PARASYMPATHOLYTICS
(CHOLINERGIC BLOCKING AGENTS)
UNIT-III

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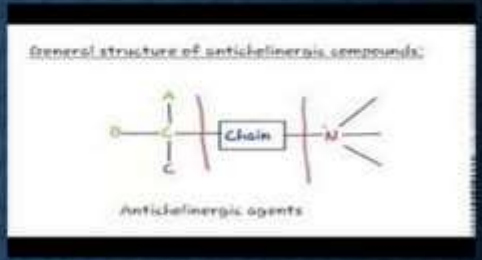
CHOLINERGIC BLOCKING AGENTS

- Definition: Drugs or chemical agents apparently reduce the number of free receptors(muscarinic and nicotinic)that can interact with acetylcholine by blocking the active site on receptor at parasympathetic ganglia or neuro muscular junction are called as cholinergic blocking agents.
- Cholinergic blocking agents will reduce the availability of AcH – receptor interactions and its biological response.
- Cholinergic blockers are also called as cholinolytics or parasympatholytics or cholinergic antagonists or anticholinergics.
- They can also reduce the activity of cholinergic agonistic drugs.
- Cholinergic blockers are differentiated as muscarinic blockers and nicotinic blockers

SAR OF CHOLINOLYTIC AGENTS



Cationic head (Quaternary N):

- Anti cholinergics containing quaternary nitrogen atom ,shows stimulative action on muscarinic receptor at neuromuscular junction in the skeletal muscle.
- Drugs should contain quaternary ammonium like AcH to show cholinergic blocking activity.
- Tertiary amine protonated with positive charge increases the potency of a drug.
- 10 to 12 carbon bridge between two nitrogens is optimal for maximum neuromuscular blockade.

- Methyl,ethyl,propyl or isopropyl substitution on quaternary N atom shows good activity and tolerated groups for the blocking activity.

Chain substitution:

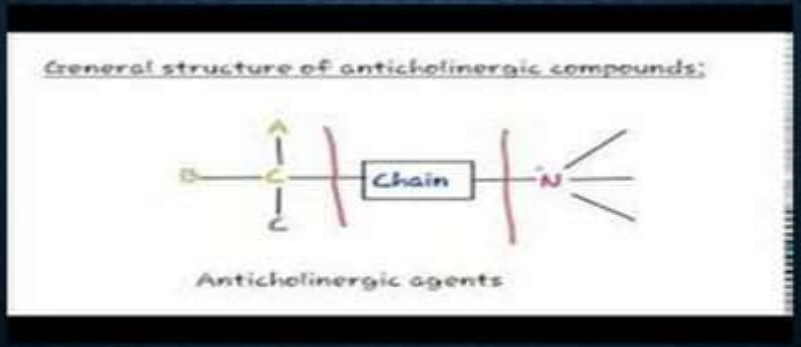
- Bridging structure between two N atoms should be lipophilic in nature to show increased potency.
- Ester group in the chain provides the most potent anticholinergic activity.
- The substituent may also be ether or aminoalcohol shows blocking action.
- No substitution in the chain decreases the activity.

A & B Substitution:

- Substitution may be cycloalkyl,aromatic or heterocyclic rings.
- Substitution with heterocyclic rings or carbocyclic groups increases antagonistic activity.
- More potent anticholinergic compounds possess different rings at position A & B.

Substitution at position C:

- The substituent can be hydrogen atom or hydroxyl group or hyroxymethyl group.
- Antagonist with hydroxyl group or hydroxymethyl group is more potent.



CLASSIFICATION

- A wide variety of compounds possess anticholinergic activity.
- Cholinergic blockers are classified based on chemical structure:

1. Solanaceous alkaloids and its synthetic derivatives
2. Synthetic aminoalcohol ethers
3. Aminoalcohols
4. Amino amides
5. Papaveraceous derivatives
6. Miscellaneous derivatives

- Solanaceous alkaloids and its synthetic derivatives:These are alkaloids that are members of solanaceous group.They found principally in henbane(Hyoscyamus niger),deadly nightshade (Atropa belladonna) and jimson weed(Datura stramonium).

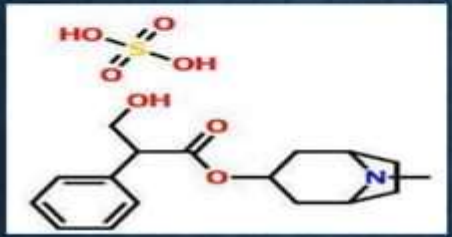
Eg:Atropine sulphate,Hyoscyamine sulphate,Scopolamine hydrobromide,Homatropine hydrobromide, Ipratropium bromide

- Synthetic cholinergic blocking agents: Synthetic drugs containing aminoalcohol ether group or amino amide group or other groups

Eg: Cyclopentolate hydrochloride,clidinium bromide,Dicyclomine hydrochloride,Glycopyrrolate,Methantheline bromide,Propanetheline bromide, Benzotropium mesylate,Tropicamide,Orphenadrine citrate,Biperidine hydrochloride,procyclidine hydrochloride,Tridihexethyl chloride,Isopropamide iodide,Ethopropazine hydrochloride

ATROPINE SULPHATE

- Structure:



- Uses: 1.Atropine produces mydriatic effect (dilation of pupil).

  2.Used in the treatment of iritis and corneal inflammations.

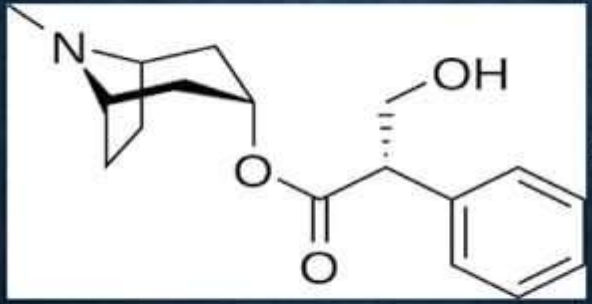
  3.To treat arrythmias by increasing heart rate.

  4. Atropine is used before general anaesthesia to reduce oral and nasal secretions

  5. Used as organophosphate antidote(to prevent muscarinic effects of AcH accumulation).

HYOSCYAMINE **SULPHATE**

- Structure:

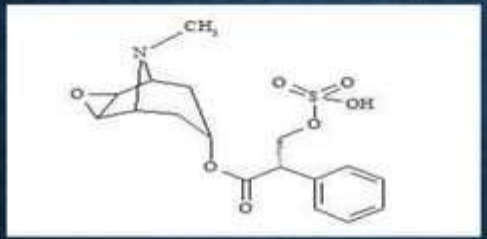


- Uses: 1. Used as a anticholinergic agent.

  2.Levorotatory form of atropine

SCOPOLAMINE HYDROBROMIDE

- Structure:



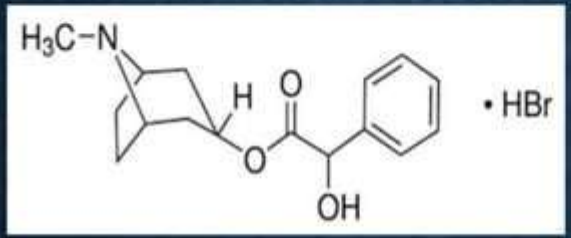
- Uses: 1.Scopolamine is also called as hyoscine

  2.Used to treat motion sickness and postoperative nausea and vomiting

  3. Scopolamine is used before surgery to decrease saliva secretion

HOMATROPINE HYDROBROMIDE

- Structure:



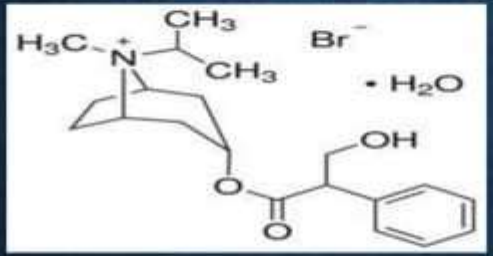
- Uses: 1. First anticholinergic agent used before eye examinations and after eye surgeries.

  2. It blocks muscarinic actions of acetylcholine

  3.It widens the pupil of eye.

IPRATROPIUM BROMIDE

- Structure:



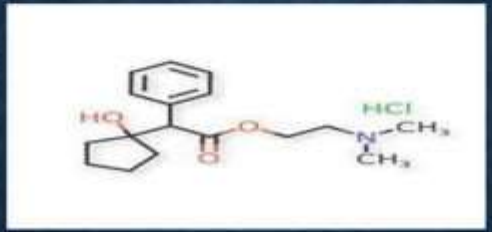
- Uses: 1.Used to control and prevent symptoms of Wheezing and shortness of breath caused by lung disease chronic obstructure pulmonary disease.

  2.It relaxes the muscles around airways to easier the breathe

  3.To treat bronchitis and emphysema.

CYCLOPENTOLATE HYDROCHLORIDE

- Structure:



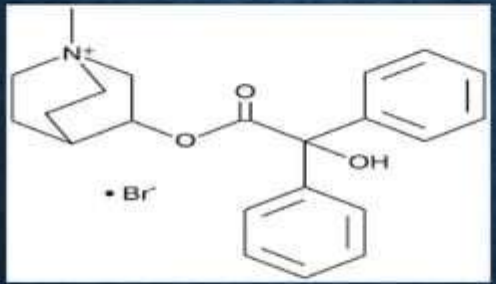
- Uses: 1. Parasympatholytic

  2.It quickly produces cycloplegia and mydriasis in the management of iritis and keratitis

  3.It is having spasmodic activity

CLIDINIUM BROMIDE

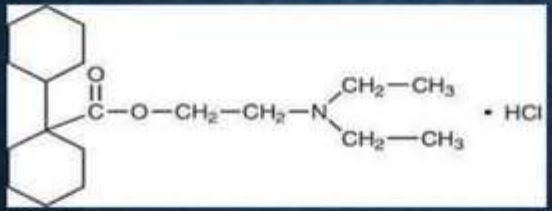
- Structure:



- Uses: 1. Anticholinergic agent in the treatment of peptic ulcer,hyperchlorhydria,ulcerative colitis and spastic colon,anxiety states with GIT disturbances.

DICYCLOMINE HYDROCHLORIDE

- Structure:



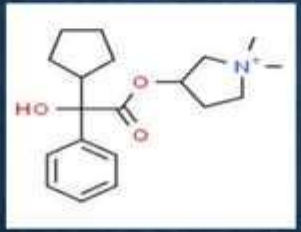
- Uses: 1.Spasmolytic effect on various smooth muscle spasms.

  2.Shows neurotropic and musculotropic effect.

  3.Also useful in dysmenorrhea,pylorospasm and biliary dysfunction

GLYCOPYRROLATE

- Structure:



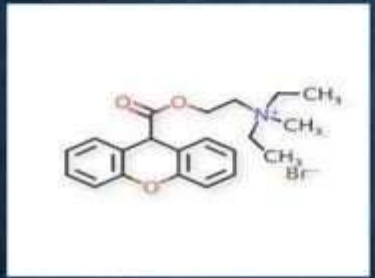
- Uses: 1.Spasmolytic effect on the musculature of the GIT and genitourinary tract.

  2.Potent antagonist on M1 receptor than M2 &M3.

  3.Used as adjunct in the treatment of peptic ulcer associated with hyperacidity,hypermotility and spasm.

METHANTHELINE BROMIDE

- Structure:

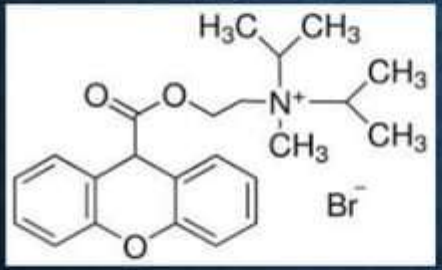


- Uses: Potent anticholinergic agents acts on nicotinic receptor

2.Used to control gastritis,intestinal hypermotility,bladder irritability,pancreatitis,peptic ulcer,hyperhidrosis

PROPANETHELINE BROMIDE

- Structure:

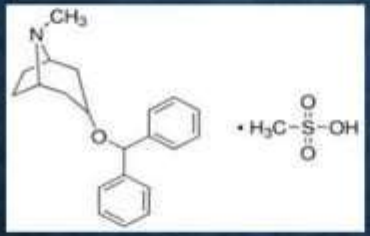


- Uses: 1.More active than methantheline

  2. It shows similar effects like methantheline

BENZOTROPIUM MESYLATE

- Structure:



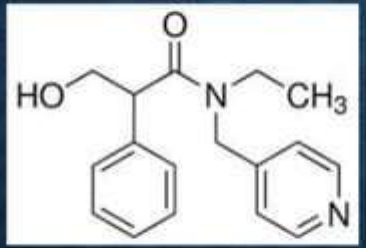
- Uses: 1.Anticholinergic,antihistaminic and local anaesthetic

  2.Used to treat parkinsonism

  3.Useful in minimizing drooling,sialorrhoea,oculogyric crisis,muscle cramps.

TROPICAMIDE

- Structure:

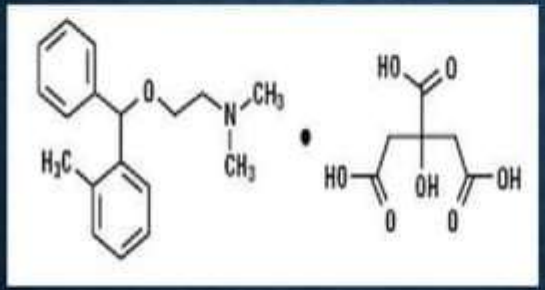


- Uses: 1. Shows mydriatic effect produced by relxation of the sphincter muscle of the iris.

  2.To treat cycloplegia

ORPHENADRINE CITRATE

- Structure:



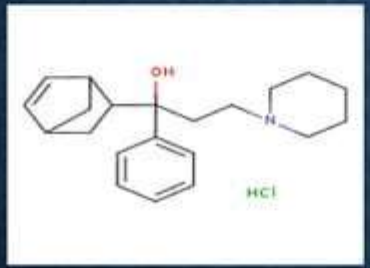
- Uses: 1. Lower antihistaminic property and higher anticholinergic action

  2.This drug is used for the symptomatic treatment of parkinsons disease.

  3.It relieves rigidity,mental sluggishness,akinesia,adynamia and lack of mobility

BIPERIDINE HYDROCHLORIDE

- Structure:

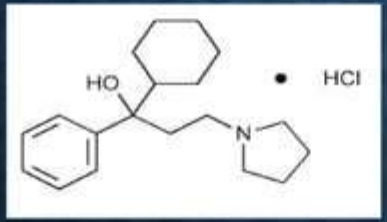


- Uses: 1. Biperidine is a mydriatic drug

  2.Used for the symptomatic treatment of parkinsonism(stiffness,tremors &spasms)

PROCYCLIDINE HYDROCHLORIDE

- Structure:



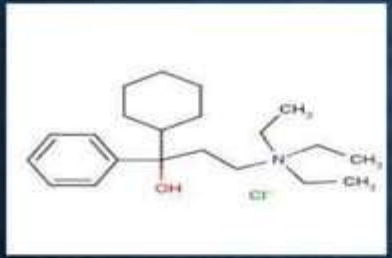
- Uses: 1. To treat parkinsonism & drug –induced parkinsonism

  2. To treat acute dystonia,idiopathic dystonia

  3.It relieves voluntary muscle spasticity by its central action

TRIDIHEXETHYL CHLORIDE

- Structure:

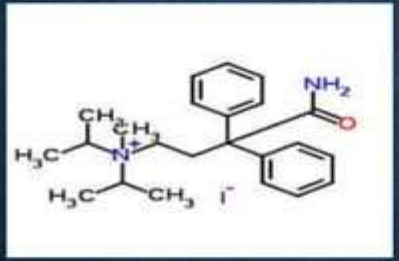


- Uses: 1. It possess antispasmodic and antisecretory activity.

2.This drug is used as adjunct therapy in peptic ulcer, GIT disturbances, spastic colon, gastric hyperacidity,pylorospasm.

ISOPROPAMIDE IODIDE

- Structure:



- Uses: 1.It shows Antispasmodic and antisecretory effect as long as 12 hours per dose.

2.Adjunctive drug in the therapy of peptic ulcer and other GIT disturbances associated with hypermotility and hypersecretion

ETHOPROPAZINE HYDROCHLORIDE

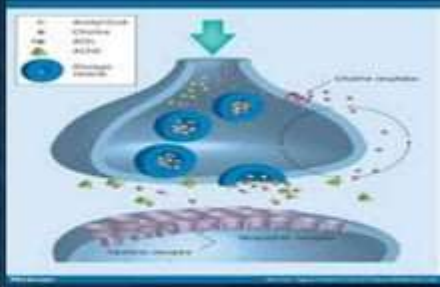
- Structure:

Parkinsonism

- Uses: 1.Antimuscarinic activity used in the symptomatic treatment of parkinsonism.

  2. One of best antiparkonism drug.

MECHANISM OF ACTION



- Cholinergic blockers are competitive antagonists
- They compete with acetylcholine.
- Cholinolytics block acetylcholine at the muscarinic receptors in the parasympathetic nervous system.
- Reversible blockade of AcH at the muscarinic receptors at neuromuscular junction occurs by receptor binding with cholinolytics.
- Reverses the levels of AcH at neuromuscular junction by decreasing the blockade.
- If these drugs(cholinergic blockers) binds to the receptors, they inhibit the nerve transmission at these receptors.

SIDE EFFECTS &TOXICITY

- Dryness of mouth(xerostomia)
- CNS Excitation
- Restlessness
- Irritability
- Hallucinations
- Delirium(memory loss)
- Increased heart rate
- Dysrrthmias
- Blurred vision
- Urinary retention
- Paralytic ileus
- Constipation
- sedation

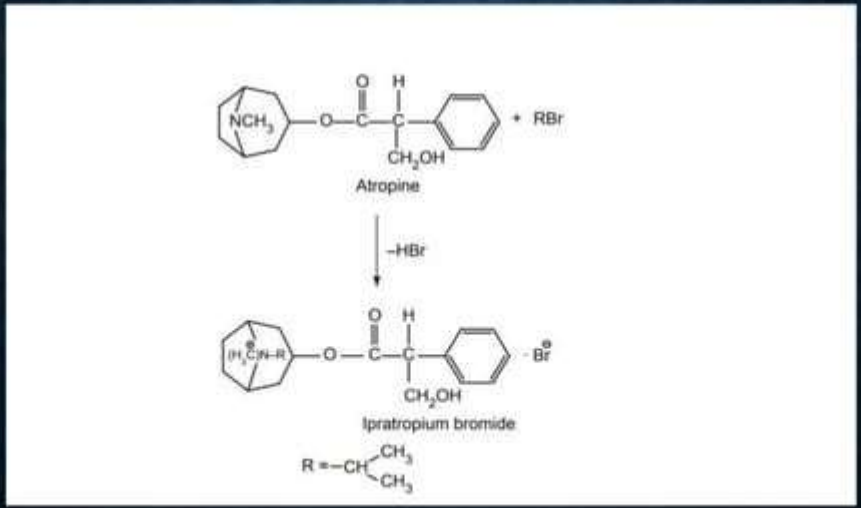
Delirium

Dryness of mouth

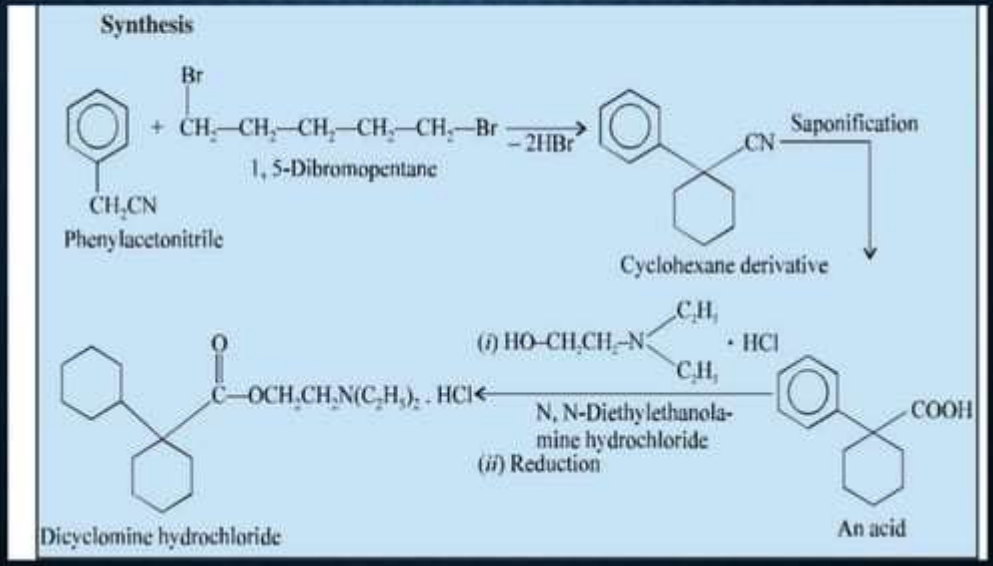
Blurred vision

Hallucinations

SYNTHESIS OF IPRATROPIUM BROMIDE

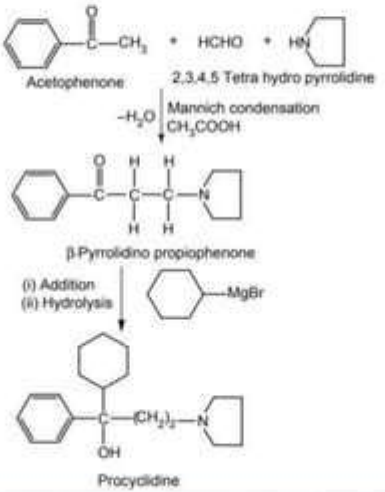


SYNTHESIS OF DICYCLOMINE



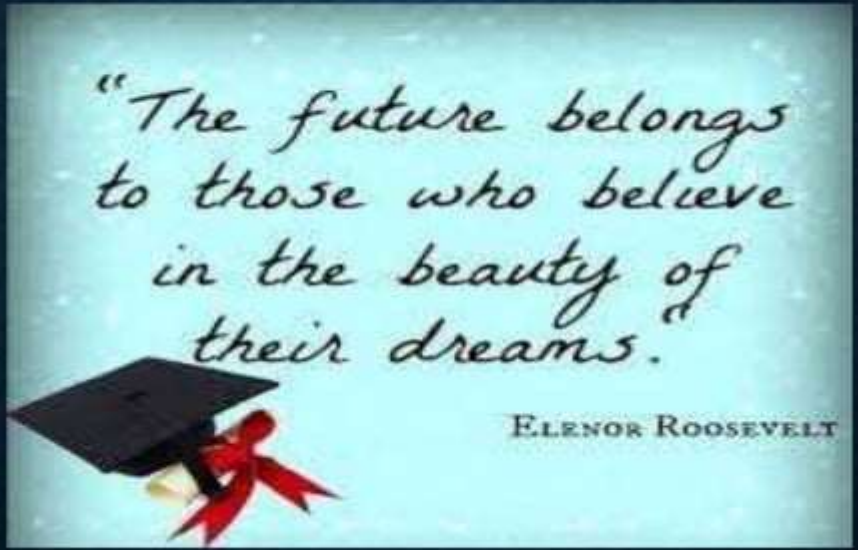
SYNTHESIS OF PROCYCLIDINE

Synthesis



REFERENCES

- Wilson and Gisvold's textbook of organic ,medicinal and pharmaceutical chemistry
- A textbook of medicinal chemistry by V.Alagarswamy
- Medicinal chemistry by Ashutosh kar
- Principles of organic medicinal chemistry by Rama rao Nadendla
- Textbook of medicinal chemistry by Valentine .Ilango
- Medicinal chemistry by Graham Patrick
- www.nlm.nih.gov.pubmed
- Pharmafactz.com – online library for medicinal chemistry


"The future belongs to those who believe in the beauty of their dreams.
Elenor Roosevelt


Thank You !