# Anticholinergic drugs

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# Muscarinic receptor antagonists, Atropinic or Parasympatholytic

**They** block actions of ACh in ANS and in the CNS exerted through **muscarinic receptors**

**Nicotinic antagonists** also block certain actions of ACh, they are generally referred to as ‘ganglionic blockers’

Synthetic atropine substitutes also possess significant nicotinic-blocking properties

All anticholinergic drugs are competitive antagonists

Many other classes of drugs like tricyclic antidepressants and anti-histamines possess significant antimuscarinic actions

# Classification

- 1. Natural alkaloids
- Atropine, Hyoscine (Scopolamine)
- 2. Semisynthetic derivatives
- Homatropine, Atropine methonitrate, Hyoscine butyl bromide, Ipratropium bromide, Tiotropium bromide.
- 3. Synthetic compounds
- (a) Mydriatics: Cyclopentolate, Tropicamide
- (b) Antisecretory-antispasmodics:
  - (i)Quaternary compounds: Propantheline, Oxyphenonium, Clidinium, Glycopyrrolate
  - (ii)Tertiary amines: Dicyclomine, Valethamate, Pirenzepine
- (c) Vasicoselective: Oxybutynin, Flavoxate, Tolterodine
- (d)Antiparkinsonian: Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden

# Natural alkaloids-1

- Are found in plants of the Solanaceae family
- **Atropine** in *Atropa belladonna* **a**nd *Datura stramonium*
- **Atropine** is the prototype drug of this class, is highly selective for muscarinic receptors
- Atropine stimulates many medullary centers—vagal, respiratory, vasomotor
- By blocking the relative cholinergic overactivity in basal ganglia, it suppresses tremor and rigidity of parkinsonism
- Atropine and glycopyrrolate are occasionally employed to prevent salivation during **dental procedures and oral surgery**

# Natural alkaloids-2

- Hyoscine in *Hyoscyamus niger*
- The levo-isomers are much more active than the dextroisomers
- Atropine is racemic while scopolamine is l-hyoscine
- Hyoscine differs from atropine in producing depressant (drowsiness, amnesia, fatigue) effects at low doses
- Hyoscine butyl bromide and atropine methonitrate are quaternary derivatives that do not produce CNS effects and are used mainly for colics and GIT disorders

# Mechanism of action

- **Heart**
- Atropine causes tachycardia prominently due to the blockade of M2 receptors on SA node through which vagal tone decreases HR
- Atropine does not have any consistent or marked effect on BP

- The sensitivity of different organs and tissues to atropine varies and can be graded as:

Saliva, sweat, bronchial secretion > eye, bronchial muscle, heart > smooth muscle of intestine, bladder > gastric glands, and smooth muscle

# Atropine substitutes -1

- Many semisynthetic derivatives of belladonna alkaloids
- Ipratropium bromide is given by inhalation in bronchial asthma and chronic obstructive pulmonary disease(COPD)
- Unlike atropine, it does not depress mucociliary clearance by bronchial epithelium
- Tiotropium bromide is along acting and more broncho-selective congener of ipratropium
- Inhaled ipratropium bromide and tiotropium bromide are useful in COPD and as an adjuvant to inhaled β2 agonists in severe bronchial asthma

# Atropine substitutes -2

- Glycopyrrolate acts rapidly, used parenterally before and during anesthesia
- Dicyclomine has antiemetic properties used in morning and motion sicknesses
- Valethamate has antispasmodic properties used to hasten dilation of the cervix during labor
- Oxybutynin, tolterodine, and flavoxate have smooth muscle relaxant properties used in urge incontinence
- Homatropine, cyclopentolate, and tropicamide are mydriatic, and cycloplegic, have quicker action than atropine
- Trihexyphenidyl, procyclidine, and biperiden have central antimuscarinic action, used in parkinsonism

# Ganglionic stimulants and blockers

# Ganglionic stimulants

- Selective nicotinic agonists
- Nicotine (small dose)
- Lobeline
- Dimethyl phenyl
- piperazinium iodide (DMPP)
- Tetramethyl ammonium(TMA)
- Varenicline

- Nonselective/muscarinic agonists
- Acetylcholine
- Carbachol
- Pilocarpine
- Anticholinesterases
- MCN 343-A

# Nicotine

- from *Nicotiana tabacum* is important in the context of smoking or chewing tobacco
- Has no clinical application of ganglionic stimulants, because no useful purpose by stimulating both sympathetic and parasympathetic ganglia
- Nicotine transdermal and nicotine chewing gum used as an aid to smoking cessation
- Varenicline
- It is a $N_N$ subtype selective nicotinic receptor partial agonist recently approved as an aid to smoking cessation

# Ganglionic blockers

- A. Competitive blockers
- Quaternary ammonium compounds
  - Hexamethonium
  - Pentolinium
- Amines
  - Mecamylamine
  - Pempidine
- Monosulfonium compound
  - Trimethaphan
  - camforsulfonate
- B. Persistent depolarising blockers
  - Nicotine (large dose)
  - Anticholinesterases (large dose)

# Ganglionic blockers

- Competitive ganglionic blockers were used in the 1950s for hypertension and peptic ulcer
- Have been totally replaced now because they produce several unpleasant side effects
- There is at present no clinical relevance of ganglion blockers

# Thank you