

# UNIT-III

## Drugs acting on Autonomic nervous system

### Points to be covered in this topic

- CHOLINERGIC NEUROTRANSMITTERS
- PARASYMPATHOMIMETIC AGENTS
- CHOLINESTERASE REACTIVATOR
- CHOLINERGIC BLOCKING AGENTS

#### PARASYMPATHETIC NERVES

Rest and Digest

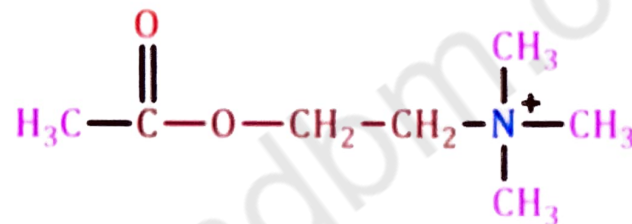


## ❑ CHOLINERGIC NEUROTRANSMITTERS

- **Synonyms:** Cholinomimetic, cholinergic Agonists, Cholinergic Drugs.
- The neurotransmitter acetylcholine (Ach) is the **only neurotransmitter used in the motor division of the somatic nervous system (neuromuscular junction) at autonomic ganglia.**

### ❖ Acetylcholine

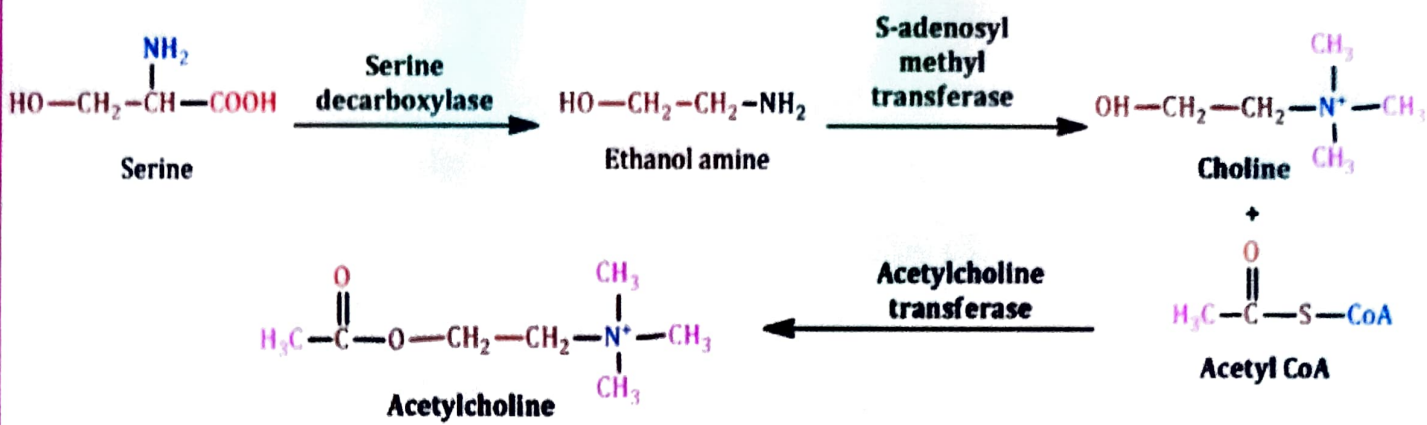
- Acetylcholine (Ach) is an **ester of choline and acetic acid.**
- Acetylcholine is the **neurotransmitter in the preganglionic sympathetic and parasympathetic neurons.**
- Acetylcholine, at the adrenal medulla and **serves as a neurotransmitter substance of nerve impulses within the central and peripheral nervous systems.**



2-acetoxy-N,N,N-trimethylethanaminium

### ❖ Biosynthesis, storage and release of acetylcholine

- **Synthesis** :- synthesis of acetylcholine (Ach) is done by cholinergic neurons.
- It was **first synthesized by Bayer in 1867 from liver by the reaction between the choline with active acetyl (CoA).**
- The active **acetyl CoA formed by the combination of acetate with Coenzyme A (CoA).**
- The reaction between acetyl Coenzyme A and choline is catalyzed by the **enzyme cholineacetylase**, then **transferred along the axon** to its terminals where the acetylcholine is formed.

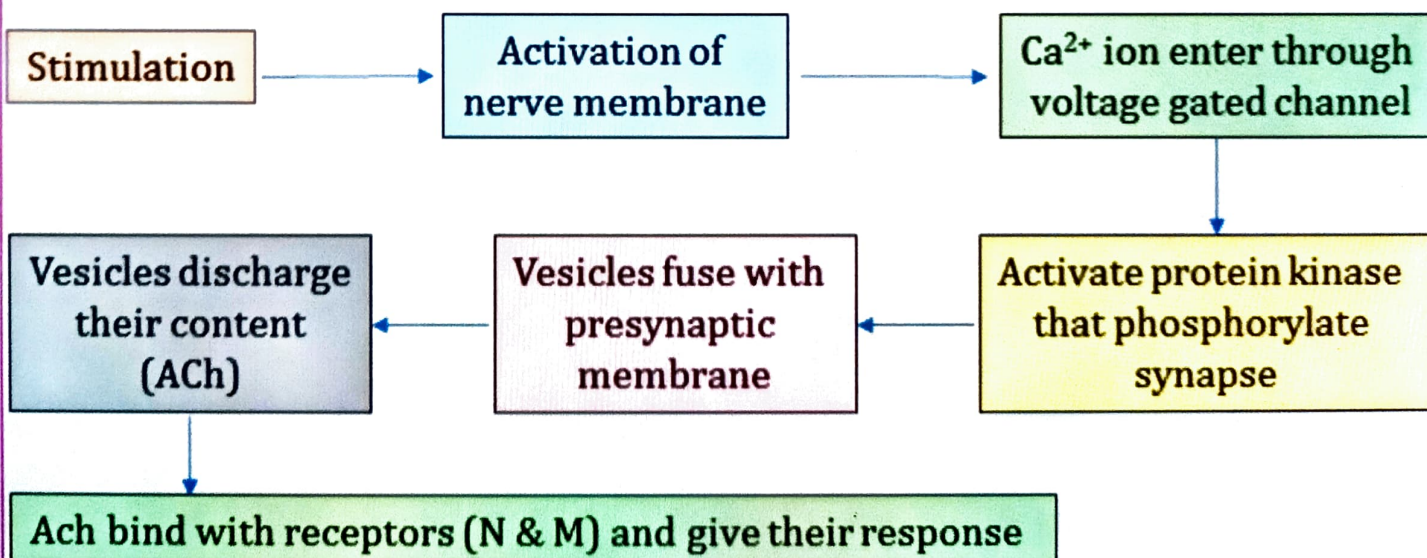


### ➤ Storage:-

- **ACh is stored in synaptic vesicles**, each vesicles contains 1000-50000 molecules of acetylcholine.
- The **mature vesicle contains** not only Ach but also **adenosine triphosphate proteoglycan**.
- The uptake of ACh into storage vesicle occurs through an **energy dependent pump that acidifies the vesicle**. The acidified vesicle then uses a vesicular ACh **transporter (VACHT) to exchange protons for ACh molecules**
- In vesicles acetylcholine is protected from hydrolysis.

### ➤ Release:-

- **Ach is released from storage granules** under the **influence of the nerve action potential and opening Ca<sup>2+</sup> ion channel** (voltage gated channel).
- This **release can be stopped by botulinum toxin**.

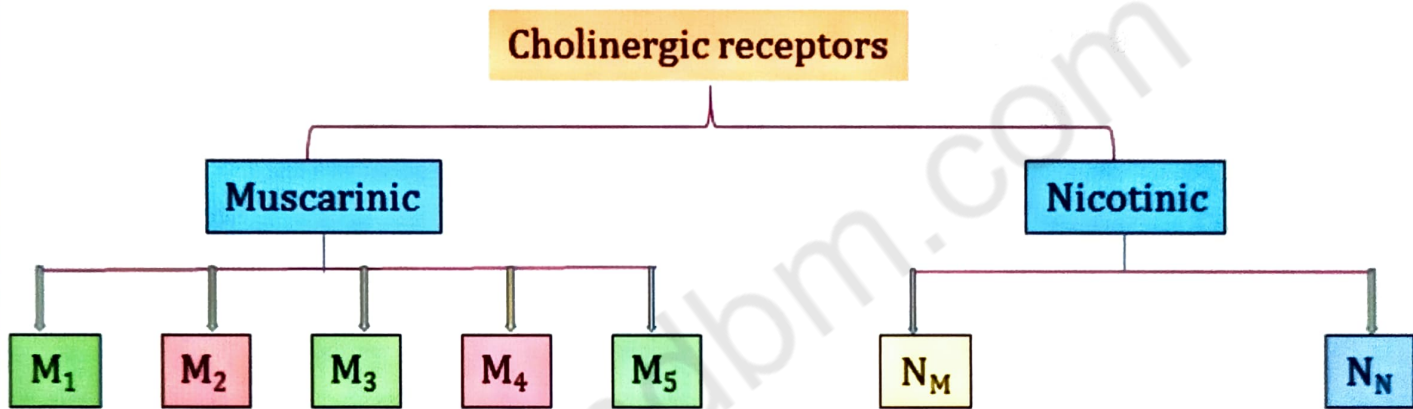


## ❖ Catabolism of acetylcholine :-

- After the release and action of acetylcholine, the function and effects of Ach can be terminated with the help of enzyme hydrolysis.
- **Cholinesterase enzyme also known as acetylcholine esterase (AChE)** and it undergoes hydrolysis, Acetylcholine (Ach) into the inactive metabolites choline and acetic acid.

## ❖ Cholinergic receptors and their distribution:-

- A cholinergic receptor are those receptor in which cholinergic neurotransmitter binds directly to induce various action or responses.



### ➤ Muscarinic Receptors:-

- It belongs to the **G-protein couple receptors family**.
- The **prototype agonist** for these receptors is muscarinic.
- It is **water soluble toxin derived from the poisonous fly agaric, Amanita muscarinic**, which cause activation of parasympathetic nervous system.

## ❖ Receptors with their locations and functions :-

Receptor	Location	Function
<b>M<sub>1</sub></b>	CNS, gastric and salivary glands, autonomic ganglia, enteric nerves	↑ Cognitive function. ↑ Seizure activity. ↑ Secretions. ↑ Autonomic ganglia depolarization. ↓ DA release and locomotion.

<b>M<sub>2</sub></b>	<b>Autonomic nerve terminals, CNS, heart, smooth muscle</b>	<p>↑ Smooth muscle contraction.</p> <p><b>Neural inhibition in periphery via autoreceptors and heteroreceptor.</b></p> <p>↓ Ganglionic transmission Neural inhibition in CNS.</p> <p>↑ Tremors hypothermia &amp; analgesia.</p>
<b>M<sub>3</sub></b>	<b>Salivary glands, heart</b>	<p>↑ Smooth muscle contraction (e.g. bladder).</p> <p>↑ Salivary gland secretion.</p> <p>↑ Food intake, body fat deposits</p> <p>Inhibits dopamine release.</p> <p>Synthesis of nitric oxide.</p>
<b>M<sub>4</sub></b>	<b>CNS and heart</b>	<p>Inhibition of autoreceptors and heteroreceptor mediated transmitter release in CNS,</p> <p><b>Analgesia, Cataleptic activity;</b></p> <p>Facilitates dopamine release.</p>
<b>M<sub>5</sub></b>	<b>CNS &amp; Periphery nervous system</b>	<p><b>Mediates dilation of cerebral arteries.</b></p> <p>Facilitates dopamine release.</p> <p><b>Augments drug seeking behavior and reward.</b></p>

➤ **Nicotinic Receptors:-**

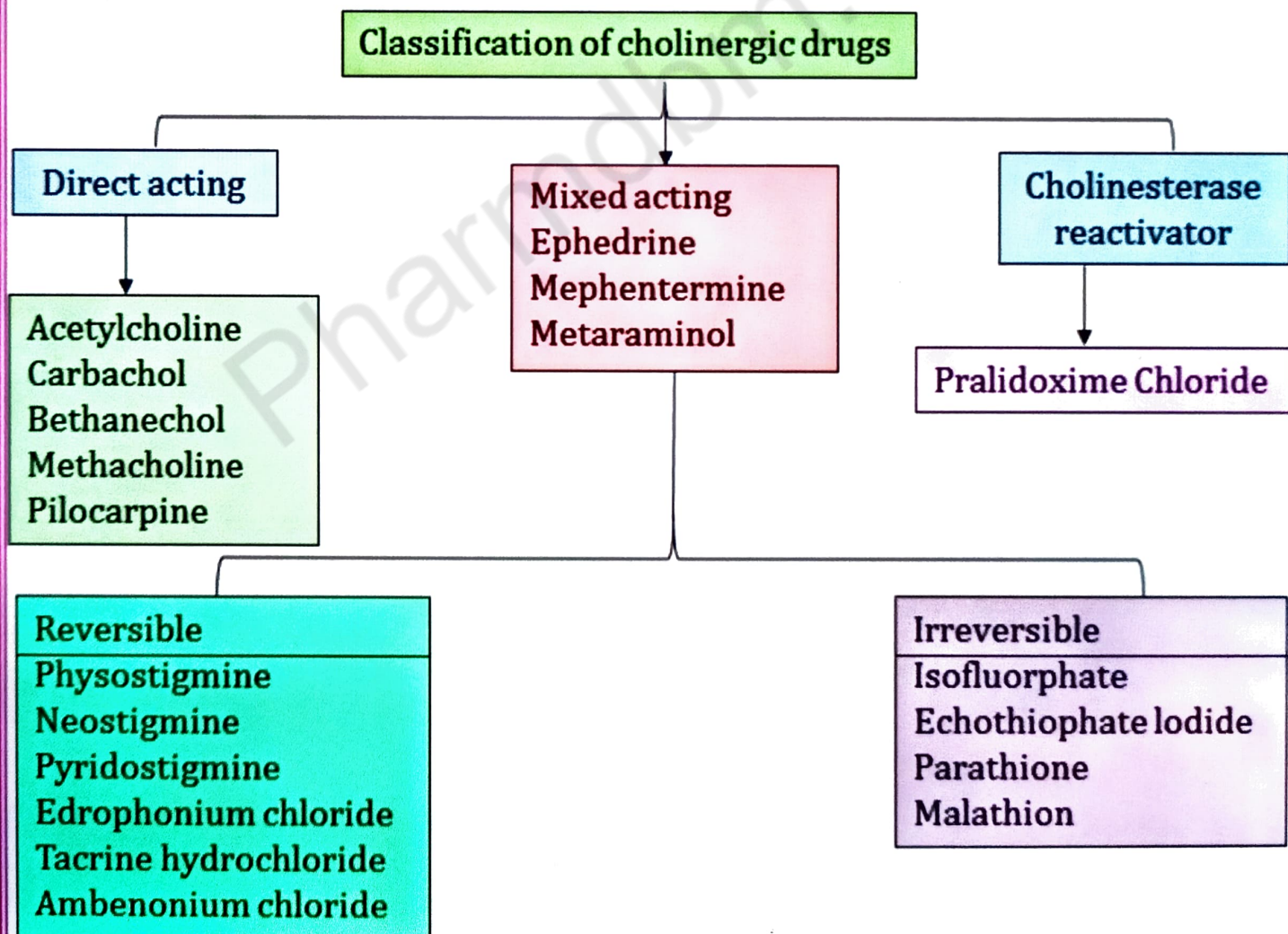
- Nicotinic receptors are directly coupled to ion channels and when activated by Ach, it shows very rapid responses.
- First neurotransmitter receptor **isolated and purified in an active form.**

Receptor	Location	Function
<b>N<sub>M</sub></b>	<b>Skeletal neuromuscular junction</b>	<b>Skeletal muscle contraction, increase cation permeability</b>

$N_N$	Ganglionic cells, Adrenal medulla, spinal cord, Brain	Depolarization & secretion of catecholamines
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## ❑ Parasympathomimetic agents:-

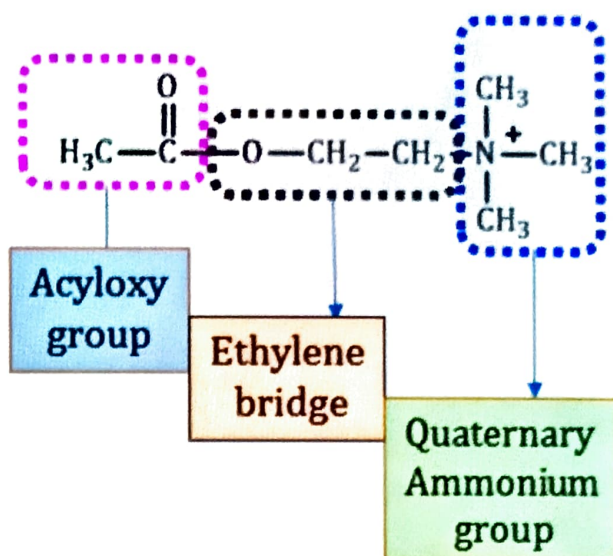
- Compounds that mimic the action of acetylcholine or produce the effect of cholinergic(parasympathetic) nerve stimulation are called as **Cholinergic or Parasympathomimetic agents**.
- Parasympathomimetic are those chemical agents **which copy the action of parasympathetic nervous system**.
- These agents or drugs bind with cholinergic receptor (N & M) and give their action.



## ❖ SAR of Parasympathomimetic agents:-

### ➤ Substitution on acetyl group:-

- Replacement of acetate group by carbamate group, Increase activity and also more stable.
- Replacement of ester group by ether & ketone group give chemically stable and potent compound and have some cholinergic activity.



### ➤ Substitution on ethylene bridge:-

- Increase in the chain length will decrease in activity.
- Branching on  $\beta$ -substitution leads to reduction of nicotinic activity but increase muscarinic activity.
- Branching on  $\alpha$ -substitution leads to increase activity for nicotinic but reduction in muscarinic activity.

### ➤ Substitution on quaternary ammonium group:-

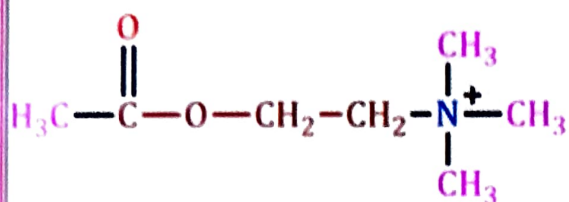
- Placement of primary, secondary, or tertiary amines leads to decrease in activity.
- Replacement of more than one methyl group of quaternary ammonium group leads to complete loss of cholinergic activity.
- The quaternary ammonium group is essential for intrinsic activity.

## ❖ Drugs acting on Parasympathomimetic agents:-

### ➤ Direct acting :-

- These are those drugs or agents which directly bind with cholinergic receptor (N&M) and gives its action.

### 1) Acetylcholine



**2-acetoxy-N,N,N-trimethylethanaminium**

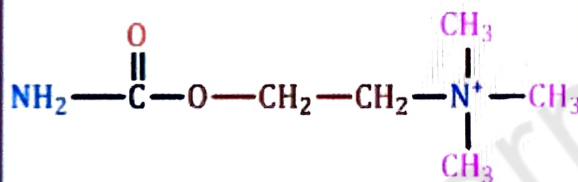
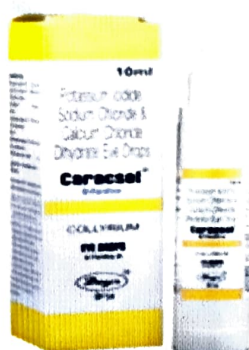
#### ✓ Mechanism of action

- It is **direct acting cholinergic drug**.
- It is **powerful but its action is destructed by cholinesterase**

#### ✓ Uses

- widely **used as eye drop to cause miosis during surgery & recovery**.
- used as **vasodilator & cardiac depressant etc.**

### 2) Carbachol



**2-(carbamoyloxy)-N,N,N-trimethylethanaminium**

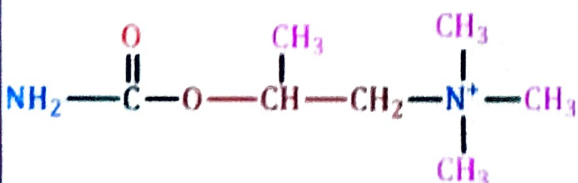
#### ✓ Mechanism of action

- **Bind with both muscarinic and nicotinic**.
- It is **not inactivated by cholinesterase so its action are more prolonged than acetylcholine**.

#### ✓ Uses

- Used **in case of severe chronic glaucoma**.
- Give **intraocular to produce miosis in ocular surgery and to reduce post operative risk**.

### 3) Bethanechol



**2-(carbamoyloxy)-N,N,N-trimethylpropan-1-aminium**

#### ✓ Mechanism of action

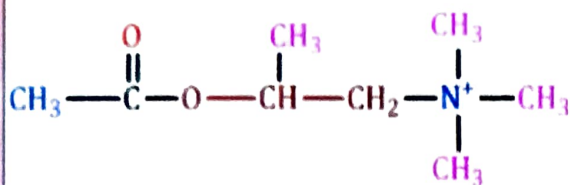
- **More selective on the muscarinic receptor**.
- It is **more stable than Carbachol due to presence of methyl group on B- Carbon**.

#### ✓ Uses

- Used to **stimulate GI tract and urinary bladder after surgery**.
- **Prolong effect than acetylcholine**.



#### 4) Methacholine



2-acetoxy-N,N,N-trimethylpropan-1-aminium

#### ✓ Mechanism of action

- It has muscarinic actions of acetylcholine.

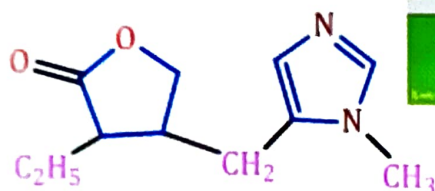
- **Prolonged action than acetylcholine**

#### ✓ Uses

- Used in the treatment of Reynaud's syndrome and glaucoma.

- Used in case of tachycardia.

#### 5) Pilocarpine



3-ethyl-4-((1-methyl-1H-imidazol-5-yl)methyl)dihydrofuran-2(3H)-one

#### ✓ Mechanism of action

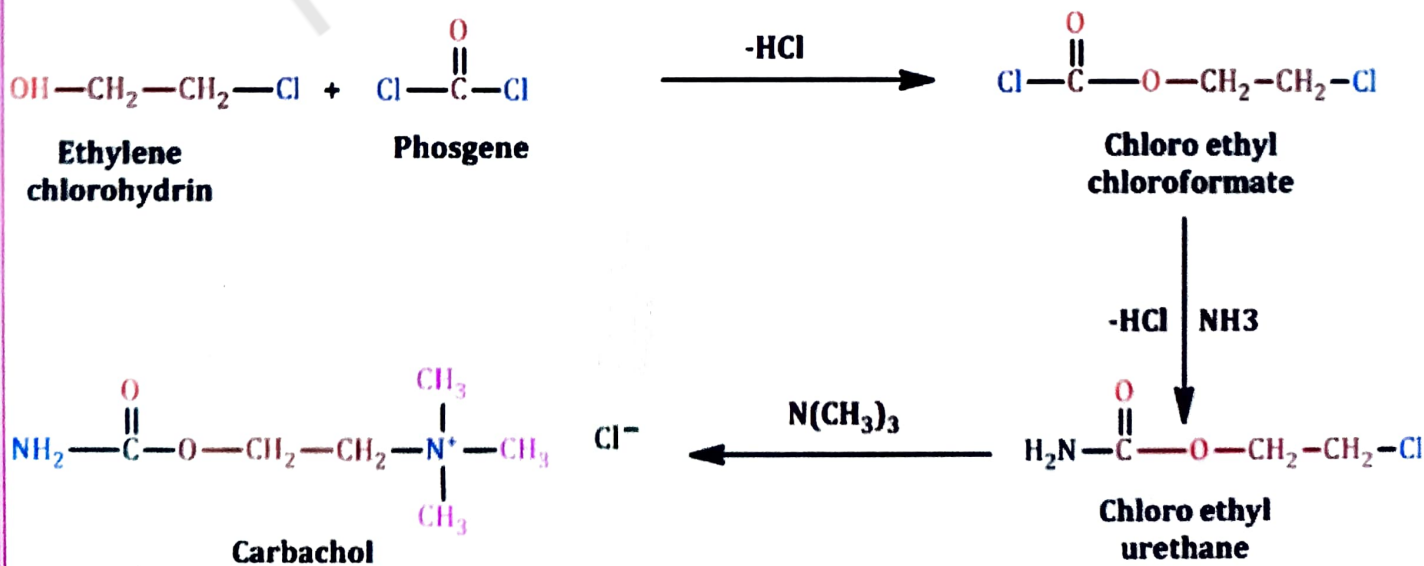
- **Direct acting cholinergic drug** that has muscarinic effect of acetylcholine.

#### ✓ Uses

- Used in treatment of glaucoma and in treatment of dry eye or dry mouth.

- Used before surgery as part of emergency treatment of acute attacks of angle-closure glaucoma.

#### ❖ Synthesis of carbachol:- From: Ethylene chlorohydrin



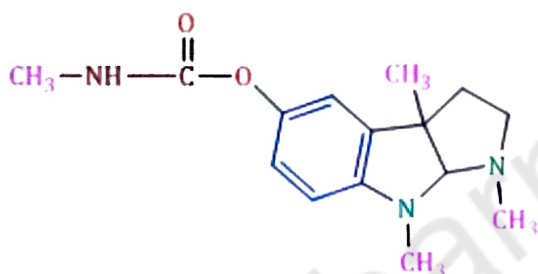
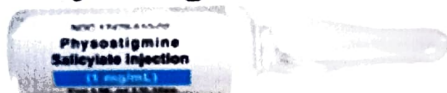
## ➤ Indirect acting :-

- Also known as **anticholinesterases**.
- These are those drug which does not directly act on receptor but **inhibit the hydrolysis of acetylcholine by acetyl cholinesterase** and hence **increase the life of acetylcholine so acetylcholine give their action**.
- They are of two types:-

### I. Reversible:-

- These are those drugs which binds reversibly to the acetyl cholinesterase enzyme.
- They are **capable of combining with the anionic and esteratic sites of cholinesterase** as well as with Ach receptor.

#### 1) Physostigmine



1,3a,8-trimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-5-yl methylcarbamate

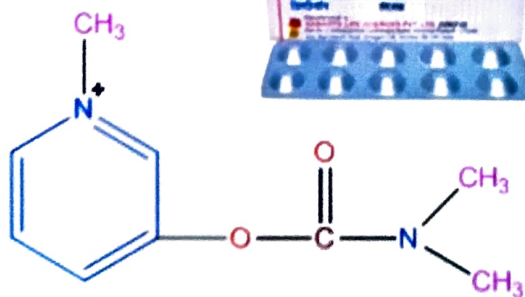
#### ✓ Mechanism of action

- **Reversible cholinesterase Inhibitor.**
- It **indirectly stimulate both muscarinic and Nicotinic receptor**.

#### ✓ Uses

- Used as **a miotic**.
- Used to **decrease intraocular pressure in glaucoma**.

#### 3) Pyridostigmine



3-((dimethyl carbamoyl)oxy)-1-methylpyridin-1-ium

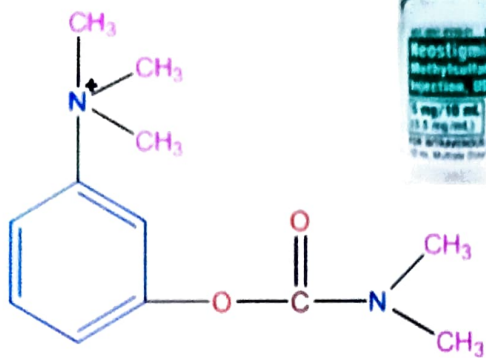
#### ✓ Mechanism of action

- **Block acetyl cholinesterase enzyme and inhibit the destruction of released acetylcholine.**

#### ✓ Uses

- Used in the **treatment of myasthenia gravis**.
- **Also helpful in nerve gas poisoning**.

## 2) Neostigmine



3-((dimethylcarbamoyl)oxy)-  
N,N,N-  
trimethylbenzenaminium

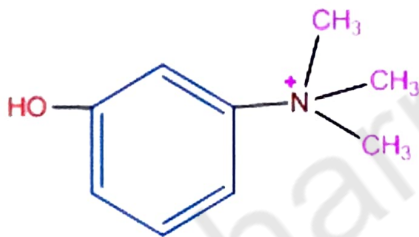
### ✓ Mechanism of action

- It indirectly stimulates both muscarinic and nicotinic receptors.
- It binds to the anionic and esteratic site of cholinesterase and blocks the activity of anticholinesterase.

### ✓ Uses

- Used in the treatment of myasthenia gravis.
- Also used in glaucoma (lower intraocular pressure).

## 4) Edrophonium chloride



3-hydroxy-N,N,N-  
trimethylbenzenaminium

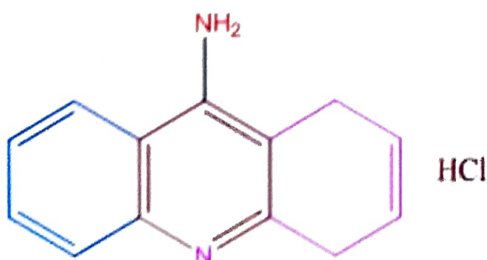
### ✓ Mechanism of action

- Reversible cholinergic inhibitor
- short duration of action than neostigmine and pyridostigmine

### ✓ Uses

- Useful for the treatment of myasthenia gravis (not for regular).
- Used in the treatment of snake bite.

## 5) Tacrine hydrochloride



1,4-dihydroacridin-9-amine  
hydrochloride

### ✓ Mechanism of action

- Centrally acting anticholinesterases.

### ✓ Uses

- Used for the treatment of Alzheimer's disease.

## 6) Ambenonium Chloride



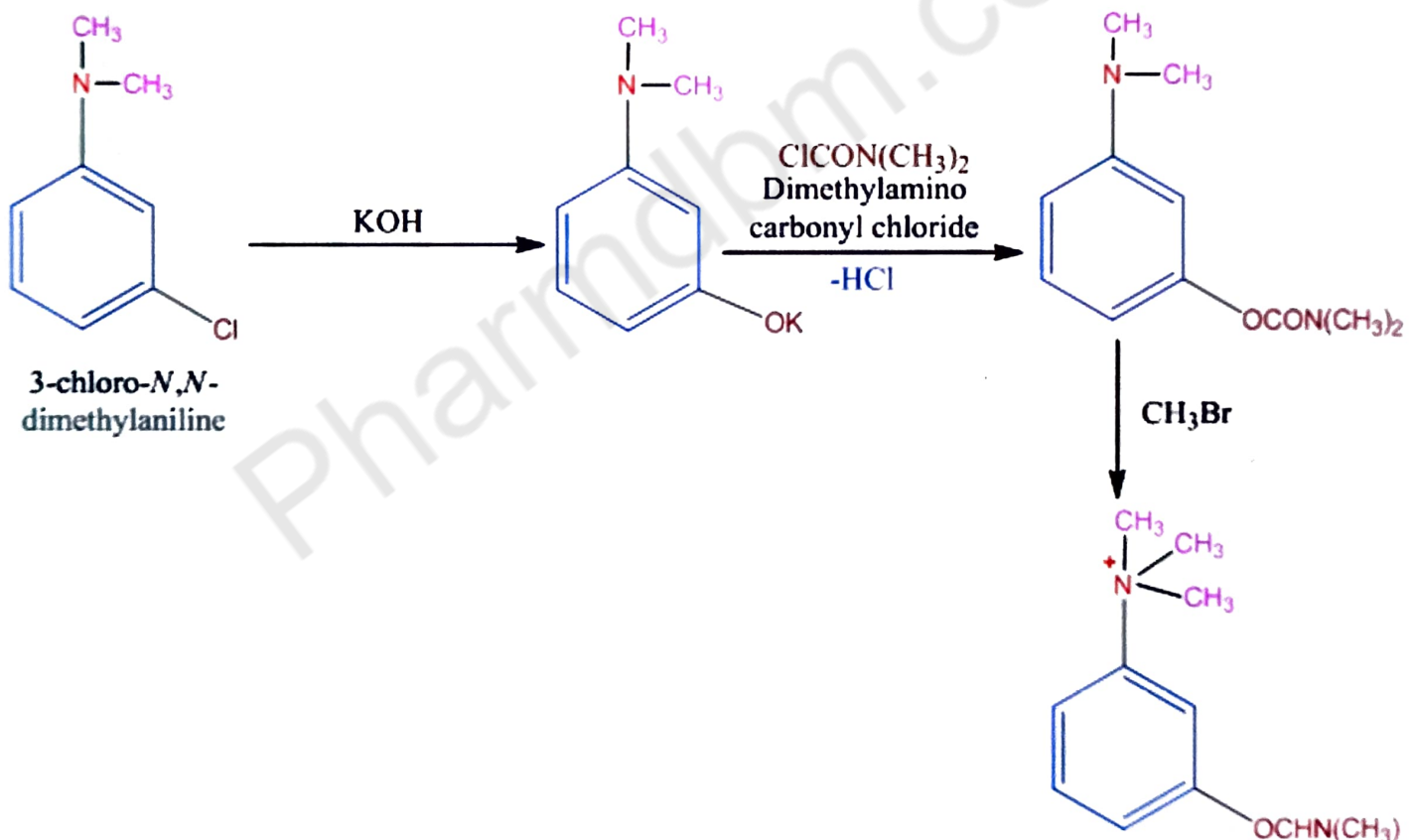
### ✓ Mechanism of action

- Reversibly inhibit acetyl cholinesterase enzyme.

### ✓ Uses

- Used in the treatment and management of myasthenia gravis.

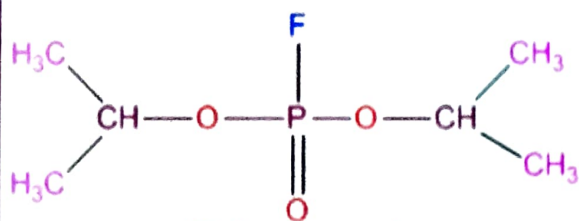
## ❖ Synthesis of Neostigmine:- From -m-chloro-N,N-dimethyl amino benzene



## II. Irreversible:-

- These are those drug which produces Irreversible inactivation of acetylcholinesterase enzyme.
- Bind to **cholinesterase** and form a permanent covalent bond.
- The body **must make new cholinesterase to break these bonds.**

### 1) Isoflurophate



Di isopropyl  
phosphorofluoridate

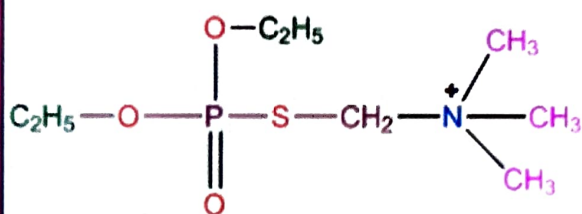
#### ✓ Mechanism of action

- Irreversible Inactivation of the acetyl cholinesterase.

#### ✓ Uses

- Used as miotic agent in treatment of glaucoma.

### 2) Ecothiophate Iodide



1-((diethoxy phosphoryl)thio)-  
N,N,N-  
trimethylmethanaminium

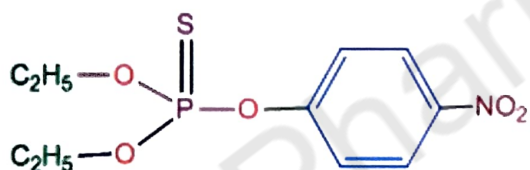
#### ✓ Mechanism of action

- Irreversible acetyl cholinesterase inhibitor.
- Permanently inactive the enzyme.

#### ✓ Uses

- Used as Chronic an Ocular antihypertensive in the treatment of glaucoma.

### 3) Parathione



O,O-diethyl O-(4-nitrophenyl)  
phosphorothioate

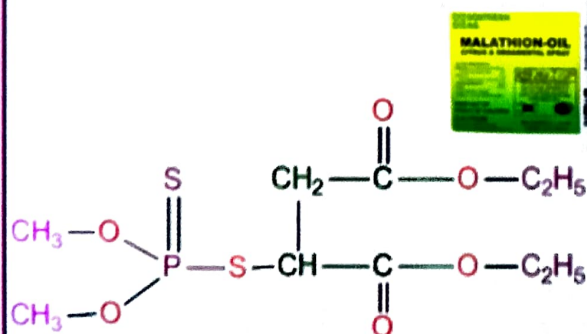
#### ✓ Mechanism of action

- Indirectly inhibitor.

#### ✓ Uses

- Used as insecticide in agriculture.

### 3) Malathion



diethyl 2-  
((dimethoxyphosphorothioyl)t  
hio)succinate

#### ✓ Mechanism of action

- Binding serine residue on cholinesterase enzyme & inactive it irreversibly.

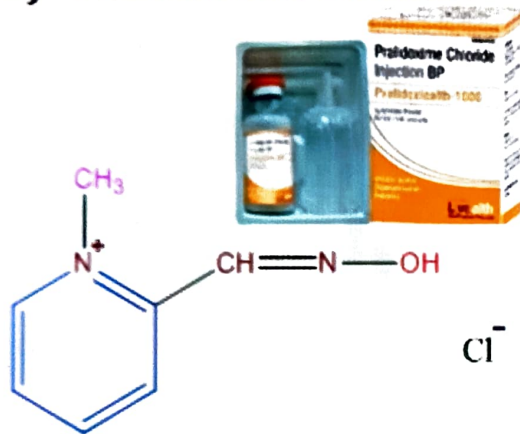
#### ✓ Uses

- Used for treatment of scabies.
- Used as insecticide.

## ❑ Cholinesterase reactivator:-

- Drugs used to reverse the inactivation of cholinesterase caused by organophosphates or sulfonates.
- They are an important component of therapy in agricultural, industrial, and military poisonings by organophosphates and sulfonates.

### 1) Pralidoxime chloride



2-((hydroxyamino)methyl)-1-methylpyridin-1-ium chloride

### ✓ Mechanism of action

- It reactivates the enzyme by binding to the anionic site of the enzyme.
- And displaces the phosphate from the serine residue.

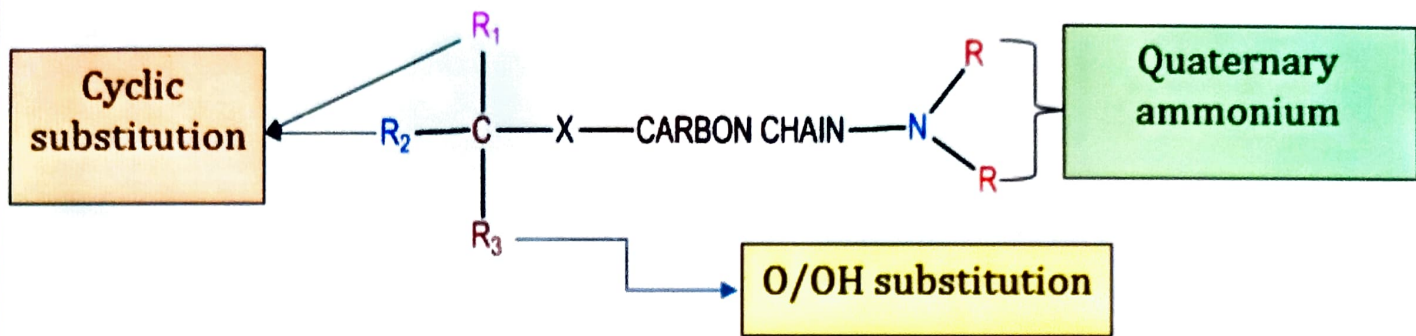
### ✓ Uses

- Used for the treatment of poisoning of organophosphorus compounds.

## ❑ CHOLINERGIC BLOCKING AGENTS:-

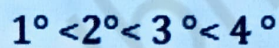
- **Synonyms:-** Cholinergic blocking agents, Cholinolytic agents, Anticholinergic agents/drugs, Cholinergic antagonist, Parasympatholytic agents, antimuscarinic agents.
- These are those agents or drugs which inhibit the effect of acetylcholine or parasympathomimetic agents by blocking the cholinergic receptors.
- These drugs are highly specific reversible competitive antagonists for muscarinic ACh receptors.
- They are rapidly absorbed from the gastrointestinal tract, slowly absorbed when applied locally on eye or skin.

## ❖ SAR OF CHOLINERGIC BLOCKING AGENTS:-



### ➤ Substitution on Quaternary ammonium groups:-

- Quaternary ammonium compounds **possess most potent anticholinergic activity.**
- Replacement of quaternary to the **tertiary, secondary or primary Cause decreases in activity.**



### ➤ Substitution in carbon chain:-

- The Substitution **may be ester, ether, alcohol amine.**
- But, Ester group provides the most potent anticholinergic activity.  
E.g.-Atropine.
- The nature of the group X effects only the duration of action, the physicochemical properties and the side effects of the drug molecule but **not its ability to bind with the receptor.**
- The **distance between the ring-substituted carbon and the amine nitrogen apparently is not critical; the length of the alkyl chain connecting these can be from two to four carbons.**
- The **most potent anticholinergic agents have two methylene units in this chain.**

## ➤ Substitution in carbon chain:-

- **Substituent  $R_1$  &  $R_2$**  should be carbocyclic or heterocyclic ring for maximal antagonist activity.
- Replacement of **heterocyclic rings to aromatic decrease activity.**
- The **rings could be identical but the more potent compounds are found to have different ring substitution.**

## ➤ Substitution on $R_3$ group:-

- Substituent  $R_3$  should be a hydrogen atom, hydroxy group, hydroxymethyl group, or methyl group.
- **H or OH attached antagonist are more potent (activity increase).**
- **In H or OH,**
  - OH → **Action (activity increase), duration of action will decrease.**
  - H → **Action (Activity decrease), duration of action will increase.**

### Classification of cholinergic blockers

#### Solanaceous alkaloids

Atropine sulphate  
Hyoscyamine sulphate  
Scopolamine hydrobromide  
Homatropine hydrobromide  
Ipratropium bromide

#### Synthetic cholinergic blockers

Tropicamide  
Cyclopentolate hydrochloride  
Clidinium bromide  
Dicyclomine hydrochloride  
Glycopyrrolate  
Methantheline bromide  
Propantheline bromide  
Benztropine mesylate  
Orphenadrine citrate  
Biperidine hydrochloride  
Procyclidine hydrochloride  
Tridihexethyl chloride  
Isopropamide iodide  
Ethopropazine hydrochloride

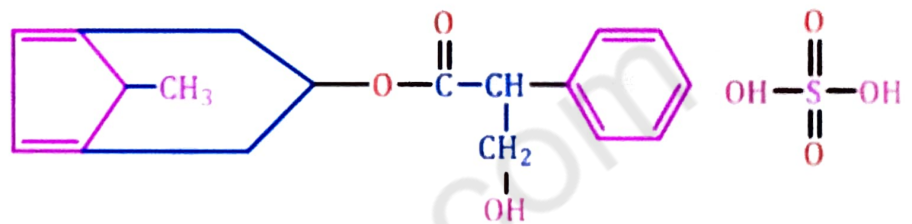


## ❖ Drugs acting on cholinergic blocking agents:-

### ➤ Solanaceous alkaloids and analogues:-

- Solanaceous alkaloids are **ester of the tropine**, these alkaloids are obtained from plants these such as atropa belladonna, Hyoscyamus niger, Datura stramonium etc.
- It is an **optically active compound** and levoform is potent.
- **(-) scopolamine is slightly water miscible viscous liquid.**
- Scopolamine occurs as Scopolamine hydrobromide salt, **which is colorless, odorless, water soluble powder.**

#### 1) Atropine sulphate



[(1S,5R)-8-methyl-8-azabicyclo[3.2.1]octan-3-yl]3-hydroxy-2-phenylpropanoate;sulfuric acid



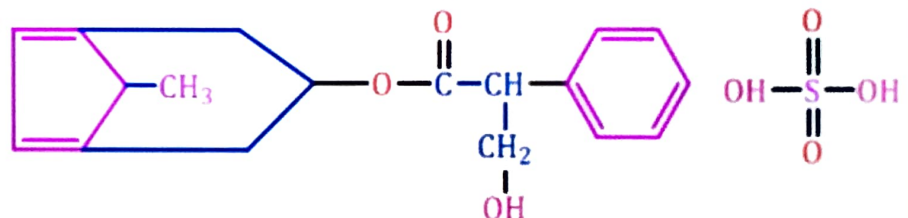
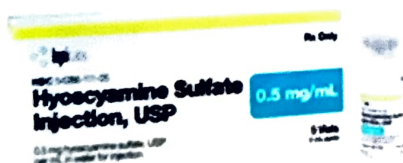
#### ✓ Mechanism of action

- It **has both central and peripheral action.**
- It first stimulates and then depresses the CNS.

#### ✓ Uses

- used in the treatment of gastric and duodenal ulcers.
- used in the **treatment of smooth muscle spasm.**

#### 2) Hyoscyamine sulphate



8-methyl-8-aza-bicyclo[3.2.1]octan-3-yl 3-hydroxy-2-phenylpropanoate;sulfuric acid

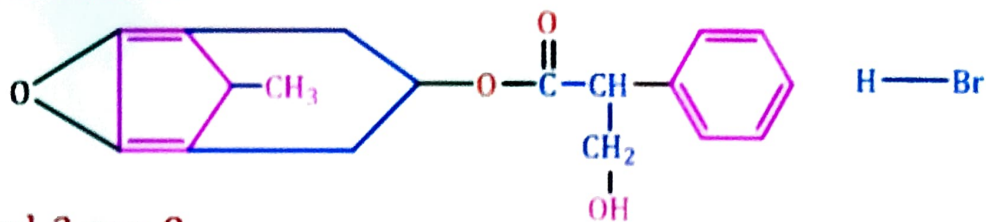
#### ✓ Uses

- **Treatment of gastric and duodenal ulcer.**
- Also **used In treatment of parkinsonism.**
- Prevent motion sickness.

#### ✓ mechanism of action

- **Similar to atropine.**
- More **potent than atropine.**

### 3) Scopolamine hydrobromide



[(1R,2R,4S,5S)-9-methyl-3-oxa-9-azatricyclo[3.3.1.0<sup>2,4</sup>]nonan-7-yl] (2S)-3-hydroxy-2-phenylpropanoate;hydrobromide



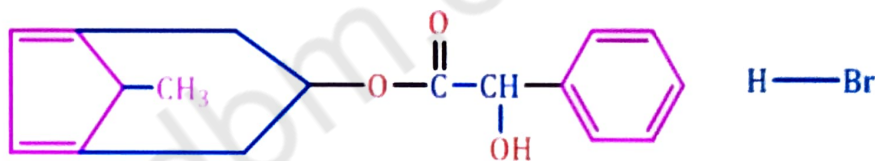
#### ✓ Uses

- Used in the **treatment of motion sickness.**
- Sometimes used before **surgery to decrease saliva**

#### ✓ Mechanism of action

- It has **more rapid onset but shorter duration of action than atropine.**
- **More potent than atropine.**
- **More toxic**

### 4) Homatropine hydrobromide



8-methylbicyclo[3.2.1]octa-1(7),5-dien-3-yl-2-hydroxy-2-phenylacetate;hydrobromide



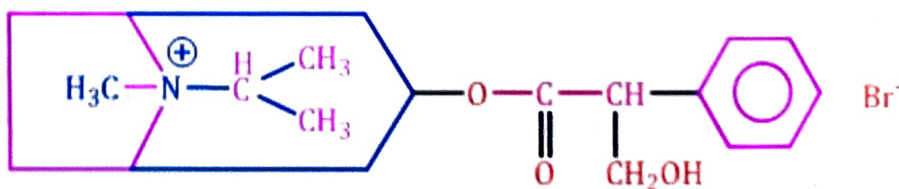
#### ✓ Mechanism of action

- It is a **competitive inhibitor of acetylcholine at the muscarinic receptor**, blocks parasympathetic stimulation.

#### ✓ Uses

- It is used to **dilate or enlarge pupils in eyes.**

### 5) Ipratropium bromide



(8-methyl-8-propan-2-yl-8-azoniabicyclo[3.2.1]octan-3-yl)3-hydroxy-2-phenylpropanoate ; bromide

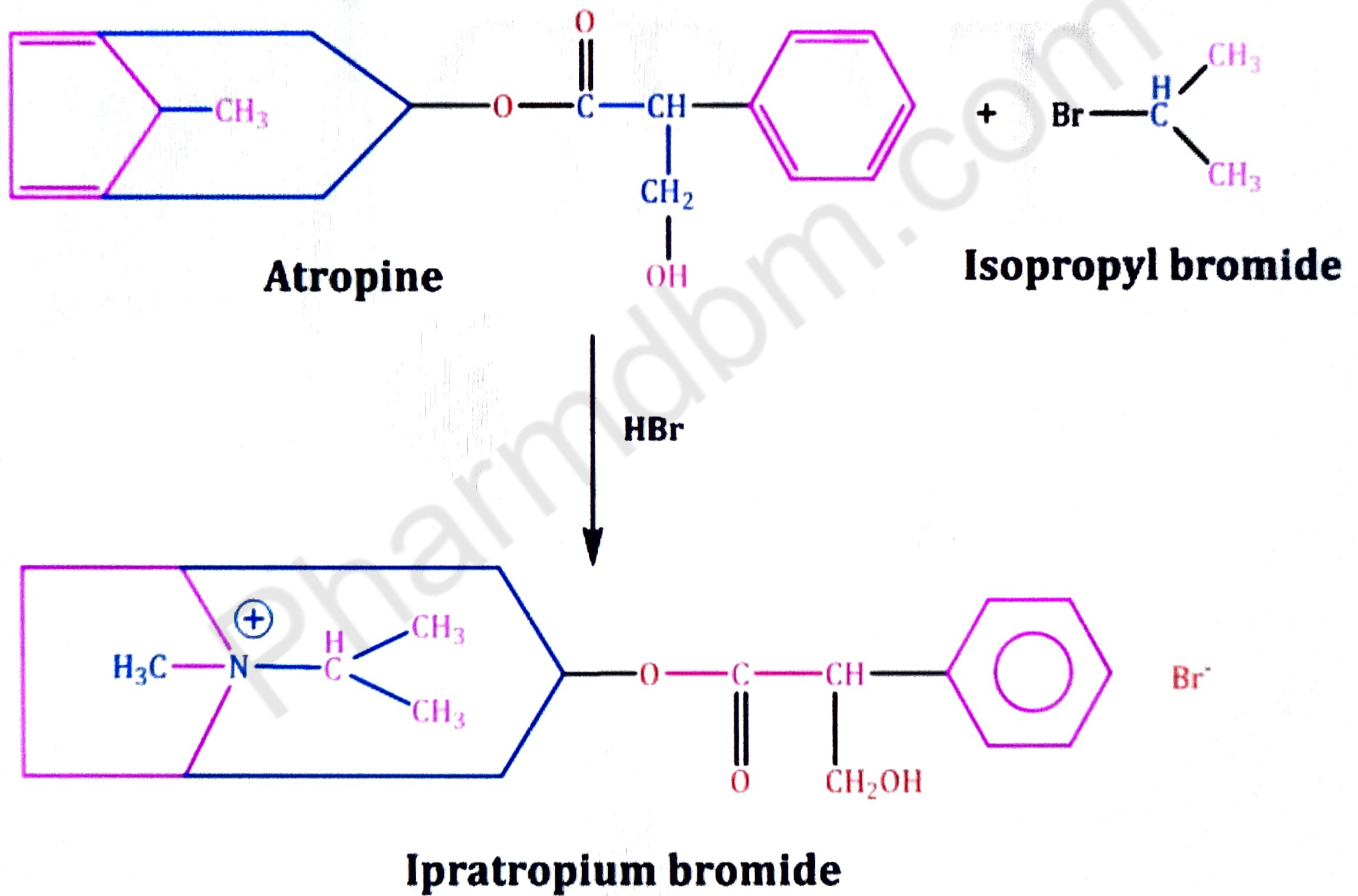
## ✓ Mechanism of action

- It is quaternary ammonium compound which blocks muscarinic acetylcholine receptors.
- It is **non-selective Muscarinic antagonist**.

## ✓ Uses

- Used in the **treatment of Asthma**.
- **treatment of chronic obstructive pulmonary disease (COPD)**.

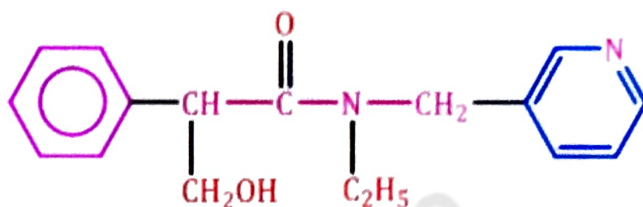
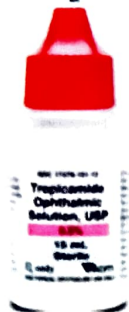
## ❖ Synthesis of Ipratropium bromide:-



## ➤ Drugs acting on synthetic cholinergic blocking agents:-

- Solanaceous alkaloids have lack selectivity and also have Some Side effects, this lead to the development of synthetic anticholinergic agents.
- Various **modification** have been made in the structure of atropine to **give various cholinergic antagonist**.

### 1) Tropicamide



#### ✓ Mechanism of action

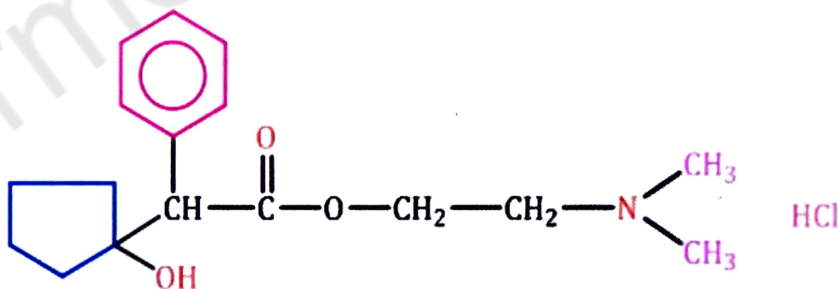
- Act as a competitive antagonist for Ach.

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

#### ✓ Uses

- Used for **dilation of pupil (before & after eye surgery)**.

### 2) Cyclopentolate hydrochloride



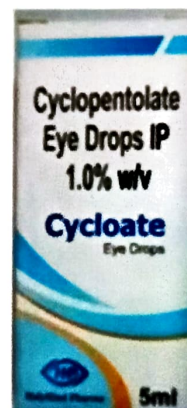
#### ✓ Uses

- Used in a eye drop for **mydriasis** (dilation of pupil).

2-(dimethylamino)ethyl-2-(1-hydroxyl cyclopentyl)-2-phenylacetate;hydrochloride

#### ✓ Mechanism of action

- Act as a **competitive antagonist for Ach**.
- Act more quickly than atropine



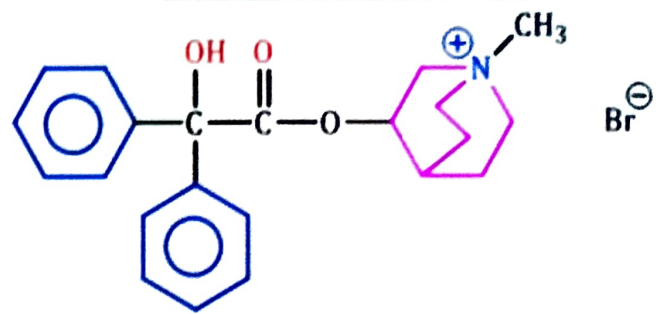
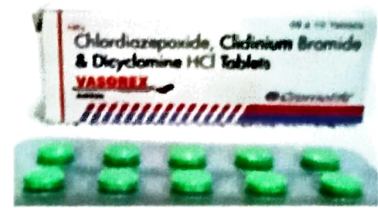
### 3) Clidinium bromide

#### ✓ Mechanism of action

- Bind with muscarinic receptor on smooth muscles and secretory gland & Inhibit the receptor.

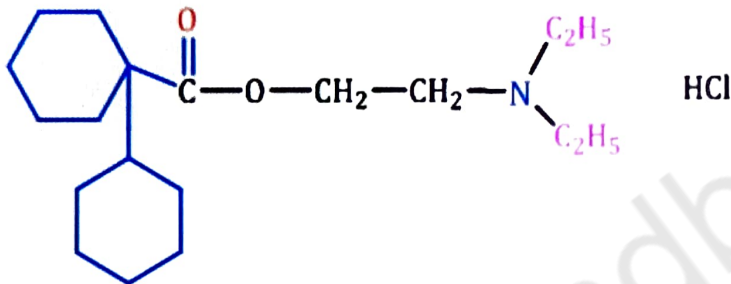
#### ✓ Uses

- it **relaxes smooth muscles and decrease biliary tract secretion.**
- Used in treatment of irritable bowel syndrome.



(1-methyl-1-azoniabicyclo[2.2.2]octan-3-yl) 2-hydroxy-2,2-diphenyl acetate; bromide

### 4) Dicyclomine hydrochloride



2-(diethylamino)ethyl 1-(cyclohexyl methyl)Cyclohexanecarboxylate hydrochloride

#### ✓ Mechanism of action

- Acts as **non selective smooth. muscle relaxant.**
- It has **specific anticholinergic effect at muscarinic receptor and has direct effect on smooth muscles.**

#### ✓ Uses

- used in **the treatment of irritable bowel syndrome.**
- Also used in the treatment of gastric and duodenal ulcer.



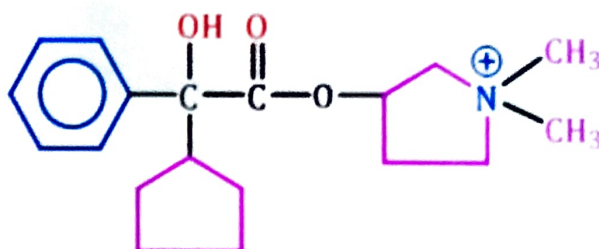
## 5) Glycopyrrolate

### ✓ Mechanism of action

- Blocks muscarinic receptor thus inhibiting cholinergic transmission.

### ✓ Uses

- Used to treat gastric ulcer by reducing acidic secretion.
- Used before surgery to reduce salivary, bronchial and gastric secretion.



(1,1-dimethylpyrrolidin-1-ium-3-yl) 2-cyclopentyl-2-hydroxy-2-phenylbromide

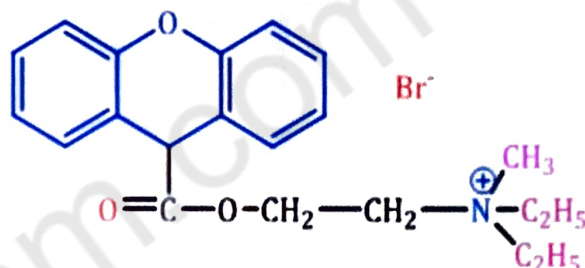
## 6) Methantheline bromide

### ✓ Mechanism of action

- Bind muscarinic receptor & blocks the action of Ach.

### ✓ Uses

- Uses It is given in the combination of antacid to treat peptic ulcer.



2-(9H-xanthene-9-carboxyloxy)-N,N-diethyl-N-methyl ethanaminium bromide

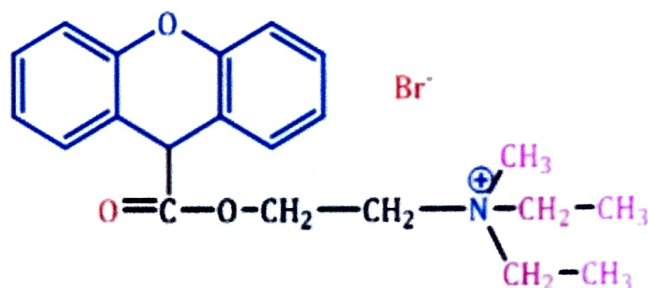
## 7) Propantheline bromide

### ✓ Mechanism of action

- It blocks the action of acetylcholine by binding to Muscarinic receptor present in various smooth muscle like gut bladder and eye.

### ✓ Uses

- treatment of spasm of the stomach, intestine & bladder.
- used in the treatment of excessive sweating.



diethyl-methyl-[2-(9H-xanthene-9-carboxyloxy)ethyl]azaium; bromide

## 8) Benztropine mesylate

### ✓ Mechanism of action

- centrally acting anticholinergic & antihistamine agent. It is selective  $M_1$  Muscarinic antagonist.

### ✓ Uses

- Used in treatment of Parkinson's disease.
- Anticholinergic, antihistaminic and local anesthetic activity.

## 9) Orphenadrine citrate

### ✓ Mechanism of action

- It is well known non selective acetylcholine receptor antagonist and also antihistamine.

### ✓ Uses

- It is used in skeletal muscles relaxant.
- Also used in treatment of Parkinson's disease.

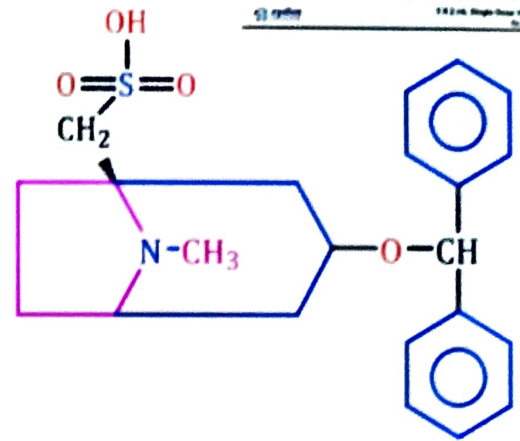
## 10) Biperidine Hydrochloride

### ✓ Mechanism of action

- Acts as a centrally blocking agent and block  $M_1$ .

### ✓ Uses

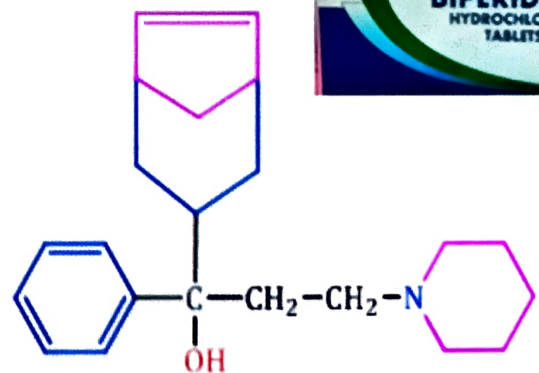
- It have strong musculotropic action.
- Used in all type of Parkinson's disease.



((1R)-3-(benzhydryloxy)-8-methyl-8-aza-bicyclo[3.2.1]octan-1-yl)methane sulfonic acid

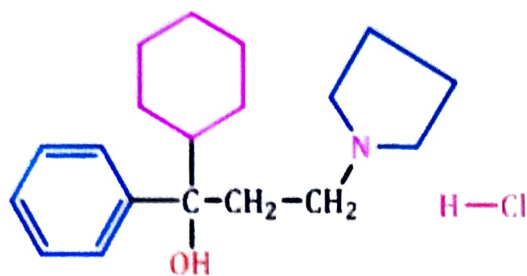


N,N-dimethyl-2-(phenyl(o-tolyl) methoxy) ethanamine



(1S)-1-(bicyclo[3.2.1]oct-6-en-3-yl)-1-phenyl-3-(piperidin-1-yl) propan-1-ol

## 11) Procyclidine Hydrochloride



1-cyclohexyl-1-phenyl-3-pyrrolidin-1-ylpropan-1-ol; hydrochloride

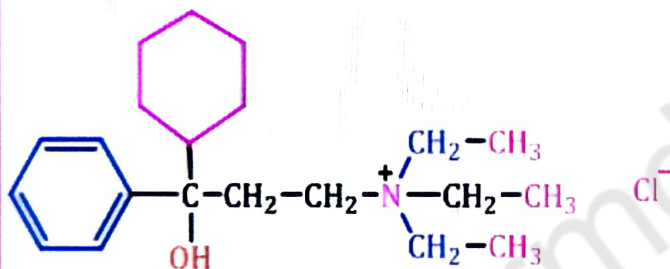
### ✓ Mechanism of action

- Acts on central cholinergic receptors, and thus balancing cholinergic and dopaminergic activity in the basal ganglia.

### ✓ Uses

- used in treatment of Parkinson's disease.
- Involuntary movements due to the side effects of certain antipsychotic drugs.

## 12) Tridihexethyl chloride



(S)-3-cyclohexyl-N,N,N-triethyl-3-hydroxy-3-phenylpropan-1-aminium chloride

### ✓ Mechanism of action

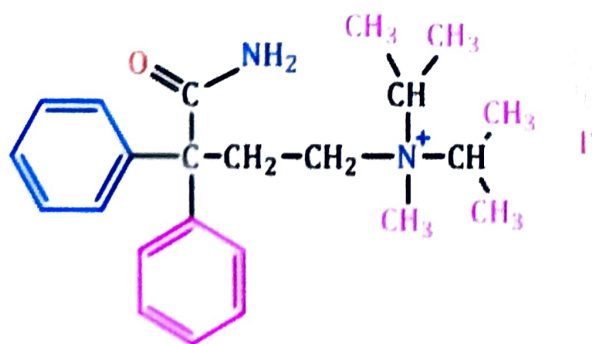
- It blocks all three muscarinic receptors i.e. M<sub>1</sub>, M<sub>2</sub> & M<sub>3</sub>.

### ✓ Uses

- Used as antispasmodic and anti-Parkinson's agents.



## 13) Isopropamide iodide



(4-amino-4-oxo-3,3-diphenylbutyl)-methyl-di(propan-2-yl)azanium; iodide

### ✓ Mechanism of action

- inhibit parasympathetic nerve impulses by blocking acetylcholine.

### Uses

- Used in the treatment of peptic ulcer.
- Potent anticholinergic, antispasmodic and antisecretory effects.



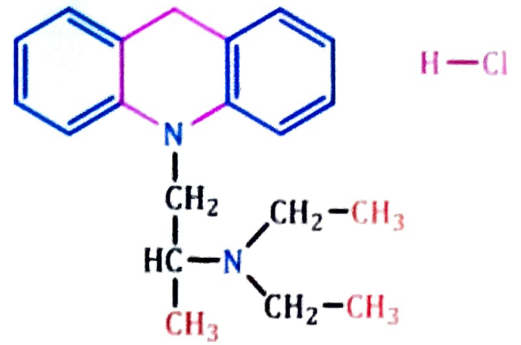
## 14) Ethopropazine hydrochloride

### ✓ Mechanism of action

- Act on An antimuscarinic receptors.

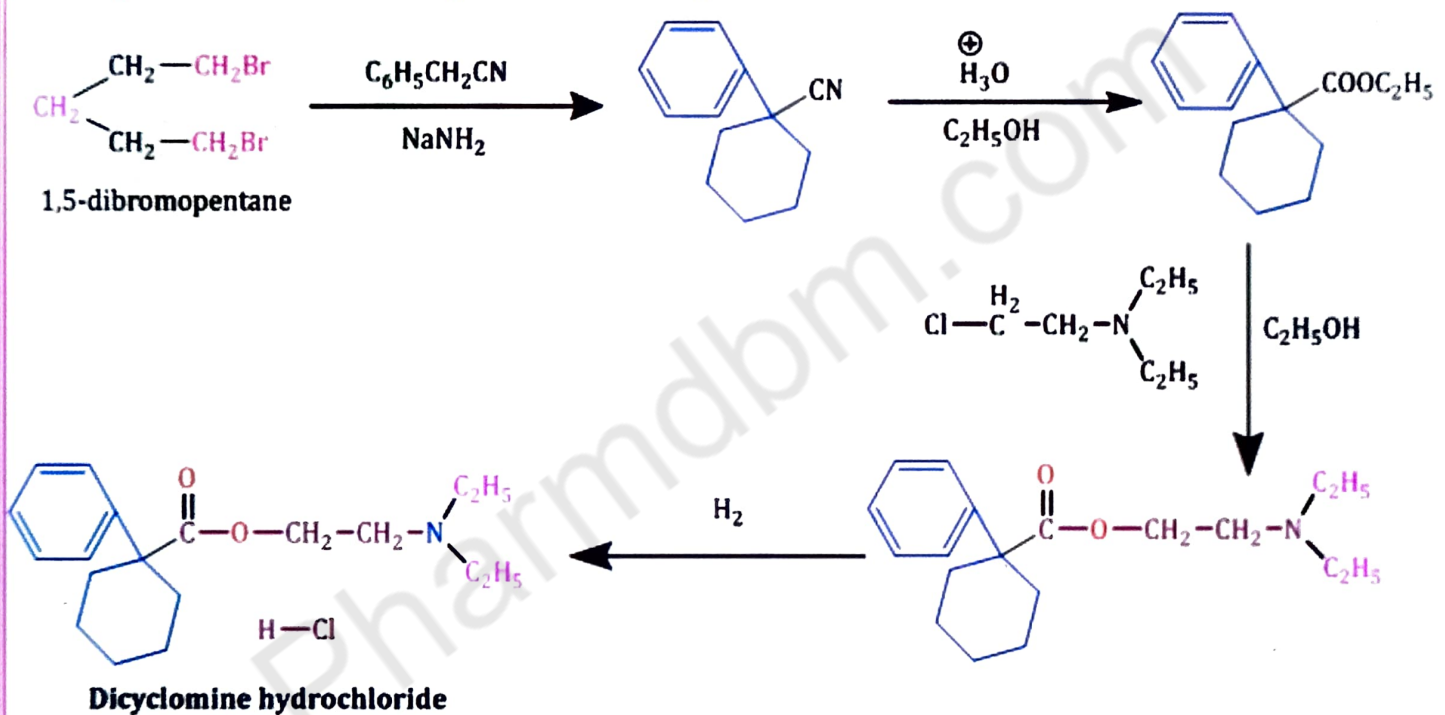
### ✓ Uses

- Used as adrenergic antagonist, Histamine antagonist and antiparkinson drugs.



N,N-diethyl-1-phenothiazin-10-ylpropan-2-amine;hydrochloride

### ❖ Synthesis of Dicyclomine hydrochloride:-



### ❖ Synthesis of Procyclidine hydrochloride:-

