Name of Unit	Cholinergic neurotransmitters
Course/Subject Code	BP402T
Class	B. Pharmacy
Semester	IV
Email id	kaurbaljeet32@gmail.com
Mobile No	9876722322
Faculty	Baljeet kaur

Learning Outcome of Module 03

LO	Learning Outcome (LO)	Course Outcome Code
LO1	Student will learn about the Cholinergic receptors, Cholinergic neurotransmitter.	BP402.1
LO2	biosynthesis and distribution.	BP402.2
LO3	Cholinergic agonist and Antagonist.	BP402.1
LO4	Structure activity relationship.	BP402.3
LO5	Synthesis of drugs.	BP402.4

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Table
• Introduction Cholinergic neurotransmitters • Biosynthesis • Direct acting drugs with Synthesis • SAR • Indirect acting drugs. • Cholinergic antagonists • Important questions

CHOLINERGIC AND ANTICHOLINERGIC DRUG

The autonomic nervous system is a part of nervous system that controls and regulates the internal organs. It controls involuntary responses eg; Breathing, digestion etc.

(i) Sympathetic: Studied in module 2.

(ii) Parasympathetic: When our body come back from sympathetic nervous system to normal condition.

EG: Normal heart rate of digestion rate etc.

Neurotransmitter:

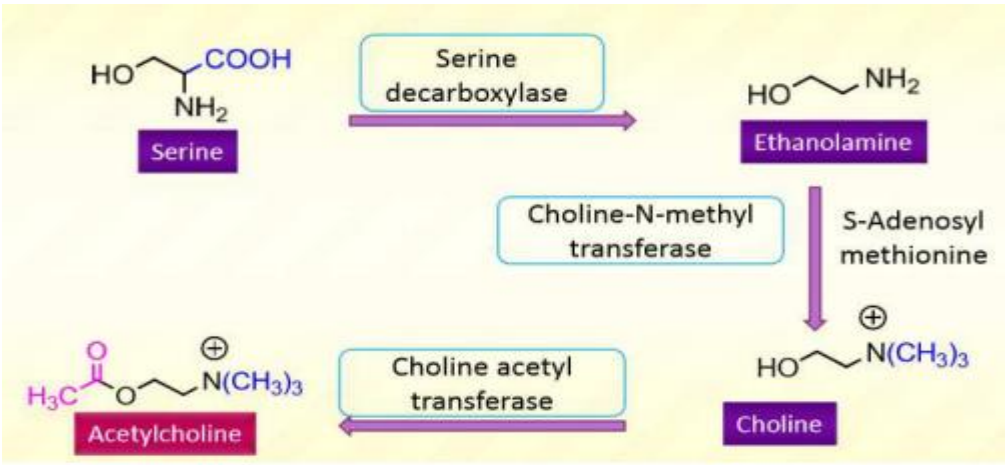
These are chemical messenger that transmit signals from a neuron to a target cell/ neuron across a synapse.

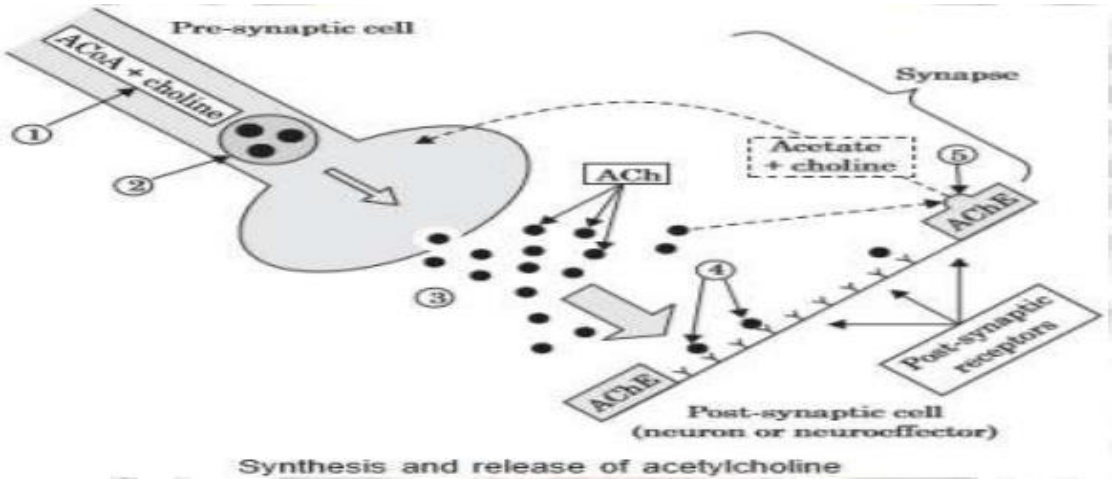
Sympathetic System release adrenaline (Adrenergic neurotransmitter).

Parasympathetic system release Acetylcholine (Cholinergic Neurotransmitter).

Acetylcholine (ACh) is the neurotransmitter of all the pre and many of the post ganglionic neurons of the parasympathetic system. Parasympathetic stimulation causes slowing down of the heartbeat, lowering of blood pressure, constriction of the pupils, increased blood flow to the skin and viscera, peristalsis of the GI tract.

Biosynthesis and catabolism of acetylcholine: The chemical transmitter at both pre and postganglionic synapses in the parasympathetic system is acetyl choline(Ach). Ach is also the neurotransmitter at sympathetic pre ganglionic synapses, some sympathetic postganglionic synapses, the neuromuscular junction (somatic nervous system), and at some sites in the CNS. Acetylcholine is the most wide spread autonomic transmitter present in the body. (a) Synthesis of acetylcholine (ACh). It was first synthesized by Bayer in 1867. Acetylcholine virtually has no therapeutic effect because of its differences of action and susceptibility to hydrolysis by acetyl cholinesterase and plasma butyryl cholinesterase. The synthesis of acetylcholine involves the reaction of choline with active acetyl (CoA). The active acetyl CoA being formed by the combination of acetate with Coenzyme A (CoA). The reaction between acetylCoenzyme A and choline is catalyzed by the enzyme choline acetylase. There is considerable evidence that the enzyme choline acetylase is synthesized with in the neuronal perikaryon, then transferred along the axon to its terminals where the formation of acetylcholine is believed to occur.





Synthesis and release of acetylcholine

Storage and release of ACh. ACh is stored in synaptic vesicles, which is released as discrete "Quanta" in response to depolarization of the nerve terminal and an increased influx of Ca++. When a nerve impulse occurs, depolarization of nerve terminal causes influx of Ca++, which facilitates the fusion of the axonal and vesicular storage membranes, and release formed acetylcholine into the synaptic cleft by exocytosis. The released acetylcholine combines with the receptors at target organ, remains bound for less than a millisecond and is quickly hydrolyzed by acetyl cholinesterase enzyme into choline and acetate.

Cholinergic receptors (Muscarinic & Nicotinic) and their distribution

Acetylcholine Receptors. There are number of different ACh receptors throughout the body. Acetylcholine acts on two different classes of receptors-nicotinic receptors and muscarinic receptors (widely distributed within both peripheral and central nervous systems).

Nicotinic Receptors. Nicotinic receptors are selectively activated by nicotine and blocked by tubocurarine or hexamethonium. These are rosette like penta meric structures which enclose a ligand gated cation channel, their activation causes opening of the channel and rapid flow of cations resulting in depolarization and generation of action potential On the basis of location and selectivity. They are divided into two types;

N1 : These are present at skeletal muscle endplate and mediate skeletal muscle contractions. They are selectively stimulated by phenyl trimethyl ammonium and are blocked by tubocurarine.

N2 : These are present in ganglionic cells, adrenal medullary cells, in spinal cord and in certain areas of brain. They are primarily stimulated by dimethylphenyl piperazine and blocked by hexamethonium.

Muscarinic Receptors. Although five muscarinic receptors have been identified, helpfully labelled M1 to M5, only three are well-characterized. The proto type agonist for these receptors is muscarine, derived from the poisonous fly a garic ,Amanita muscaria.

M1 receptors are mainly found in the nervous system. They mediate excitatory effects, lowering transmembrane potential by a decrease in K+ ion conductance; as an added wrinkle, they mediate increased gastric acid secretion seen with vagalstimulation. M1 receptors work via phospholipase C, increasing IP3 andDAG levels.

M2 receptors mediate the cardiac effects of vagal stimulation. They are inhibitory (hyperpolarizing membranes by increasing potassium conductance).

M2 receptors are found presynaptically in a variety of situations. This fits on cardiac cells and smooth muscle. M2 receptors lower intracellular cAMP levels

M3 receptors are responsible for all the other effects of parasympathetic stimulation, as they are the cholinergic excitatory receptors found on glands and smooth muscle. M3 receptors are similar to M1 in their use of phospholipase C. Physiology is however never simple, vascular smooth muscle relaxes in some situations due to M3 receptor stimulation. This relaxation is mediated by endothelial release of nitric oxide (NO) and occurs in some vascular beds thatappear devoid of parasympathetic innervation.

M4 are similar to M2.

M5 receptors seem similar to M1 and M3 in their effect

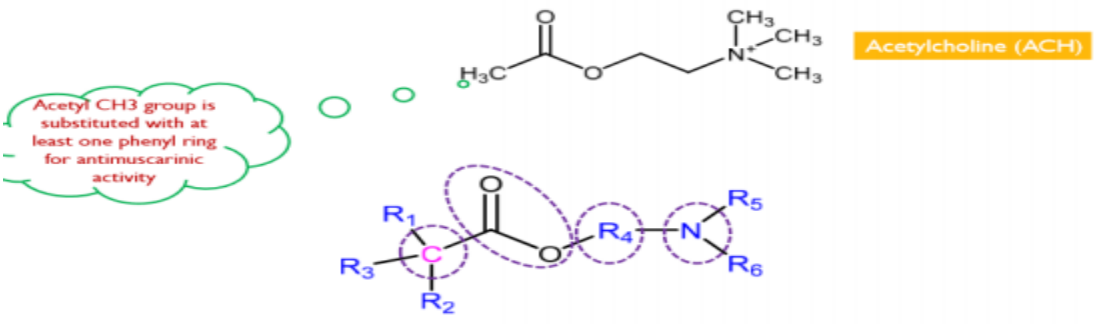
Difference Between Nicotinic receptors and Muscarinic receptors

Nicotinic receptors Central cholinoceptor	Muscarinic receptors Peripheral cholinoceptor
Ion channel linked receptors	G protein linked receptors
Autonomic ganglia (sympathetic & parasympathetic) stimulation (Nn)	On all peripheral organs that receive postganglionic parasympathetic fibers
Adrenal medulla (Nn) release of catecholamines (Adrenaline & Noradrenaline)	Heart (M2) inhibition exocrine glands (M3) contraction
Skeletal muscle (Neuromuscular junction) (Nm) Contraction	Smooth muscles (GIT, urinary tract, bronchial muscles) (M3) contraction
Almost excitatory	Excitatory or inhibitory

CHOLINOMIMETIC (PARASYMPATHOMIMETIC) DRUGS

The cholinomimetic or para sympathomimetic or cholinergic drugs are those which cause a muscarinic action on the receptors of the effector organs provided by the post-ganglionic cholinergic nerves. Invariably, these drugs exert their action in two different ways, namely: direct action, whereby they act on the cholinoceptive receptors like acetylcholine; indirect action, by rendering the cholinesterase enzymes inactive and preserving endogenously secreted acetylcholine, e.g.,anticholinesterase drugs like physostigmine (naturally occurring neostigmine and pyridostigmine (synthetic).

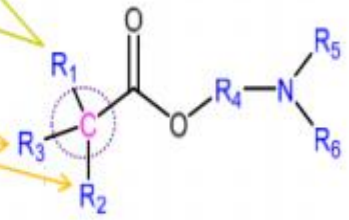
SAR OF CHOLINERGIC DRUGS



1. Substitutions at α-carbon with respect to ester group

1. May be a hydrogen atom, a hydroxyl group, a hydroxymethyl group, or a carboxamide
2. Hydroxyl group or a hydroxymethyl group, the antagonist usually is more potent

R_2 and R_3 should be carbocyclic or heterocyclic rings (phenyl, cyclohexyl, cyclopentyl) for maximal antagonist potency



Substitution of naphthalene rings at R_2 and R_3 affords inactive compounds, because of steric hindrance at the muscarinic receptor.

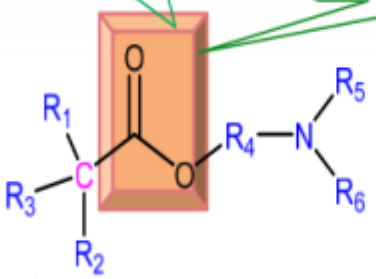
Bigger R_2 and R_3 groups bind to the hydrophobic region outside the Ach receptor site

The hydroxyl group at R_1 presumably increases binding strength by participating in a hydrogen bond interaction at the receptor.

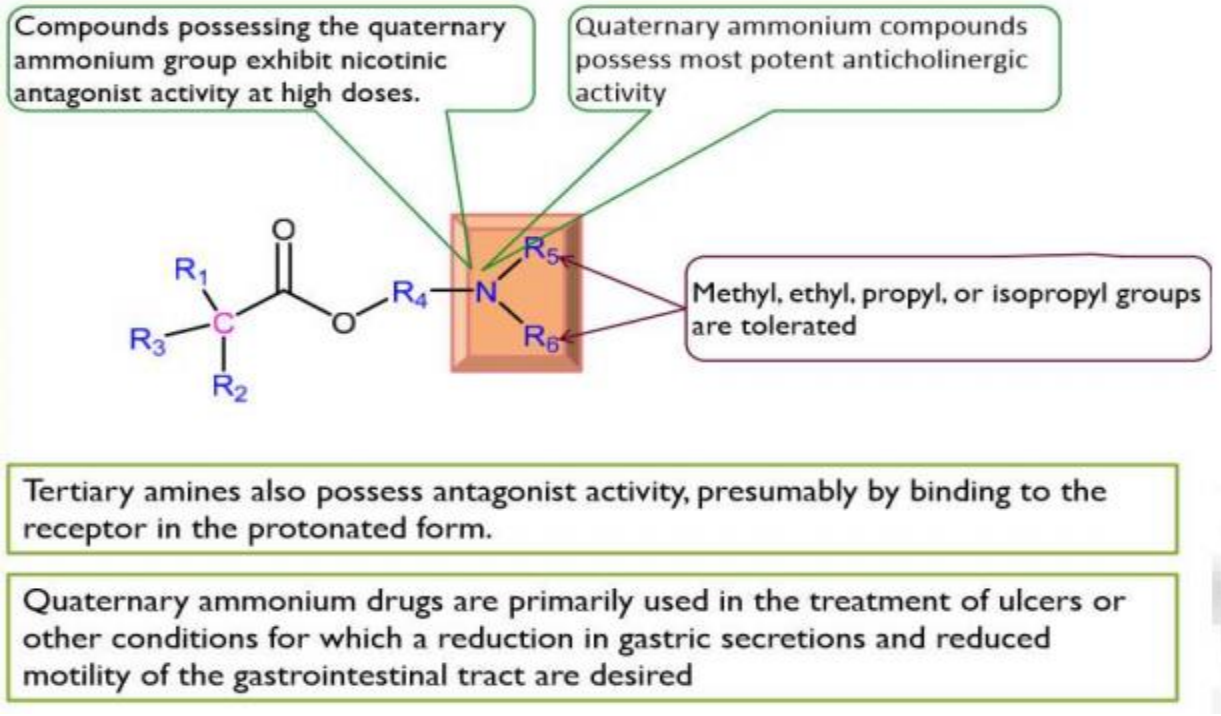
2. Changes at ester group

This substituent may also be an ether oxygen, or it may be absent completely.

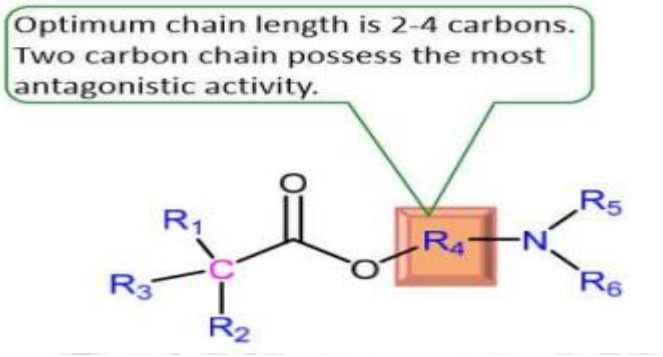
Ester group provides most potent anticholinergic activity



3. Substitution at the amine group



4. Changes at R4 position



Classification: -

Cholinomimetic drugs may be broadly classified under the following two categories.

1.Direct acting agents:

a. choline ester: Acetylcholine, Carbachol*, Bethanechol, Methacholine

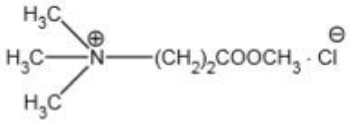
b. Natural alkaloids: Pilo carpine.

2. Indirect acting/ Cholinesterase inhibitors

a. Reversible: Physostigmine, Neostigmine*, Tacrine hydrochloride

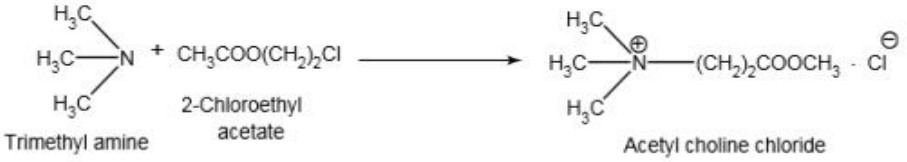
b. Irreversible: Pyridostigmine, Edrophonium chloride, Ambenoniumchloride, Isofluorphate, Echothiophate iodide, Parathione, Malathion.

i. Acetylcholine chloride (Miochol)



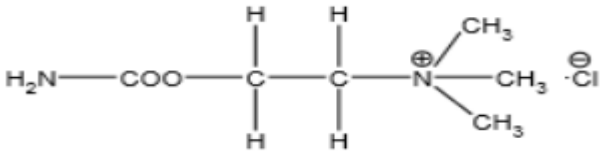
(2-Acetoxyl ethyl)-trimethyl ammonium chloride

Synthesis



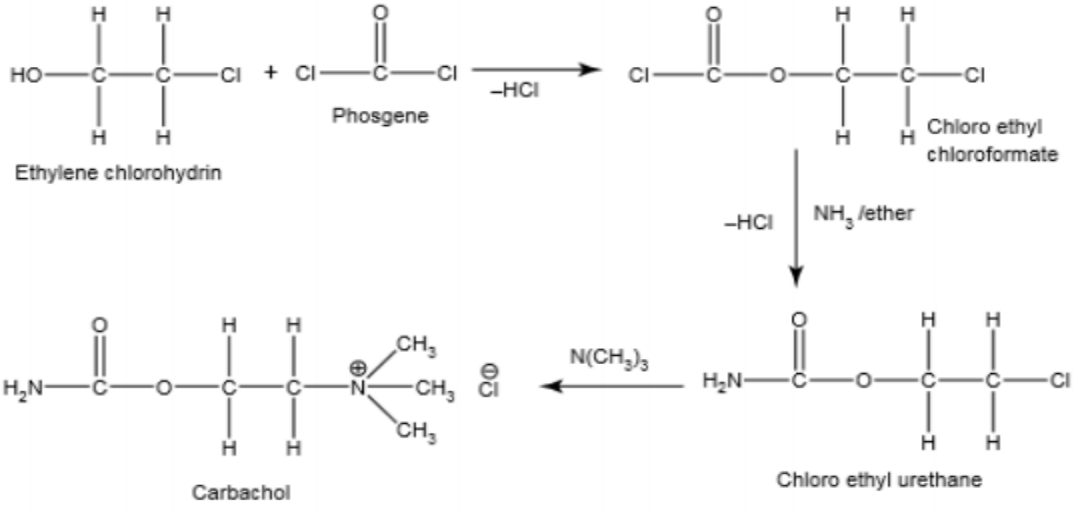
Properties and Uses: It is a white or almost white crystalline powder or colourless crystals, very hygroscopic in nature, slightly soluble in methylene chloride,soluble in water and alcohol. It is a topical ophthalmic drug to induce miosis, during certain intraocular surgical procedures, such as cataract surgery, other anterior-segment surgery. Systemically administered Ach is rapidly hydrolyzed by acetyl cholinesterase, hence, it has no clinical use. It is a cardiac depressant and effective vasodilator.

Carbachol*

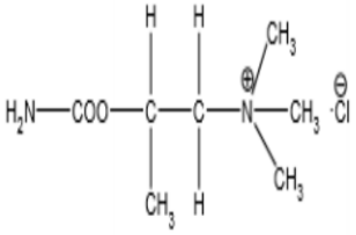


Synthesis

Route I: From Ethylene chlorohydrin



Properties and uses: It is a white crystalline, hygroscopic powder, soluble in water, sparingly soluble in alcohol, insoluble in acetone. It is an ester of carbamic acid, the terminal methyl group of Ach is replaced by amino group. It possesses both muscarinic and nicotinic properties by cholinergic receptor stimulation. It is more slowly hydrolyzed by acetyl cholinesterase. It is used for its miotic actions in the treatment of glaucoma to reduce intraocular pressure.

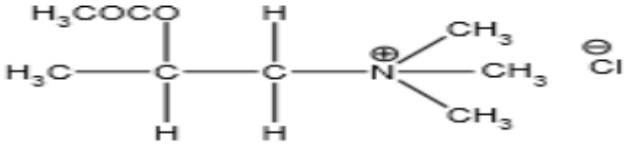


ii. Bethanechol chloride

2-[(Amino carbonyl) oxy] N,N,N trimethyl propan ammonium chloride.

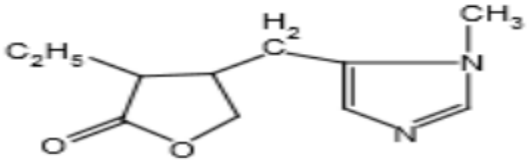
Properties and uses: It is a white crystalline hygroscopic powder, and it exhibits polymorphism, soluble in water and alcohol. it has pharmacological properties similar to those of methacholine. The presence of -CH3 gives prolonged activity due to steric hindrance.It produces smooth muscle contractions. It is not well absorbed from the gastro-intestinal tract. It can be given subcutaneously, but not by intramuscular (IM) or intravenous (IV) because of its severe side effects. It is used to relieve urinary retention and abdominal distention after surgery. This is one of the post vagotomy gastric drug.

3.Methacholine



Properties and uses: It is highly deliquescent, has faint fishy odour, and aqueous solutions are neutral, soluble in water, alcohol, and $CHCl_3$. It is used to treat Reynaud's syndrome and glaucoma.

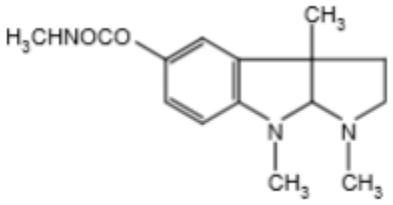
4. Pilocarpine.



Properties and uses: It is a white or almost white crystalline powder or colourless crystals, hygroscopic, very soluble in water and in alcohol. Pilocarpine is an alkaloid obtained from the dried leaflets of Pilocarpus jaborandi and Pilocarpus cmicrophyllus in which it occurs to the extent of about 0.5% together with other alkaloids. Pilocarpine is a nonselective agonist on the muscarinic receptors. It acts on M3 receptors in smooth muscles and cause contractions in the gut, trachea, and eyes. It is used for the treatment of symptoms of dry mouth caused by radiotherapy for cancer of head and neck and the symptoms associated with Sjogren's syndrome.

2. Reversible & Irreversible:

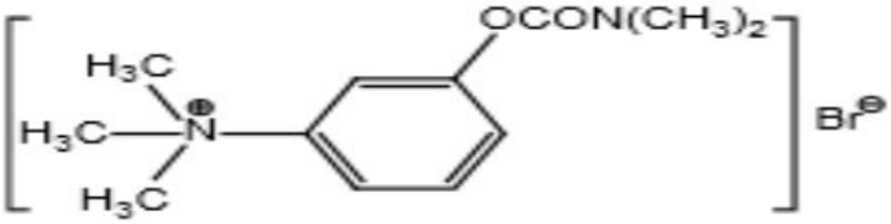
1.**Reversible & Irreversible**:



Properties and uses: It exists as a white or almost white crystalline powder, hygroscopic, very soluble in water, and freely soluble in alcohol. It gradually becomes red when exposed to air and light; the colour develops more quickly

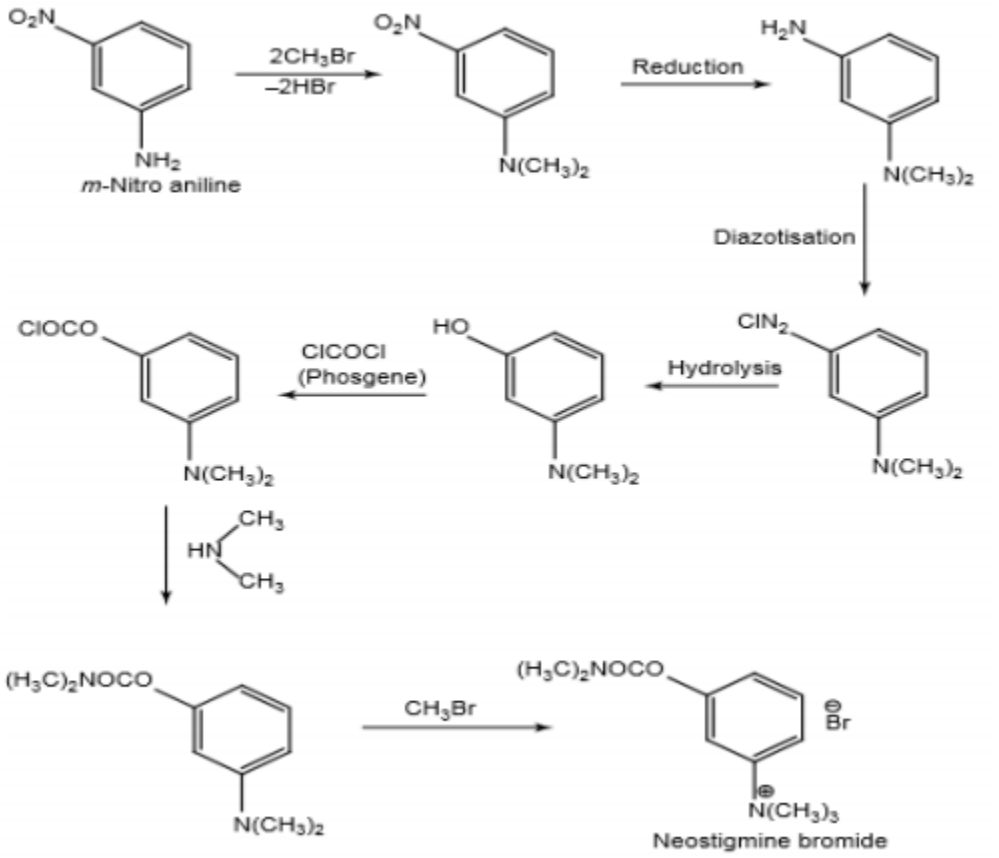
Physostigmine is an oldest anticholinesterase agent. It is used in the treatment of glaucoma. It can penetrate the blood brain barrier and is employed to antagonize the toxic CNS effects of anti-muscarinic drugs, tri cyclic depressants, H1 anti histamines, and benzodiazepines. It is also used in the treatment of Alzheimer's disease.

1. **Neostigmine***

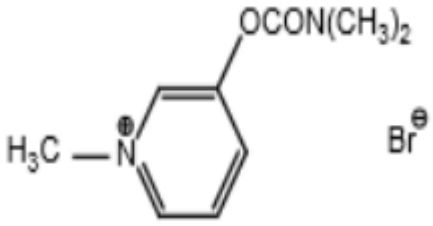


Properties and uses: It exists as white, odourless, crystalline powder with a bitter taste, freely soluble in water, alcohol, and insoluble in ether. Its solutions are neutral to litmus. It acts as a cholinesterase inhibitor

Synthesis



3. Pyridostigmine



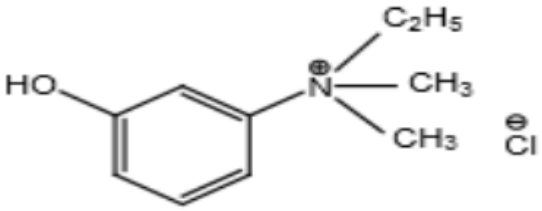
Properties and uses:

It exists as white, crystalline powder with a characteristic odour and bitter taste, soluble in water, alcohol, chloroform, slightly soluble in hexane, and insoluble in ether.

It is hygroscopic in nature.

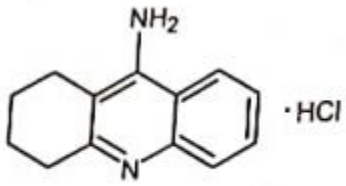
It is used in the treatment of myasthenia gravis and it antagonizes the effects of neuro muscular blocking (NMB) agents.

4.**Edrophonium chloride**



Properties and uses: It exists as a white crystalline powder, soluble in water and alcohol, insoluble in methylene chloride. On parenteral administration, edrophonium has a more rapid onset and shorter duration of action than neostigmine. It is used as an anti arrhythmic drug in paroxymal atrial tachycardia. It is also used in the diagnosis of myasthenia gravis.

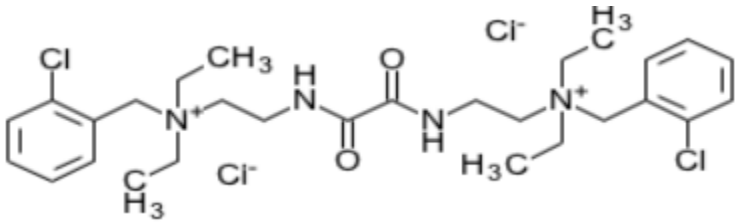
4.Tacrine hydrochloride



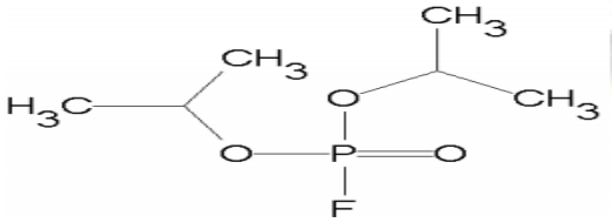
1,2,3,4-tetrahydro-9-aminoacridine hydrochloride.

Uses- It is used in the treatment of Alzheimer disease. It is also used in mild to moderate Alzheimer demetia.

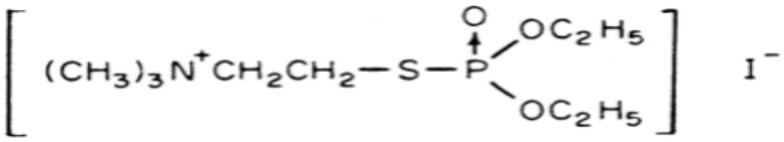
6. Ambenonium chloride



7. Isofluorphate

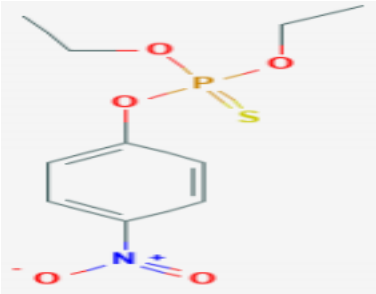


8. Echothiaphate iodide

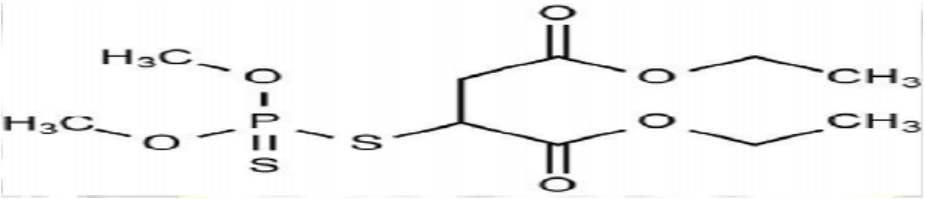


Properties and uses: It exists as a white crystalline powder, soluble in water and alcohol, insoluble in methylene chloride. On parenteral administration, edrophonium has a more rapid onset and shorter duration of action than neostigmine, pyridostigmine, or ambenonium. It is used as an anti arrhythmic drug in paroxymal atrial tachycardia. It is also used in the diagnosis of glaucoma

9. Parathione



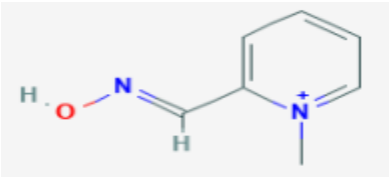
10.Malathion.



CHOLINESTERASE REACTIVATOR:

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

1.Pralidoxime chloride.

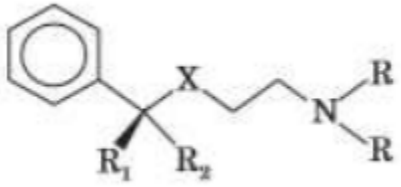


CHOLINERGIC BLOCKING AGENTS

Cholinergic Blocking agents: Cholinergic antagonists inhibit the actions of endogenous acetyl choline and muscarinic agonists at muscarnic receptors in peripheral tissues and in the CNS. These drugs are highly specific reversible competitive antagonists for muscarinic ACh receptors. The pharmacological effects are blockage of parasympathetic stimulation at effector organs. They are rapidly absorbed from the gastrointestinal tract, slowly absorbed when applied locally on eye or skin. The potent anti cholinergics are used to control the secretion of saliva and gastric acid, slow down gut motility, and to prevent vomiting. They also have a limited therapeutic use for the treatment of Parkinson's disease.

SAR of cholinolytic agents

1. Anticholinergic agents are bulky. They combine with muscarinic receptors and shield the binding site from acetylcholine. The general structure of the compounds in this category is



2. Substituent R1 should be carbo cyclic or heterocyclic ring for maximal antagonist activity.

3. Substituent R2 should be a hydrogen atom, hydroxy group, hydroxyl methyl group, or methyl group.

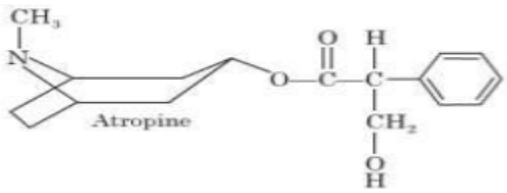
4. The nature of the group X effects only the duration of action, the physicochemical properties and the side effects of the drug molecule but not its ability to bind with the receptor.

5. There is a limitation for the N-substitution. Optimal potency is associated with 2-3 ethyl groups.

6. The stereochemistry at the benzylic carbon is critical for muscarinic antagonist activity. Any compound that can place the phenyl group in the same absolute configuration as depicted in the general formula above will have potent muscarinic antagonist activity.

7. The phenyl ring cannot tolerate any their substituent than F at the p position without losing its antagonist activity

8. A negative site for binding of the positive charged N; positive charged proton formal positive charge while tertiary amines have a positive charged proton



9. Atropine is a racemic mixture (equal number of d- and l-isomers) and like most chemicals acting on the peripheral nervous system, atropine is stereo specific; l-isomer (l-hyoscyamine) is 250 times more active than thed-isomer

10. The presence of an N-methyl group on atropine or scopolamine changes the activity of the ligand, possibly by preventing a close interaction between the ligand and the membrane or lipophilic sites onthe receptor. The methyl group also prevents the penetration into the brain.

Therapeutic uses of anticholinergic drugs

1. Peripheral: Therapeutic uses following inhibition of para sympathetic transmission, e.g., mydriasis , decrease saliva production, decrease motility of smooth muscle, inhibition of vagal transmission toheart, decrease bronchial secretions, decrease in urinary in continence,etc.

2. Central: Anti-parkinson and anti-motion sickness

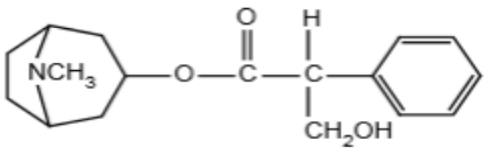
3. If anti cholinergic drugs are non-quaternary amine derivatives, they will cross the blood brain barrier. They may have therapeutic actions, or side effects, involving the central nervous system; if anti cholinergic drugs are quaternary amines, they will not cross the blood brain barrier, thus they are devoid of CNS activity.

4. Expected ‘side effects’ of anti cholinergic therapy include: peripheral photophobia, cycloplegia, dry mouth, tachycardia, difficult urination, redskin (‘atropine flush’), and increase in skin temperature, central-sedation or excitement.

SOLANACEOUS ALKALOIDS AND ANALOGUES

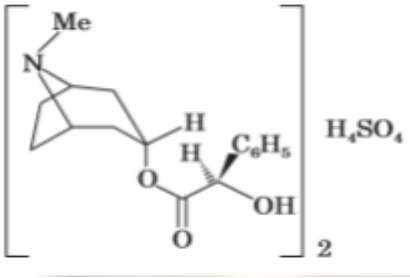
Scopolamine is an alkaloid isolated from various members of solanaceae. It is an optically active compound and levo form is potent. (-) Scopolamine is slightly water miscible viscous liquid. Scopolamine occurs as Scopolamine hydrobromide salt, which is a colorless, odorless, water soluble powder

1.**Atropine sulphate**



Properties and uses: It is a white crystalline powder or colour less crystals, freely soluble in alcohol and well soluble in water. It is the tropine ester of racemic tropic acid and is optically inactive. The greater molar potency of atropine helps it to block several moles of acetylcholine. The umbrella like atropine molecule may mechanically or electrostatically inactivate adjacent receptors on the cell surface so that these receptors are also unavailable for acetylcholine or other para sympathomimetic stimulants. Atropine has all the actions and uses of anti muscarinic drugs.

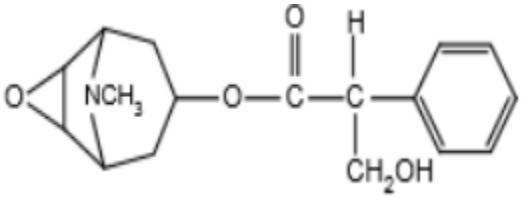
2.Hyoscyamine sulphate



Properties and uses: Hyoscyamine sulphate is available as white, crystalline powder or colorless needles, very soluble in water, sparingly soluble or soluble in alcohol, practically insoluble in ether. It melts at about 203°C, with decomposition. It should be stored in an airtight container, protected from light

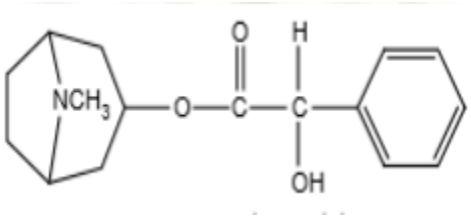
Use: Hyoscyamine is an anti cholinergic drug used to treat peptic ulcers.

3. Scopolamine hydrobromide



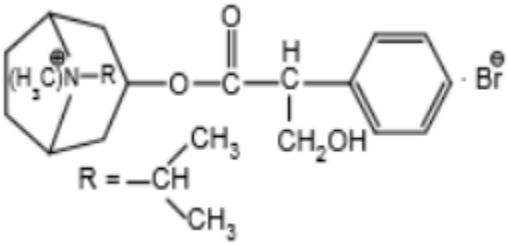
Properties and uses: It exists as colour less or white crystals or white granular powder, odourless, slightly efflorescent in dry air, and is an anhydrous salt, soluble in water or alcohol and in chloroform, insoluble in ether. Scopolamine is the levo component of the racemic mixture that is known as Hyoscine. It is effective in the prevention of motion sickness. It is a competitive blocking agent of the parasympathetic nervous system like atropine, but it differs markedly from atropine in its action on the higher nerve centres

4. Homatropine hydrobromide

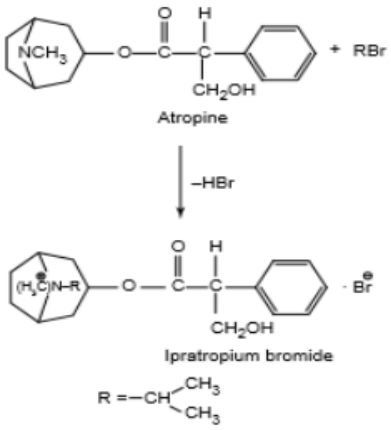


Properties and uses: It is a white crystalline powder or colour less crystals, sparingly soluble in alcohol, but freely soluble in water. It is used topically on the ciliary structure of the eye and to effect mydriasis.

5. Ipratropium bromide*.



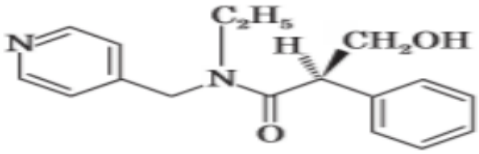
Synthesis



Properties and uses: It is a white or almost white crystalline powder, freely soluble in methanol, soluble in water, but slightly soluble in ethanol. It is used in the inhalation therapy to produce dilation of bronchial smooth muscle for acute asthmatic attacks. It produces broncho-dilation by competitive inhibition of cholinergic receptors bound to the smooth muscles of the bronchioles.

Synthetic cholinergic blocking agents:

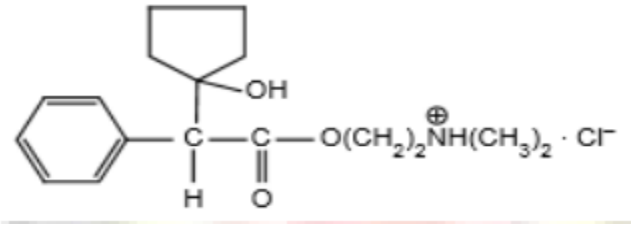
1.Tropicamide



Properties and uses: Tropicamide is (RS)-N-ethyl-2-phenyl-N-(4-pyridylmethyl) hydrocrylamide. It is white, crystalline powder, slightly soluble in water, freely soluble in

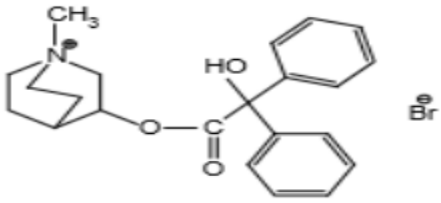
alcohol and in methylene chloride. It is an effective anti cholinergic drug for ophthalmic use. It antagonizes M4 receptors.

2. Cyclopentolate hydrochloride



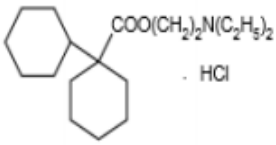
Properties and uses: It exists as white crystalline powder, soluble in water, methanol, and ethanol, but insoluble in toluene. Cyclopentolate is usually employed as eye drops to cause cycloplegia and mydriasis. It acts much faster than atropine and possesses a relatively shorter duration of action.

3.**Clidinium bromide**



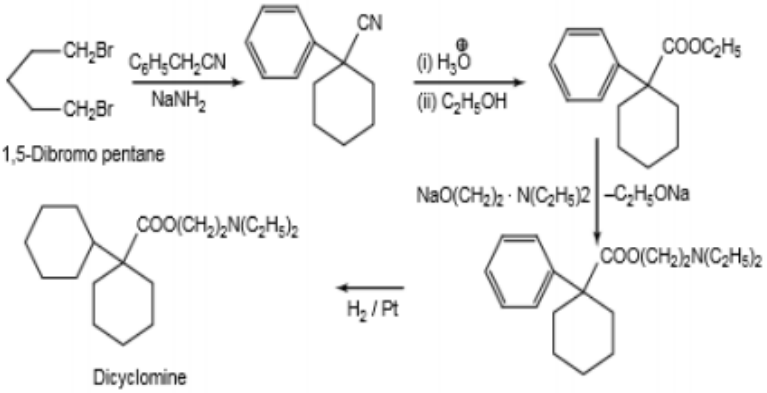
Uses: Used as a bronchodilator in asthmatic conditions. It has a longer lasting effect as compared to β-agonists

4. Dicyclomine hydrochloride*



2-(Dimethylamino) ethyl bicyclohexyl-1-carboxylate HCl

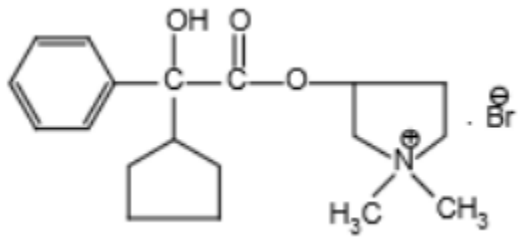
Synthesis



Dicyclomine

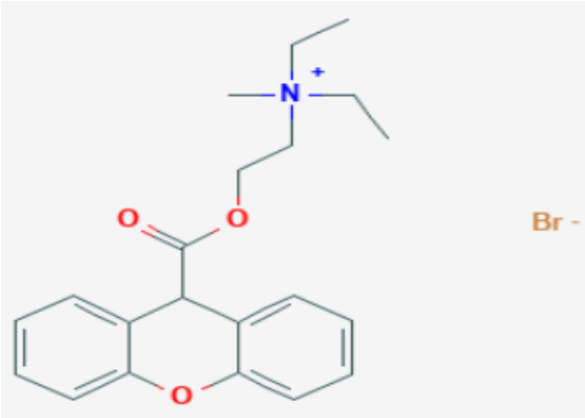
Properties and uses: It exists as a white, crystalline powder with a bitter taste, soluble in water and chloroform. Dicyclomine HCl behaves both as an antimuscarinic and a nonspecific antispasmodic agent. It was first introduced in 1950 and had minimized the adverse effects associated with the atropine type of compounds. Dicyclomine has spasmolytic effect on various smooth muscle spasms particularly those associated with the gastrointestinal (GI) tract. It is also used in dysmenorrhoea, pylorospasm, and biliary dysfunction.

5. Glycopyrrolate

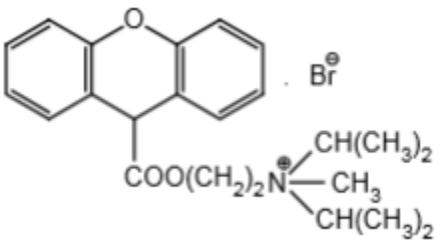


Properties and uses: It exists as a white, crystalline powder with a bitter taste,soluble in water and alcohol. It is used for suppressing gastric secretion and in the treatment of peptic ulcer and gastrointestinal disorder associated with spasm.

6**. Methantheline bromide**

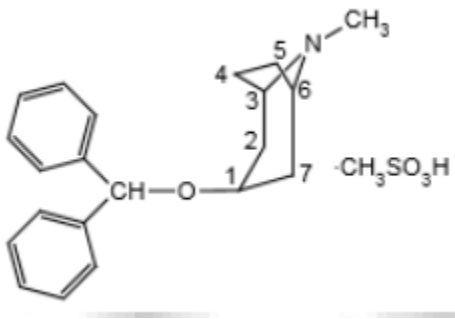


7**. Propantheline bromide**



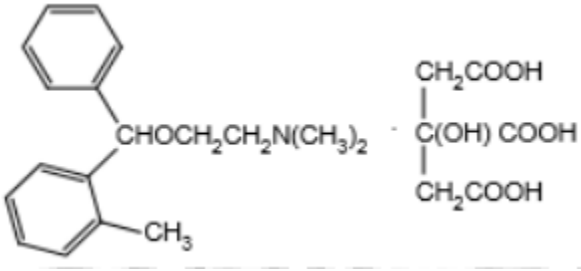
Properties and uses: It is a white or yellowish-white powder, slightly hygroscopic, soluble in water, in alcohol, and in methylene chloride. It is beneficial for the treatment of peptic ulcer, due to the decreased gastric motility by this drug, and it may relieve the pain in this condition.

8. Benztropinemesylate



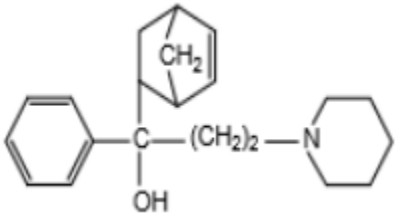
Properties and uses : It is a white crystalline powder, insoluble in ether, but soluble in water and ethanol. It has anti cholinergic, antihistaminic, and local anaesthetic activities. It is used in the treatment of Parkinsons's disease.

9**. Orphenadrine citrate**



Properties and uses: It is a white or almost white crystalline powder, sparingly soluble in water, slightly soluble in alcohol. It is used for the symptomatic treatment of Parkinson's disease. It is also used as a skeletal muscle relaxant.

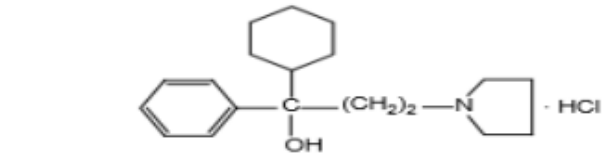
10. Biperidine hydrochloride



Properties and uses: It is a white crystalline powder, slightly soluble in methylene chloride, in water, and in alcohol. It has a relatively strong Musculo tropic action, which is about equal to

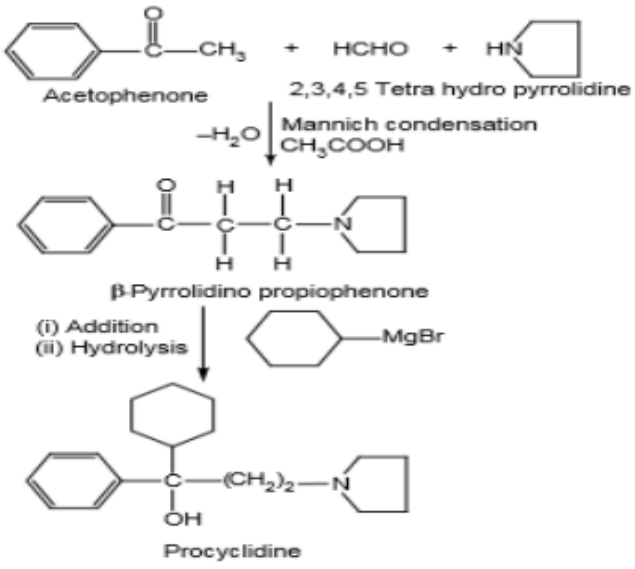
that of papaverine, in comparison with most synthetic anti cholinergic drugs. It is used in all types of Parkinson's disease.

11. Procyclidine hydrochloride*



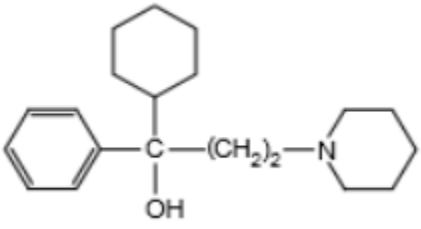
1-Cyclohexyl-1-phenyl-3-pyrrolidin-1-yl-1-propanol HCl

Synthesis



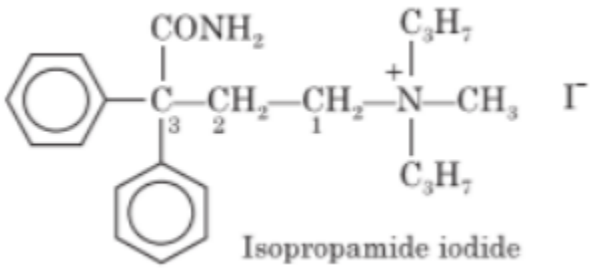
Properties and uses: It exists as white crystalline powder, and it has been used for peripheral effects that are similar to methantheline. Its clinical usefulness lies in its ability to relieve voluntary muscle spasticity through its central action. Procyclidine is used in the treatment of Parkinson's disease.

12. **Tridihexethyl chloride**



Properties and uses: It is a white crystalline powder, slightly soluble in water, sparingly soluble in alcohol and in methylene chloride. It is used as antispasmodic and anti parkinsonian agent. Trihexylphenidyl is more effective than levodopa against Parkinson's tremor.

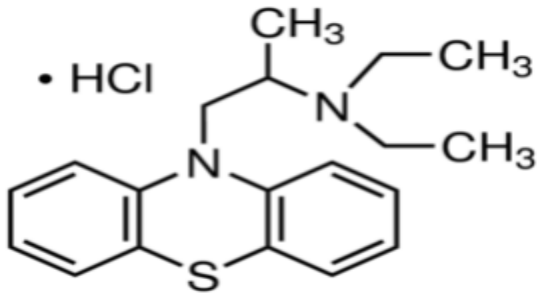
13. Isopropamide iodide.



Isopropamide iodide

Properties and uses: Isopropamide iodide is pale yellow coloured, bitter taste crystalline powder. It is sparingly soluble in water and freely soluble in chloroform and alcohol. Isopropamide is a potent anticholinergic drug. It has antispasmodic and anti secretory effects. It is used in the treatment of pepticulcer.

14. Ethopropazine hydrochloride



Multiple choice questions:

1. Which of the following is a clinical use for a muscarinic agonist?
   A. Treatment of myasthenia gravis
   B. Swifting off the GIT prior to surgery
   C. Swifting on the urinary tract after surgery
   D. Increasing heart muscle activity in certain heart defects.
2. Acetylcholine can exist in how many number of conformation?
   A. 2
   B. 3
   C. 5
   D. 4
3. Why the quaternary ammonium group is essential for intrinsic activity of ach?
   A. Because it acts as electron donor
   B. Because it acts as electron acceptor
   C. Because of its action as a detecting group.
   D. None of above
4. On substitution of methyl group on quaternary ammonium with amine group, which amine group shows more activity?
   A. Primary
   B. Secondary
   C. Tertiary
   D. None of above
5. Which group of Ach contributes to the binding of compound to the muscarinic receptor?

A. Ammonium group
B. Methyl group
C. Ester group
D. All of above

6. Effects of cholinergic nerve stimulation are called

A. Sympathetic
B. Parasympathomimetic
C. Cholinergic
D. B&C both

7. Replacement of methyl group by ethyl group or large alkyl group cause?

A. Increase in activity of compound

B. Decrease in activity of compound

C. Inactivation of compound

D. No change

8. Ester of aromatic or higher molecular weight acids possess:

A. Cholinergic agonist activity

B. Cholinergic antagonist activity

C. Anticholinergic agonist activity

D. Anticholinergic antagonist activity

9. In ethylene bridge incorporation of beta-substitution leads to reduction of:

A. Muscarinic activity

B. Nicotinic activity

C. No change

D. All of above

10.Placement of alpha substitution in choline moiety results in:

A. Decrease in nicotinic activity

B. Decrease in muscarinic activity

C. Increase in nicotinic activity

D. Both A and B

ANSWERS

1.C, 2. D, 3. C, 4.A, 5.C, 6. D, 7.C, 8.B, 9.B, 10.D

Short Question answers (5 marks)

1.Write in short M1 and M2 receptors.

2. Define cholinergic system and its functions.

3. Highlight direct action Ach agonists.

4. Write a note on direct acting drugs.

5. Highlight in short release of Ach.

6.Write any two Irreversible indirect acting parasynpathomimetic drugs.

7. Write MOA and uses of Ipratropiumbromide.

8. Write two examplesc of synthetic amino alchol ester drugs.

Long Question Answers (10 marks)

1. Explain acetylcholine biosynthesis, storage and catabolism.
2. Explain classification of parasympathomimetic agents.
3. Classify muscarinic receptors.
4. Highlight SAR of para sympathomimetic agents.
5. Give synthesis of neostigmine and carbachol.
6. Give detailed account of solanaceous alkaloids.
7. Give classification of anti-cholinergic drugs with examples and write mode of action and uses.
8. Write a note on SAR of anticholinergic drugs.