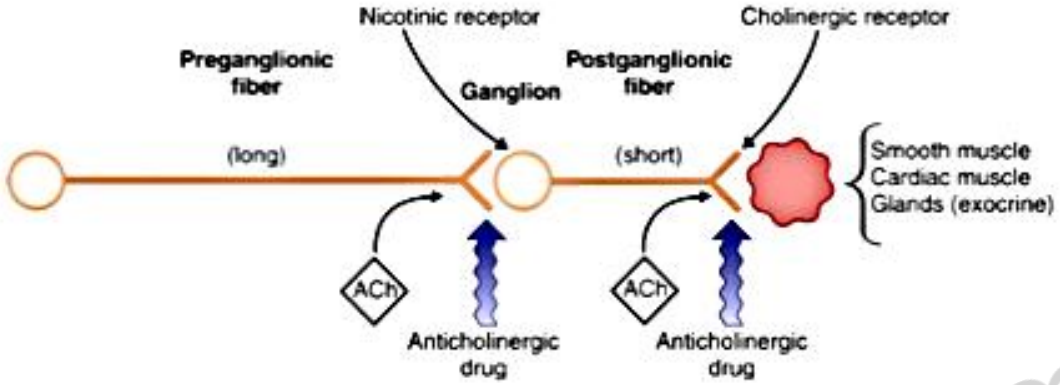
- Its usual dose is 2 drops/day.

❖ Medicinal Uses

- When applied locally, its distribution in tissues is less, which can be very desirable.
- It is used as an anticholinesterase agent in the treatment of glaucoma.
- Echothiopate iodide ophthalmic (for the eyes) reduces pressure in the eye. This medicine is used to treat chronic open-angle glaucoma, and other types of glaucoma, especially after cataract surgery.
- This medicine is also used to treat certain eye-focusing disorders.

6.5 CHOLINERGIC BLOCKING AGENTS

- Cholinergic blocking drugs are a group of drugs that block the action of acetylcholine (ACh), a neurotransmitter, in synapses of the cholinergic nervous system.
- They block acetylcholine from binding to cholinergic receptors, namely the nicotinic and muscarinic receptors.



6.5.1 Classification of Cholinergic Blocking Agents

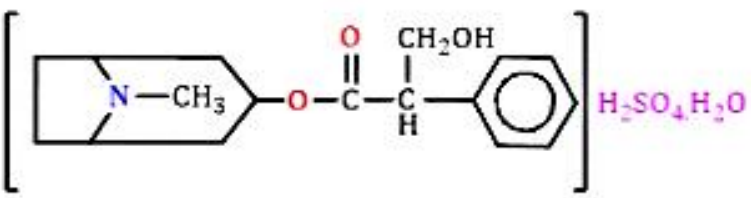
NATURAL ALKALOID	SYNTHETIC DERIVATIVE
ATROPINE	TROPICAMIDE
IPRATROPIUM	CYCLOPENTOLATE
HYOSCINE	CLIDINIUM BROMIDE
	DICYCLOMINE

❑ ATROPINE SULPHATE

- Atropine is obtained from Atropa belladonna.
- It is a chemically tropyl ester of tropine it is called as tropyl tropine.

❖ **Chemical Formula** $C_{17}H_{23}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- (RS)-(8-Methyl-8-azabicyclo[3.2.1]oct-3-yl) 3-hydroxy-2-phenylpropanoate

❖ **Physiochemical Properties**

- It is a white crystalline powder or colourless crystals, freely soluble in alcohol and well soluble in water.

❖ **Stability And Storage**

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

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of Eye drops, tablet, intramuscular and intravenous injection.

❖ **Popular Brand Names**

- Atropen
- Lomoten
- Lomotil

❖ **Dose**

- 0.6–2.0 mg I.M. / I.V. (Child 10 µg/kg), 1–2% topically in eye.

❖ **Medicinal Uses**

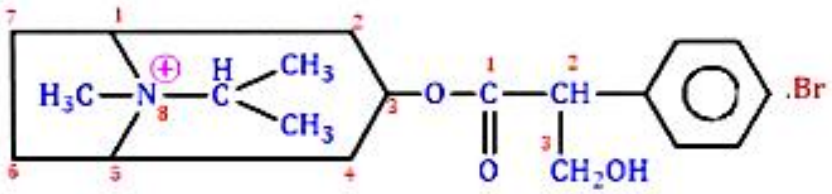
- Used as antispasmodic.
- In peptic ulcer.
- In biliary colic.
- As a pre-anaesthetic medication.
- To treat insecticidal poisoning.
- It is used as an Anti-sialagogue/anti-vagal effect.
- Organophosphate/muscarinic poisoning,
- Treatment of Bradycardia.
- It is also useful in symptomatic treatment of Parkinsonism.

❑ IPRATROPIUM BROMIDE

- Ipratropium bromide is a type of anticholinergic (SAMA - short-acting muscarinic antagonist) medication which opens up the medium and large airways in the lungs.

❖ **Chemical Formula** $C_{20}H_{30}BrNO_3$

❖ **Structure**



❖ IUPAC Nomenclature

- [8-methyl-8-(1-methylethyl)- 8-azoniabicyclo[3.2.1] oct-3-yl] 3-hydroxy-2-phenyl-propanoate

❖ Physiochemical Properties

- It is a white or almost white, odorless, and tasteless crystalline powder.
- It is a quaternary ammonium derivative. It is freely soluble in water and ethanol but insoluble in chloroform and ether

❖ Stability And Storage

- Store at room temperature 20°C to 25°C.

❖ Pharmaceutical Formulation

- This drug is formulated in the form of inhalant, and nasal solution spray.

❖ Popular Brand Names

- Atrovent
- Apovent
- Ipraxa

❖ Dose

- 40–80 µg by inhalation/nasal spray.

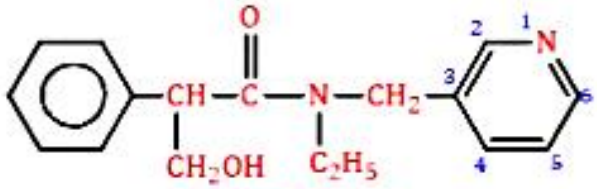
❖ Medicinal Uses

- Ipratropium oral inhalation is used to prevent wheezing, shortness of breath, coughing, and chest tightness in people with chronic obstructive pulmonary disease COPD a group of diseases that affect the lung and airways such as chronic bronchitis (swelling of the air passages that lead to the lungs) and emphysema.

❑ TROPICAMIDE

❖ **Chemical Formula** $C_{17}H_{20}N_2O_2$

❖ **Structure**



❖ **IUPAC Nomenclature**

- N-ethyl-3-hydroxy-2-phenyl-N-(pyridin-3-ylmethyl)propanamide

❖ **Physiochemical Properties**

- It is a white or almost white crystalline powder.

❖ **Stability And Storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of topical eye drops.

❖ **Popular Brand Names**

- Mydriacyl
- Paremyd

❖ **Dose**

- 0.5–1.0% topically in eye.

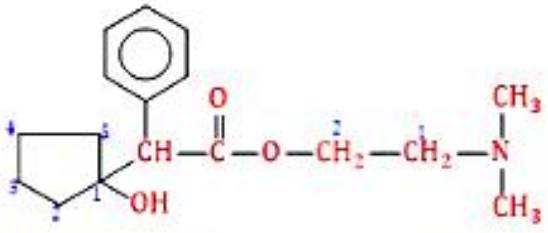
❖ **Medicinal Uses**

- It is used to dilate the pupil and help with the examination of the eye.
- Tropicamide may also be used before and after eye surgery.
- Tropicamide is used to dilate (enlarge) the pupil so that the doctor can see into the back of your eye.

❑ CYCLOPENTOLATE HYDROCHLORIDE

❖ **Chemical Formula** $C_{17}H_{25}NO_3$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 2-(dimethylamino)ethyl 2-(1-hydroxycyclopentyl)-2-phenylacetate

❖ **Physiochemical Properties**

- It exists as white crystalline, odourless powder.
- It is soluble in water, methanol, and ethanol, but insoluble in toluene.

❖ **Stability And Storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of eye drops.

❖ **Popular Brand Names**

- Cyclogyl
- Ak-Pentolate

❖ **Dose**

- 0.5–1.0% topically in eye.

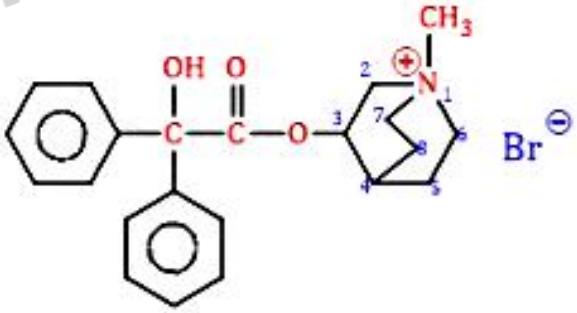
❖ **Medicinal Uses**

- It is used to dilate the pupil and help with the examination of the eye.
- Prevent the eye from focusing/accommodating (cycloplegic).

❑ **CLIDINIUM BROMIDE**

❖ **Chemical Formula** $C_{22}H_{26}NO_3^+$

❖ **Structure**



❖ **IUPAC Nomenclature**

- 3-(2-hydroxy-2,2-diphenylacetoxy)-1-methylquinuclidin-1-ium bromide

❖ **Physiochemical Properties**

- It is a white or nearly white, almost odourless, crystalline powder that is optically inactive.
- It is soluble in water and alcohol but only very slightly soluble in ether and benzene.

❖ **Stability And Storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of Tablet.

❖ **Popular Brand Names**

- Librax, Aborax, Normaxin

❖ **Dose**

- Its usual dose is 2.5–5 mg oral.

❖ **Medicinal Uses**

- It is commonly prescribed in combination with chlordiazepoxide.
- It may help symptoms of cramping and abdominal/stomach pain by decreasing stomach acid, and slowing the intestines.

❑ DICYCLOMINE HCL (DICYCLOVERINE)

❖ **Chemical Formula** $C_{19}H_{35}NO_2$

❖ **IUPAC Nomenclature**

- 2-(Diethylamino)ethyl 1-cyclohexylcyclohexane-1-carboxylate

❖ **Physiochemical Properties**

- It exists as a white, crystalline powder with a bitter taste.
- Dicyclomine is the ester, it is soluble in water and chloroform.

❖ **Stability And Storage**

- Store at room temperature, away from heat, moisture, and direct light. Keep from freezing.

❖ **Pharmaceutical Formulation**

- This drug is formulated in the form of Tablet, Syrup or intramuscular injection.

❖ **Popular Brand Names**

- Byclomine,
- Bentyl
- Dibent
- Diclospas

❖ **Dose**

- 20 mg orally four times a day, it may be increase after one week with 40 mg.

❖ **Medicinal Uses**

- Dicyclomine is used to treat the symptoms of irritable bowel syndrome, specifically hypermotility in adults.