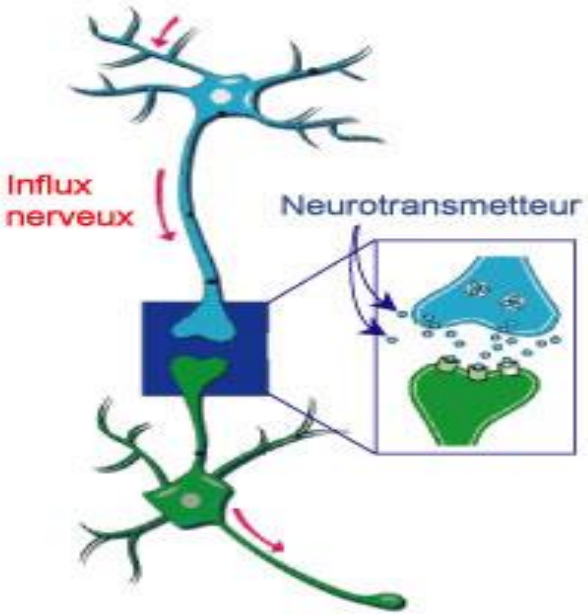
Cholinergic Antagonist Drugs



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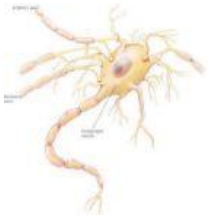


- **Anti-muscarinic drug:** Atropine-like drugs, Hyoscine (Scopolamine)
- **Anti-nicotinic drugs**

a) **Ganglion blockers**: Used in experimental pharmacology. E.g. Nicotine, Trimethapan.

b) **Neuro-muscular blockers**: Used in surgery to produce complete muscle relaxation.

Anti-muscarinic anti-cholinergic drugs

- Natural agents:
  - **Atropine, Hyoscine**
- Semi-synthetic
  - **Homatropine**
- Synthetic
  - **Ipratropium, Pirenzepine, Propantheline**

Anti-muscarinic

- Atropine (Hyoscyamine)
  - Alkaloids obtained from Atropa Belladona,
  - Considered as prototype for parasympatolytics

- Hyoscine (Scopolamine)
  - Obtained from Hyocyamus niger plant (Datura Stramonium)

Note: Antihistamines, phenothiazides and some antidepressants have anti-muscarinic effects

Clinical pharmacology of anti-muscarinic drugs

Mechanism of action:

- **Reversible blockade** of **M** receptors
- **Exocrine glands** are most **sensitive**
- **Gastric secretion** is the **least** affected
- **Heart** is **intermediate**

Note: Atropine blocks all 3 subtypes receptors (M_1,M_2,M_3)

Pharmacokinetics

- **Absorption**:
  - **Natural** and most **tertiary amines**: **good**
  - **Wide distribution** and **cross BBB**
  - **Quaternary amines**: **poorly absorbed** and poor crossing **BBB** (Ipratropium)
- Atropine t½: 2hrs
- **Partly metabolized** and partly **excreted unchanged**

Routes of administration

Oral

Parenteral

Topical (suppositories)

Some by inhalation (Ipratropium)

Pharmacodynamics

- **Exocrine glands: at low doses reduced secretions**
- Salivary
- Bronchial
- Sweet glands

CNS

- Central **stimulant** effects (Atropine) due to increased release of excitatory transmitters after blocking the presynaptic muscarinic receptors.
- Some may produce **sedation** (Hyoscine)
- Hyoscine blocks M receptors in vomiting centre and has **anti-emetic effect**
- **Toxic doses**: hallucination, convulsion, coma

Eye

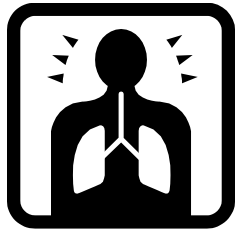
- **Mydriasis** (dilatation of pupil)
- **Cycloplegia** (relaxation of the ciliary muscle) cause: blurred vision and impaired accommodation to near vision
- **Decreased lacrimation**
- **Increase IOP**

CVS

Depending in the doses

- **Central** effect (temporary & with very small doses):
- **Decrease heart rate (due to stimulation of vagal center in the medulla)**
- **Peripheral** effect (prominent effects):
- Blockade of cardiac M2 receptors and prevent vagal nerve action this lead to **increase heart rate**
- **ABP**:
- **No** change

Respiratory system

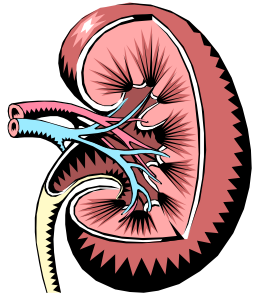


- **Bronchodilatation**
- **Reduced** bronchial **secretion**
- Ipratropium (quaternary amine derivate of Atropine) inhalation:
  - Useful in asthma and chronic obstructive pulmonary disease (COPD), also in patient who are unable to take adrenergic agonists.

GIT

- Decrease salivation
- Decrease acid secretion
- Decrease motility
- Delay gastric emptying
- Prolong intestinal transit time
- Anti-diarrhoeal and anti-spasmodic effects

GUT



- **Relaxation of bladder** wall
- Useful in **inflammatory spasm** and **pains** of the urinary tract
- **Risky** in patients with **BPH** (Benign Prostatic Hypertrophy)

Therapeutic uses

CNS disorders:

- **Parkinson's** disease
- Drug-induced parkinsonism as Phenothiazine (induced acute dystonias)
- Benztropine, Benzhexol: useful
- **Motion sickness**: Hyoscine oral, injection, trans-dermal patches

Therapeutic uses

Ocular uses:

- In **eye examination** (Tropicamide) produce mydriasis and cycloplegia
- In **iritis** (Atropine eye drop) prevent synechia (adhesion of the iris to the lens)

Note:

- Atropine eye drops effects: 7 days
- Tropicamide eye drops effects: 4-12hrs

Therapeutic uses

- **Premedication**: Hyoscine and Atropine (use as **adjunct in anaesthetic** procedure)
- **Bronchial asthma**: Ipratropium inh. (produce bronchodilatation)

Cardiovascular:

- **Bradycardia and heart block following AMI**: Atropine

Therapeutic uses

GI disorders:

- **Anti-diarrhoeal**
  - Lomotil= atropine + diphenoxylate
- **Anti-spasmodics** (in intestinal colic, IBS)
  - Atropine, hyoscine, clidinium, prifinium

Urinary disorders:

- **Urinary urgency** with UTI
- Renal **colic**

Therapeutic uses

- **Cholinergic poisoning** as:
  - Irreversible CEI insecticide poisoning
  - Chemical warfare intoxication
- To **counteract muscarinic effects**
- (nicotinic effects can not be reversed)
- Atropine IV

Adverse effects of anti-muscarinic agents

- Dry mouth
- Blurred vision
- Tachycardia
- Constipation
- Hot flushed dry skin & hyperthermia may occur with high doses

Contraindications

- **Glaucoma**
  - Increase IOP
- **BPH**
  - Bladder wall relaxation & sphincter contraction

Atropine poisoning

- Hot flushed dry skin & hyperthermia,
- Agitation, delirium, hallucination,
- Convulsions & coma
- Treatment is symptomatic

Individual drugs

- **Atropine**
- **Hyoscine**
  - Buscopan
- **Clidinium**
  - Libraxam
- **Prifinium**
  - Riabal