

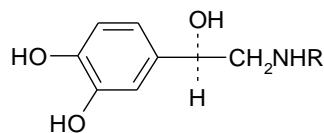
- Drugs and chemicals that cause the parasympathetic division to react are termed parasympathomimetic, whereas those blocking agents are called parasympatholytics
- Agents that mimic the sympathetic division are called sympathomimetic and those block the actions are sympatholytics.
- Drugs acting on the ANS are divided into the adrenergic, for those postganglionic sympathetic fibres that release norepinephrine and epinephrine, and cholinergic, for the remaining fibres in the ANS and the motor fibres of the somatic nerves that release acetylcholine.

....ADRENERGIC DRUGS...

- Adrenergic drugs are chemical agents that contain pharmacological and therapeutic effects by either enhancing or reducing the activity of the various components of the sympathetic division of the autonomic nervous system.
- Substances that produce effects similar to the stimulation of sympathetic nervous activity are known as sympathomimetics or adrenergic stimulants.
- Substances that decrease sympathetic nervous activity are referred to as sympatholytics, antiadrenergics or adrenergic blocking agents.
- Sympathomimetics therapeutically are used in the treatment of asthma and bronchodilatory effects (heart block) and similar effects like nasal congestion and hypotension.

ADRENERGIC NEUROTRANSMITTERS

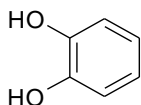
- Norepinephrine (NE) is the neurotransmitter of postganglionic sympathetic neurons, it is released from sympathetic nerve endings into the synaptic cleft, where it interacts with specific presynaptic and postsynaptic adrenergic receptors.
- Another endogenous adrenergic receptor agonist is epinephrine, which is synthesized and stored in the adrenal medulla.
- Epinephrine is often referred to as a neurohormone.
- Epinephrine is also biosynthesized in certain neurons of the CNS, where both epinephrine and norepinephrine serve as neurotransmitters.



Noradrenaline) Norepinephrine R=H

Adrenaline) Epinephrine R=CH₃

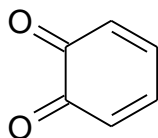
- Epinephrine and Norepinephrine belong to the chemical class of substances k/a catecholamines. This name was given because they contain an amino group attached to an aromatic ring that contains two hydroxyl groups situated ortho to each other. Same type of arrangement of hydroxyl groups as found in catechol.



Catechol

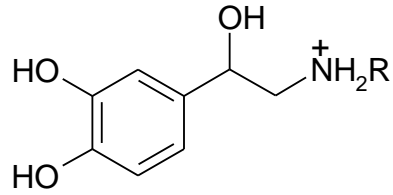
- Aromatic compounds that contain such type of arrangement of hydroxyl substituents are highly susceptible to oxidation.
- Catecholamines such as epinephrine and Norepinephrine, undergo oxidation in the presence of oxygen or other oxidising agents to produce ortho quinone like compounds, which undergoes further reaction to give mixtures of coloured products.

Note- Solutions of catecholamine drugs are stabilized by the addition of antioxidant such as ascorbic acid or sodium bisulphate.

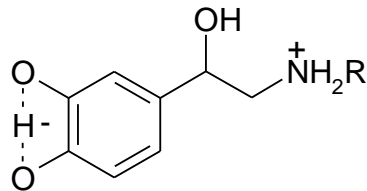


Orthoquinone

- Epinephrine and Nor epinephrine have achiral carbon atom (enantiomeric pair with R configuration).
- Catecholamine's are polar substances that contain both acidic (Aromatic hydroxyls) and basic (Aliphatic amine) functional groups.



Cationic

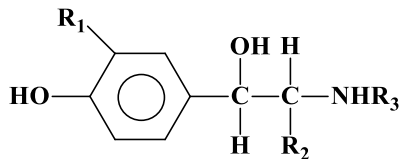


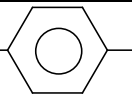
Zwitter ion

Classification of Adrenergic (Sympathomimetic) drugs:

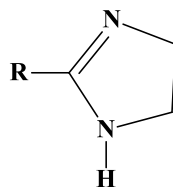
A. Direct-Acting Sympathomimetics:

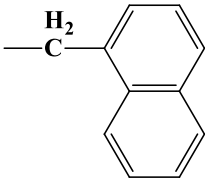
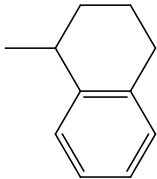
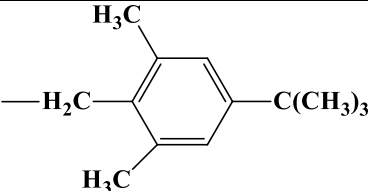
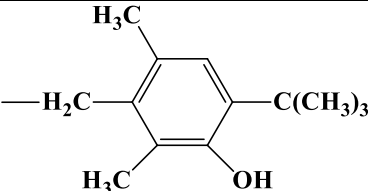
1. Phenylethylamine derivatives:



Name	R ₁	R ₂	R ₃
Noradrenaline (NE)	OH	H	H
Adrenaline (Epinephrine)	OH	H	CH ₃
Isoproterenol	OH	H	CH(CH ₃) ₂
Albuterol (Salbutamol)	-CH ₂ OH	H	C(CH ₃) ₃
Ritodrine	H	CH ₃	-CH ₂ CH ₂ -  -OH

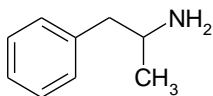
2. Imidazole derivatives:



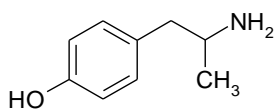
Name	R
Naphazoline	
Tetrahydrozoline	
Xylometazoline	
Oxymetazoline	

- **B)- Indirect acting sympathomimetics:-**

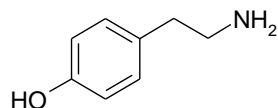
Ex:-



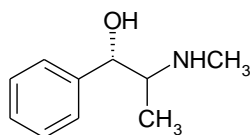
Amphetamine



Hydroxyamphetamine

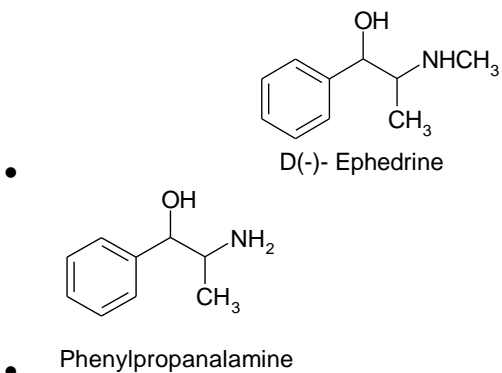


P- Tyramine



L(+)-Pseudoephedrine

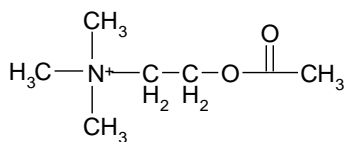
- **C) Sympathomimetics with mixed action:-**



Note:- Ephedrine has two asymmetric carbon atoms (four optical active form). The erythro racemate is called ephedrine and threo racemate is k/as Pseudoephedrine. Natural ephedrine is D(-) isomer.

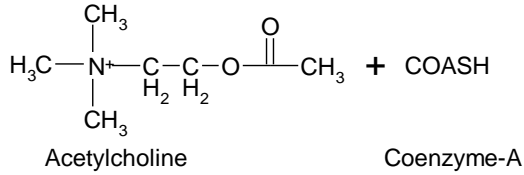
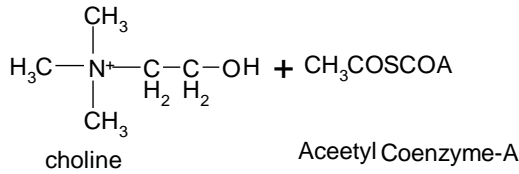
Cholinergic

- Compounds that mimic the action of acetylcholine or produce the effect of cholinergic(parasympathetic) nerve stimulation are called as Cholinergic or Parasympathomimetic agents.
- Compound that inhibit or inactivate hydrolysis of acetylcholine by acetylcholinesterase are called Anticholinesterases or anticholinesterase agents.
- Cholinergic agents and anticholinesterases are used therapeutically in the reduction of intraocular pressure in glaucoma, by increasing drainage of intraocular fluid through the canal of schlemm, relief of muscular weakness in Myasthenia gravis and in the treatment of cardiac arrhythmias.
- Cholinergic nerves are found in the peripheral nervous system and central nervous system of humans.



Acetylcholine

- Acetylcholine is a neurohumoral transmitter which mediates impulses at four different kinds of synaptic sites. These are :-
Autonomic effector sites innervated by postganglionic parasympathetic (cholinergic) fibres, the ganglionic synapses which are nerve to nerve junction in the ANS. (All ganglia of sympathetic and parasympathetic system), motor end plate on skeletal muscle innervated by somatic motor nerves (Neuromuscular junction) and certain synapses in CNS.
- Acetylcholine is synthesized, stored and released by cholinergic neurons. The neurons also synthesize two enzymes Cholineacetyltransferase (chat) and Acetylcholinesterase(AChE), which are involved in the synthesis and hydrolysis of Ach, is synthesized within the cytoplasm of nerve ending.



Note:- Cholinesterase (ChAT), the enzyme which catalyses the transfer of acetyl group from acetyl coenzyme-A to choline is inhibited invitro by trans-N-methyl-4-(1-naphthylvinyl) pyridinium iodide.

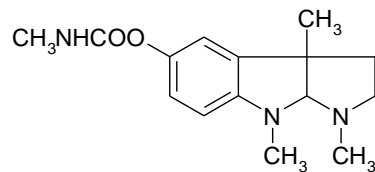
Cholinergic receptor:- There are two types of receptor for Ach that differ in composition, locations and pharmacological functions and have specific agonists and antagonists.

1. Nicotinic
2. Muscarinic

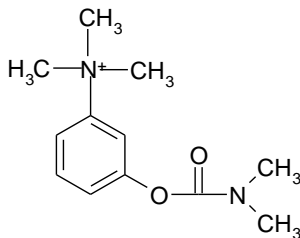
- **Anticholinesterase can be classified into two category-**

A. Reversible inhibitors:- They are capable of combining with the anionic and esteratic sites cholinesterase as well as with Ach receptor. The complex which they form with the esteratic site complex which they form with the esteratic site of cholinesterase is much less readily hydrolysed than the acetyl esteratic site complex formed with Ach.

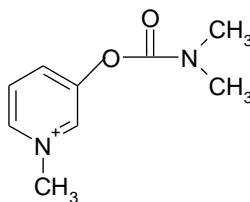
- In contrast to other reversible anticholinesterases, forms reversible complex only with the anionic sites.



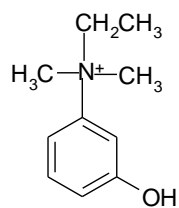
Physostigmine



Neostigmine



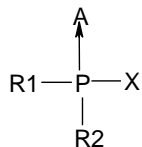
Pyridostigmine



Edrophonium

B. Irreversible inhibitors (Organophosphorus compound):- They are capable to combine only with esteratic site of cholinesterase and consequently the esteratic site is Phosphorylated. The hydrolysis of the phosphorylated site, is slow and in certain cases does not occur at all.

- In contrast to other organophosphorus compounds, forms complex with both anionic and esteratic sites and hence, is much more potent than other compounds.
- A general formula for such compounds as:-



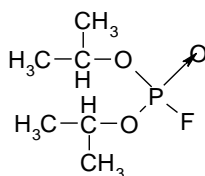
Where R_1 =Alkoxy

R_2 =Alkoxy, Alkyl, Tertiary amine

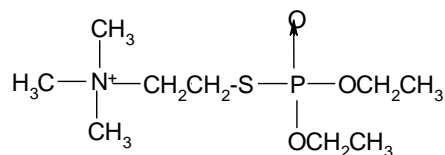
X= A good leaving group.

A= Usually oxygen or sulfur, sometime selenium.

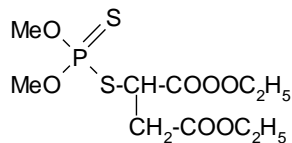
Ex-



Isofluorophate



Ecothiophate



Malathion

Cholinergic Antagonists

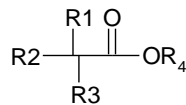
- Drugs that inhibit the action of Ach with the Ach receptors are called as Anticholinergics or Cholinergics blocking agent or parasympatholytics.
- Anticholinergic antagonize the muscarinic action of Ach, they are known as Antimuscarinic or muscarinic blocking agent.
- Anticholinergic agents may be classified in to following category:-

A)- Solanaceous alkaloids and analogues:-

Exam.- .Hyoscine

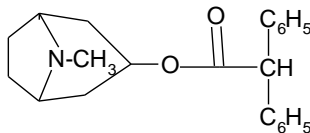
.Hyoscyamine

B)- Synthetic anticholinergics:- The synthetic atropine like anticholinergic agents have some structural features in common.

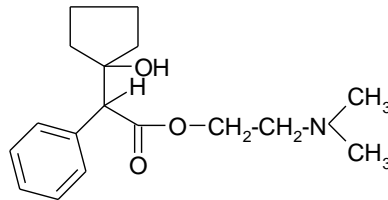


- Depending on the nature of the functional group in the main chain, the synthetic anticholinergics may be classified as:-

1)- Aminoalcohol esters:-

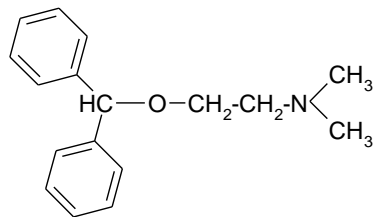


Atropine

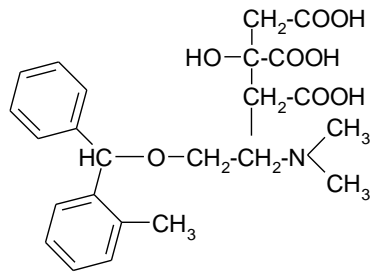


Cyclopentolate

2)-Aminoalcohol ethers:-

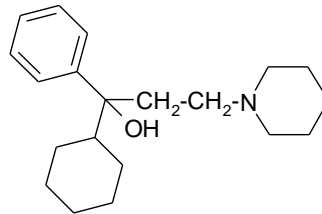


Diphenhydramine



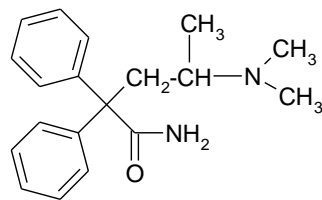
Orphenadrine citrate

3)-Aminoalcohols:-

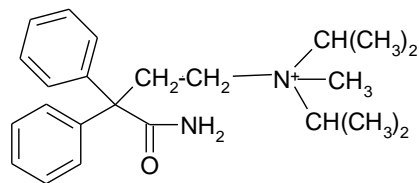


Benzhexol

4)-Aminoamides:-

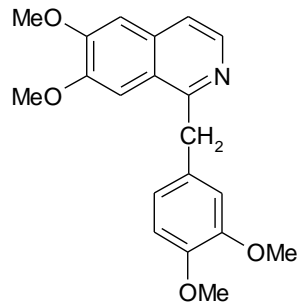


Aminopentamide



Isopropamide

5)-Miscellaneous types:-



Papaverine