MED.CHEM, BPH 4.2

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SYMPATHOMIMETIC AGENTS

Introduction

Catecholamines are the Biologically-active water-soluble amines derived from tyrosine that serve as neurotransmitters in the CNS and as hormones in circulation in response to psychological stress ("fight or flight response") or hypoglycemia

It consist of one core structure of catechol and an amine group.This group of neurotransmitters includes dopamine (DA), norepinephrine (NE)/noradrenaline, and epinephrine (EPI)/adrenaline, and they are found within the CNS, PNS, and adrenal glands.

Bio-Synthesis of Catecholamines

The Biosynthesis of catecholamines (norepinephrine, epinephrine and dopamine) takes place in adrenergic and dopaminergic neurons in the central nervous system (CNS), sympathetic nerves and in the chromaffin cells of the adrenal medulla. Non-neuronal cells in the gastrointestinal tract and the kidneys are among other tissues capable of producing catecholamines.

The enzymes involved in the biosynthesis have been identified and characterised. The key enzyme is tyrosine hydroxylase which converts L-tyrosine to L-3,4-dihydroxyphenylalanine(L-DOPA).The formation of DOPA takes place in cytoplasm of neurons.Dopa decarboxylase catalyses the decarboxylation of L-3,4-dihydroxyphenylalanine to form 3,4- dihydroxyphenyl-ethyl-amine(DOPAMINE).Dopamine formed in the cytoplasm of the neuron and it is transported by an uptake mechanism in to storage vesicles where it is hydroxylated by dopamine β-hydroxylase(dopamine β-mono-oxygenase) to form Nor-adrenaline.After that nor-adrenaline catalysed by phenyl-etanol-amine-N-methyltransferase(PNMT).This enzyme is highly localised in adrenal medula.

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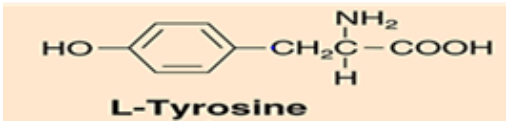
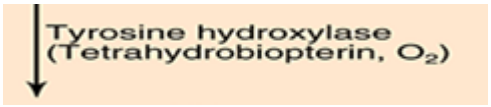
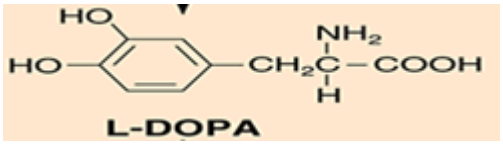


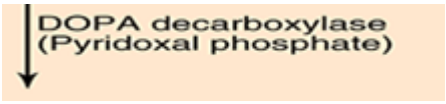
α-Amino-4-hydroxy-Benzenepropanoic acid

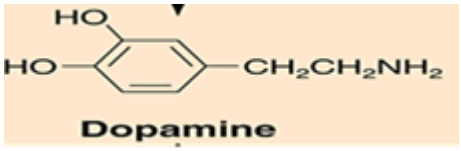




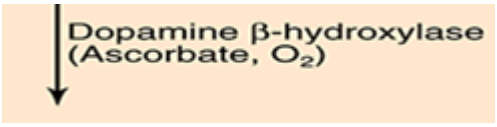
2-Amino-3 (3I, 4I-dihydroxy phenyl) propanoic acid.

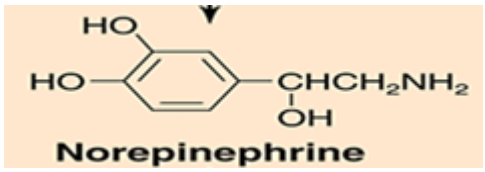
OR 3, 4-Dihydroxy-L-phenylalanine



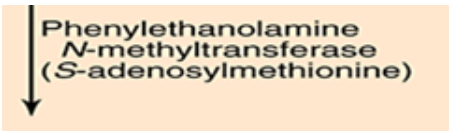


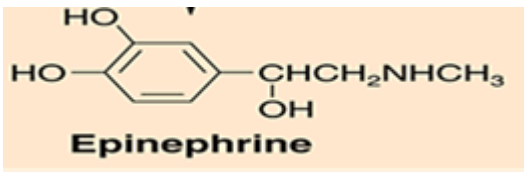
4-(2-aminoethyl) benzene-1, 2-diol



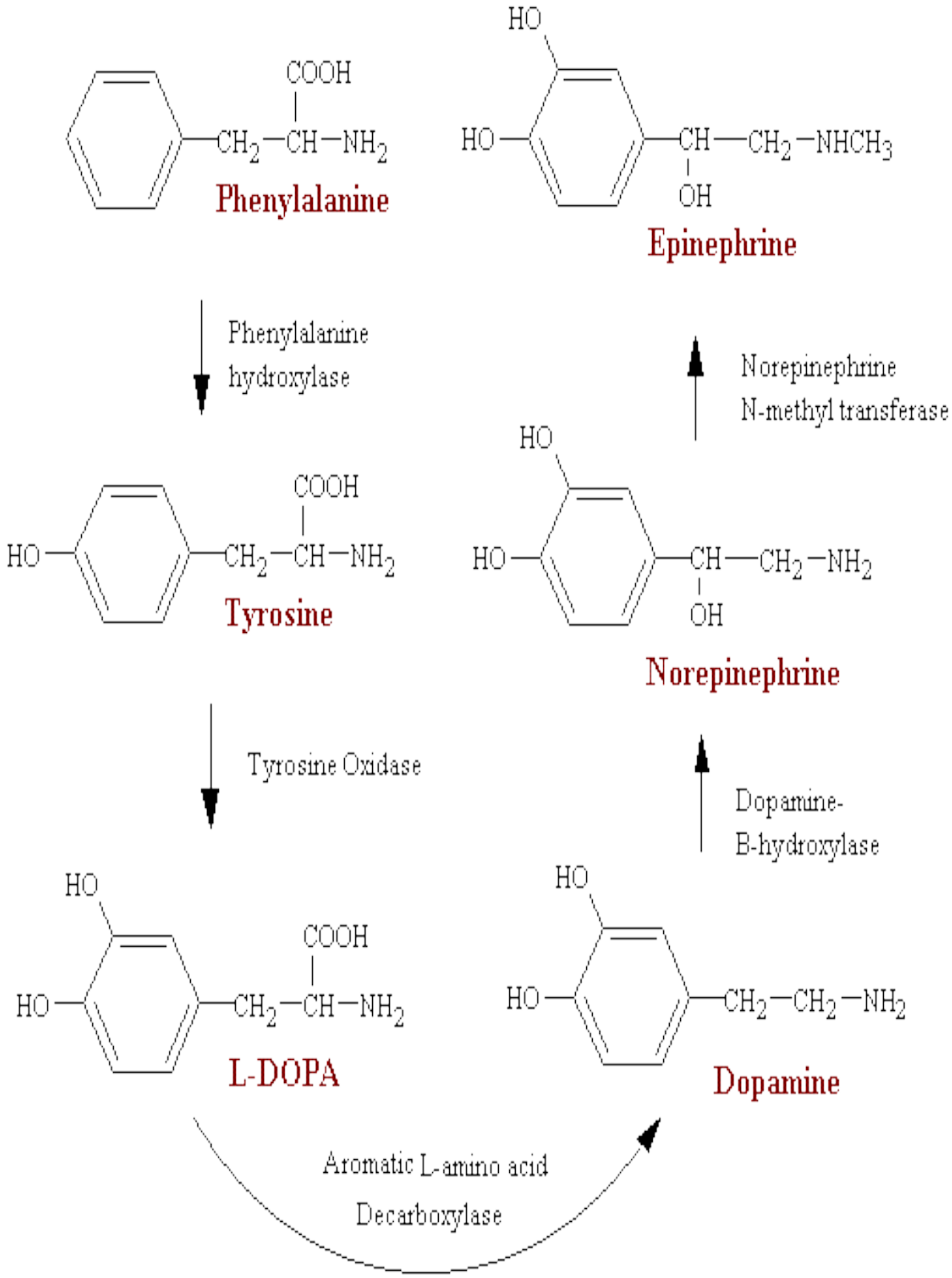


2-amino-1-hydroxyethyl]benzene-1,2-diol

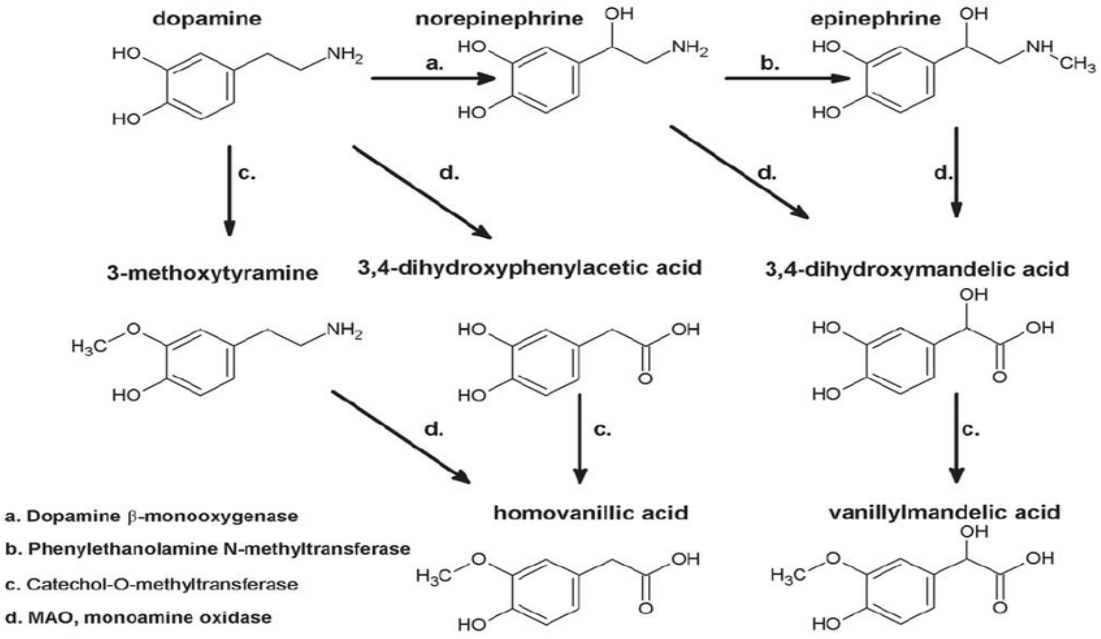


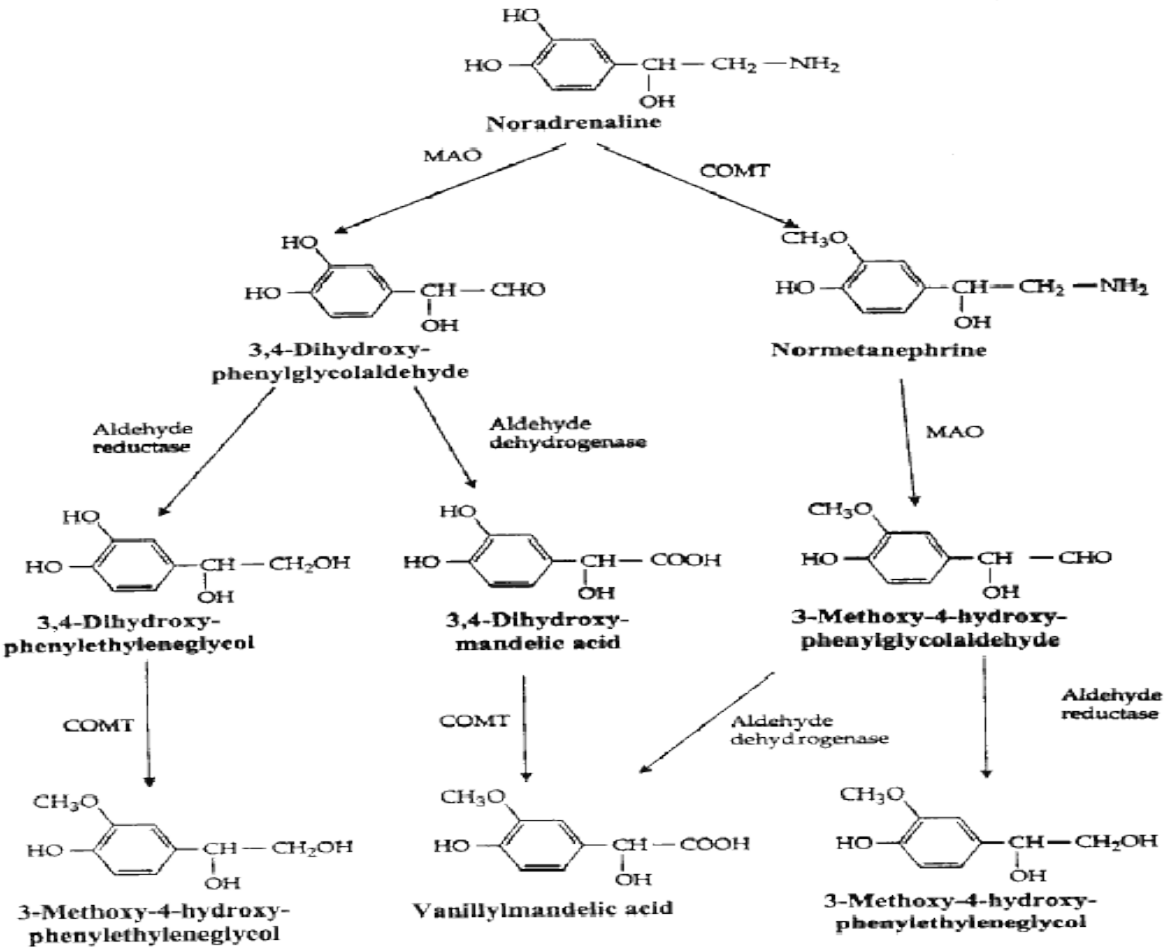


3, 4-dihydroxy-α-[(methylamino)methyl]-Benzyl alcohol


Phenylalanine
Epinephrine
Phenylalanine hydroxylase
Norepinephrine N-methyl transferase
Tyrosine
Norepinephrine
Tyrosine Oxidase
Dopamine-B-hydroxylase
L-DOPA
Dopamine
Aromatic L-amino acid Decarboxylase

Catabolism of catecholamine





Adrenergic Receptors

Sympatho-mimetic or Adrenergic drugs exert their effects by direct action on adrenergic receptors. There are two types.

1. alpha-Adrenergic receptors

2. beta- Adrenergic receptors

1. alpha-Adrenergic receptors

alpha-Adrenergic receptor sites have three parts

i) Anionic site(Phosphate) which binds with +ve ammonium group.

ii) One hydrogen binding area

iii) One flat area for aromatic ring binding.

Nor epinephrine activates primarily alpha-Adrenergic receptors

alpha-Adrenergic receptors have two types

a) alpha-1-Adrenergic receptors- which are found in smooth muscles of iris, arteries, arterioles and veis. It exerts their effect on post synoptic nerves. a1-Adrenergic receptor activation increase the influx of extracellular Ca2+ at calcium channels.

b) alpha-2-Adrenergic receptors – which mediate the inhibition of adrenergic neuro transmitter release. It exerts their effect on pre synoptic nerves. Activation of a2-Adrenergic receptors leads to a reduction in the catalytic activity of adenylyl cyclase.

2. beta- Adrenergic receptors

beta- Adrenergic receptor sites have the following parts

i) Anionic site which binds with +ve ammonium group.

ii) One hydrogen binding area

iii) One flat area for aromatic ring binding.

Epinephrine activates primarily b- Adrenergic receptor. b- receptor activation relaxes bronchial smooth muscles which cause bronchi of the lungs to dilate and also increases the rate and force of heart contractions.

beta- Adrenergic receptors are three types. They are

a) beta-1-Adrenergic receptors- found in myocardium where their stimulation increases the rate and force of myocardial contractions. They are located mainly in the heart, where they mediate the +ve inotropic and chronotropic effects of the catecholamines. They exhibit the agonist potency in the order of Isopreterenol > Epinephrine = Nor Epinephrine.

b) beta-2-Adrenergic receptors- found in bronchial and vascular smooth muscles where their stimulation causes smooth muscle dilatation and relaxation. They exhibit the agonist potency in the order of Isopreterenol > Epinephrine > Nor Epinephrine.

c) beta-3-Adrenergic receptors- They are expressed on fat cells and their stimulation causes lipolysis. They are located on brown adipose tissue and is involved in the stimulation of

lipolysis. They exhibit the agonist potency in the order of Isopreterenol = Nor Epinephrine > Epinephrine.

Classification of Adrenergic Drugs

1.Direct acting Adrenergic Agonists

They are bind and activate a1, a2, b1, b2 receptors

Examples – Nor Epinephrine (binds with a1, a2, b1, receptors), Epinephrine (binds with a1, a2, b1, b2, receptors), Dopamine (with a1, a2, b1, , receptors), Xylometazoline, Phenyl ephrine, Methoxamine, Isoprenaline, Salbutamol.

2. Indirect acting Adrenergic Agonists

They produce Nor Ephidrine (NE) like actions by stimulating NE release, preventing its reuptake and thus its inactivation.

Example – Tyramine

3.Dual acting Adrenergic Agonists

These agents act as direct and indirect adrenergic agonists. They binds to adrenergic receptors and stimulate NE release.

Example – Ephedrine, Amphetamine, Mephentermine.

Chemical classification

1.**Phenyl ethylamines and related compounds**

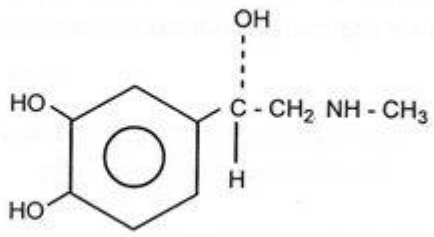
Adrenaline, Nor Adrenaline(NE), Dopamine, Phenyl ephrine, Methoxamine, Methyl dopa, Isoproterinol(Isoprenaline), Salbutamol, Terbutaline, Dobutamine, Amphetamine, Ephedrine, Pseudo Ephedrine, Ritodrine, Salmeterol

2**. Imidazoline derivatives**

Naphazoline, Tetrahydrazoline, Oxymetazoline, Xylometazoline, Clonidine.

Direct acting Adrenergic Agonists

Epinephrine: (Adrenaline)

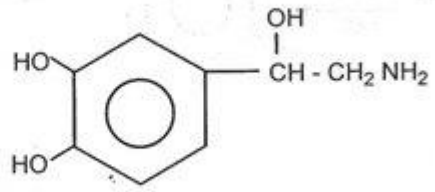


1 – (3, 4 - Dihydroxyphenyl) – 2- methyl amino ethanol.

Use:

1. Act as bronchodilator in acute asthma
2. To treat heart block that means to treat cardiac arrest.
3. To treat acute allergic reaction.
4. To control superficial haemorrhage of nose and throat.
5. Along with local anaesthetic, it is used to prolong local anaesthetic effect.

Norepinephrine (Noradrenaline)

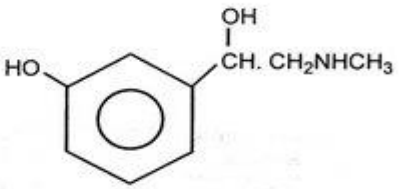


L - 1- (3, 4̇ Dihydroxy phenyl) - 2 - amino ethanol

Use:

1. To treat heart block that means to treat cardiac arrest.
2. To control superficial haemorrhage of nose and throat.
3. Along with local anaesthetic, it is used to prolong local anaesthetic effect.
4. Due to its vasoconstriction effect, it is also used to treat blood pressure in acute hypertensive states.

Phenylephrine

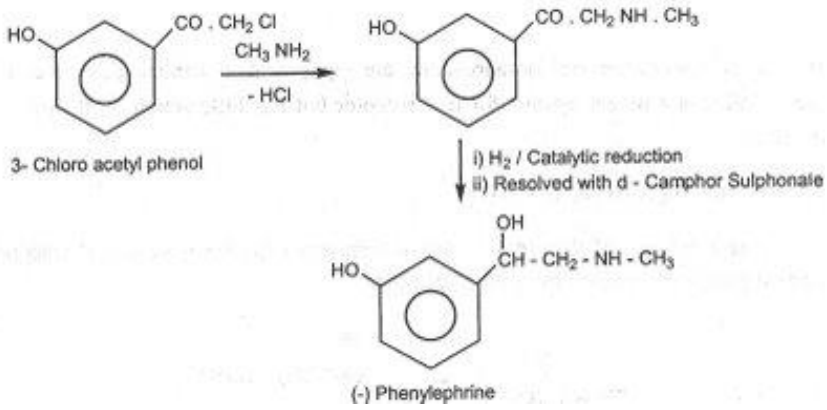


(-) - 1 - (3 – Hydroxyphenyl) – 2 – methyl amino ethanol

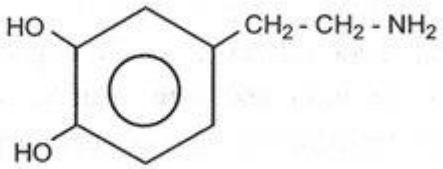
Use:

1. To treat heart block that means to treat cardiac arrest.
2. To control superficial haemorrhage of nose and throat.
3. Along with local anaesthetic, it is used to prolong local anaesthetic effect.
4. Due to its vasoconstriction effect, it is also used to treat blood pressure in acute hypertensive states.
5. It is used locally in nasal congestion and also used as a mydriatic.

Synthesis

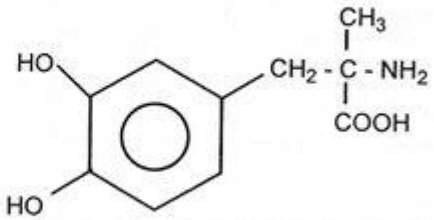


Dopamine



1- (3, 4 – Dihydroxy phenyl) -2-amino ethane

Methyl Dopa

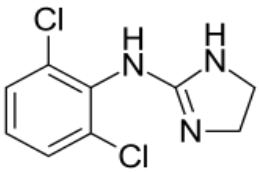


L – α – methyl – 3, 4 - dihydroxy phenyl alanine.

Use:

1. To control blood pressure in primary hypertension.
2. To control renal hypertension
3. To treat hypertension in pregnancy.
4. It is also used to treat carcinoid tumour.

Clonidine

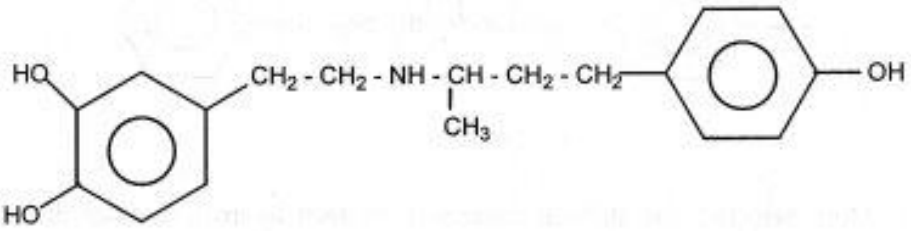


2-(2,6-Dichloroanilino)-2-imidazoline

Use:

1. It is used to treat primary hypertension.
2. To treat dysmenorrhoea.
3. To treat migraine
4. To treat postmenopausal vasomotor instability.
5. It is act as a vasodilator and decreases rennin release.

Dobutamine



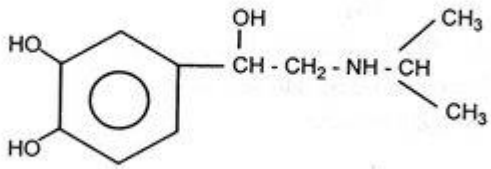
N – [1 – Methyl – 3 – (4 – hydroxyphenyl) propyl] 3, 4 - dihydroxy phenyl ethyl amine

4-(2-4[4-(4-hydroxyphenyl) butane-2-yl -amino] ethyl) benzene-1, 2-diol

Use:

1. Act as a cardiac stimulant for heart failure.
2. It is also used in case of open heart surgery and cardiomyopathy
3. It is also commonly used in the hospital setting as a pharmacologic stress testing agent to identify coronary artery disease.

Isoproterenol (Isoprenaline)



(dl) – β – (3,4 - Dihydroxy phenyl) – α – isopropyl amino ethanol.

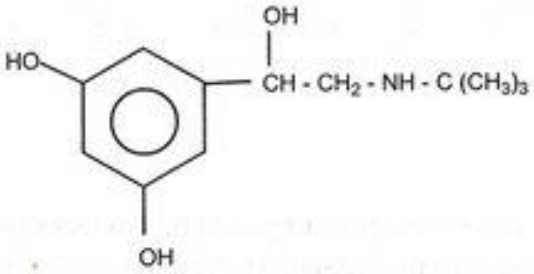
OR

1-(3, 4-dihydroxy phenyl)-2-isopropyl amino ethanol.

Use:

1. It is mainly used to treat bronchial asthma and chronic bronchitis.
2. In emergency, it is used to treat cardio-toxic shock, heart block.
3. It is also used in the form solutions having 0.5% and 1% of drug as inhaler.

Terbutaline



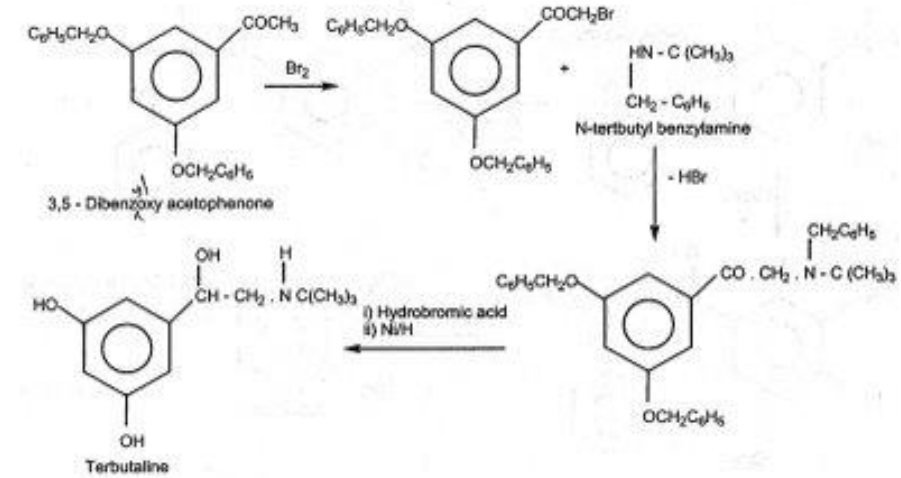
N – tert Butyl – 2 – [(3,5 - dihydroxy phenyl) – 2 – hydroxy] ethyl amine.

2-tert-butylamino-1-(3, 5-dihydroxyphenyl) ethan-1-ol.

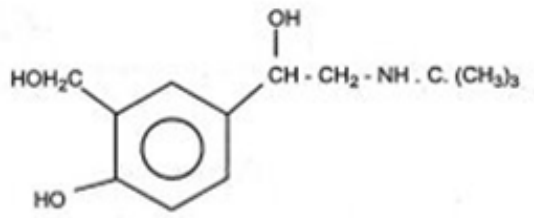
Use:

1. It is mainly used to treat bronchial asthma and chronic bronchitis.
2. In emergency, it is used to treat cardio-toxic shock, heart block.

Synthesis

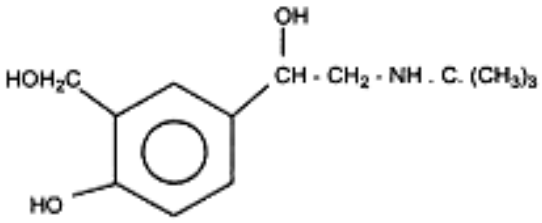


Salbutamol



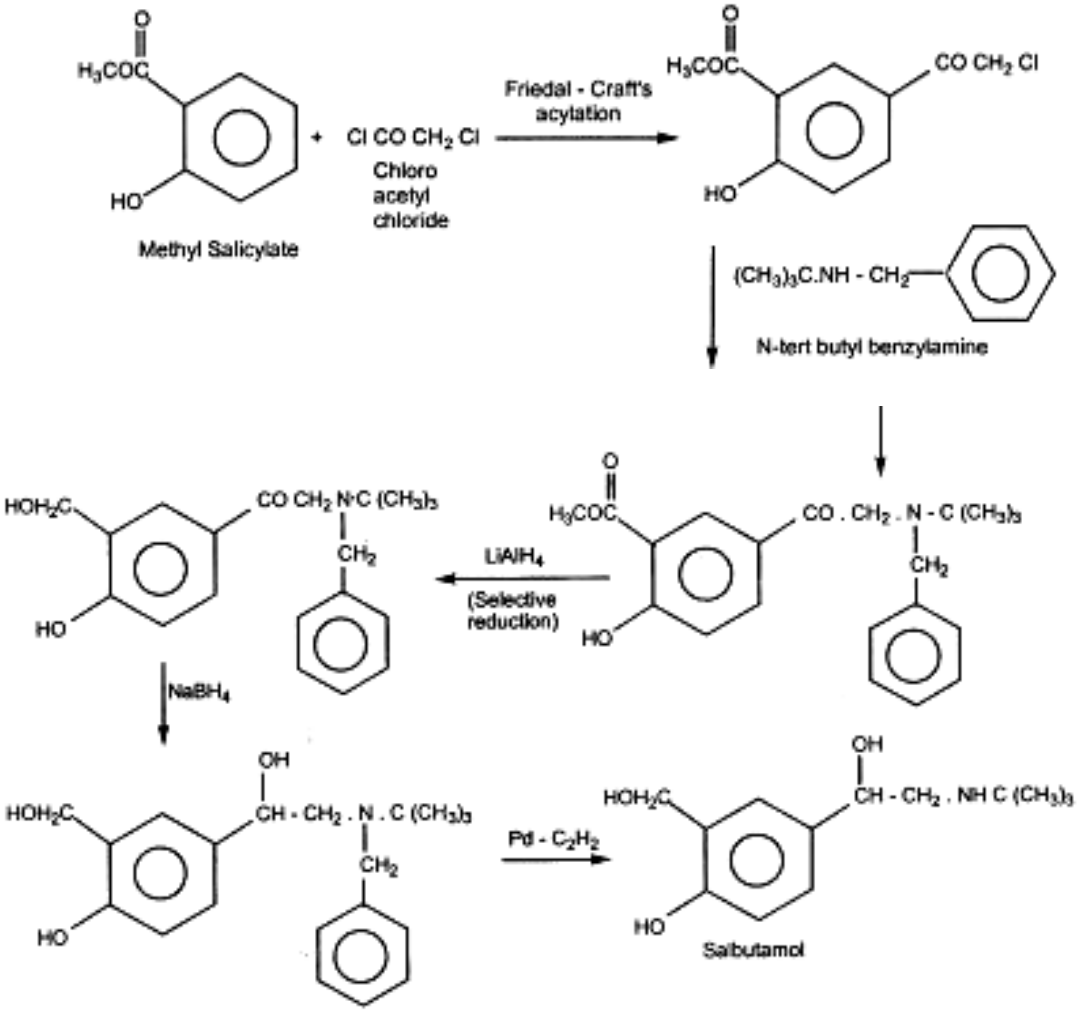
4-Hydroxy-3-hydroxy methyl-N- [(tet-butyl amino) methyl] benzyl alcohol

Salbutamol (Albuterol)



4 – Hydroxy – 3 – hydroxy methyl - α - [(tet - butyl amino) methyl] benzyl alcohol.

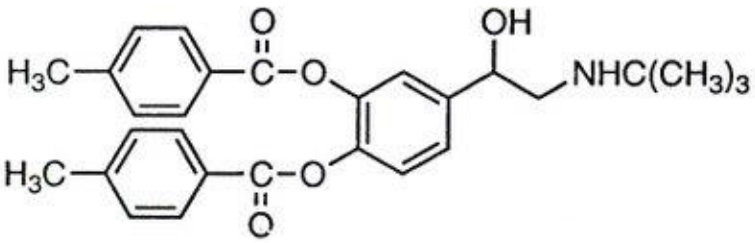
Synthesis



Use:

1. In emergency, it is used to treat cardio-toxic shock, heart block.
2. It is mainly used to treat bronchial asthma and chronic bronchitis.
3. It is also used to relax the uterine smooth muscle and prevent premature labour.
4. It is also used in the treatment of acute hyperkalemia.

Bitolterol



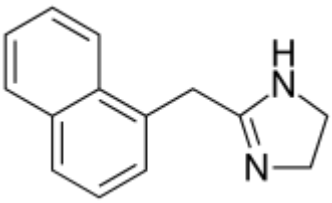
Bitolterol

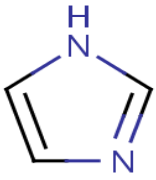
4-[2-(tert-butylamino)-1-hydroxyethyl] benzene-1, 2-diyl bis (4-methylbenzoate)

Use:

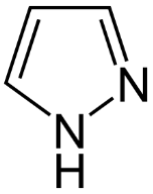
1. Commonly used for the treatment of bronchial asthma due to its bronchodilator effect.

Naphazoline





Imidazole



Pyrazole

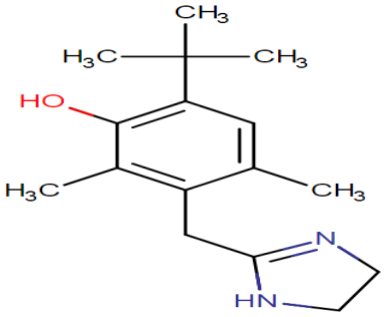
2-(naphthalen-1-yl-methyl)-4, 5-dihydro-1H-imidazole

or

2-(naphthalen-1-yl-methyl)-2-imidazoline

Use:

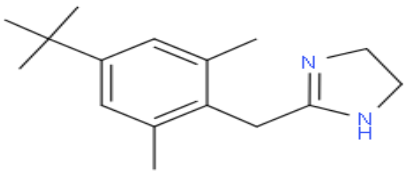
2. It is used topically as a nasal decongestant.
3. It is also used as a vasoconstrictor.
4. It helps in the relief of sinusitis.



3-(4, 5-Dihydro-1H-imidazol-2-yl-methyl)-2, 4-dimethyl-6-(2-methyl-2-propanyl) phenol

Use: It is used topically as a nasal decongestant.

Xylometazoline

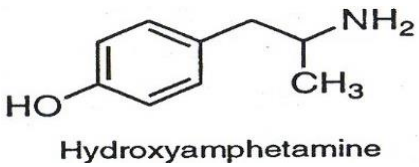


2-(4-tert-butyl-2,6-dimethylbenzyl)-4,5-dihydro-1H-imidazole OR
2-[2, 6-Dimethyl-4-(2-methyl-2-propanyl) benzyl]-4, 5-dihydro-1H-imidazol

Use: It is used as a vasoconstrictor to reduce swelling and nasal discharge.

Indirect acting agents:

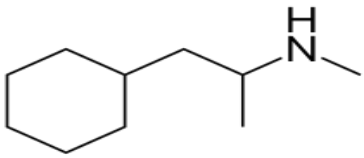
Hydroxyamphetamine



4-(2-aminopropyl)-phenol

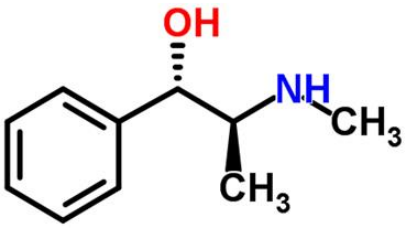
Use: It is used as mydriatic, to treat narcolepsy sudden attack of sleep and also used in the treatment of obesity.

Propylhexedrine



1-Cyclohexyl-2-methylaminopropane, or 1-Cyclohexyl-N-methyl-2-propanamin, or 1-cyclohexyl-N-methylpropan-2-amine

Pseudoephedrine

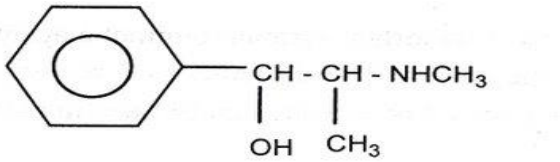


2-(Methyl amino)-1-phenyl-1-propanol or 1-(Methyl amino) ethyl] benzene methanol

Use: It is used as a nasal decongestant.

Agents with mixed mechanism

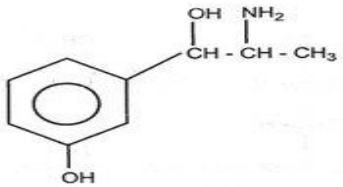
Ephedrine



(1R,2S) - 2-Methyl amino -1-phenyl propan -1-ol

Use: 1. It is used as a bronchodilator, cardiac stimulant, and nasal decongestant.

Metaraminol

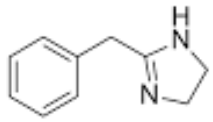


2 - Amino – 1- (3' - hydroxy phenyl) propanol

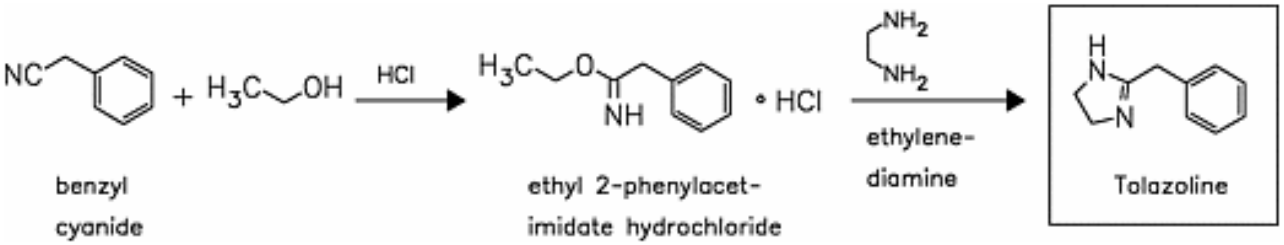
Use: It is used to maintain blood pressure with spinal anaesthesia similar to methoxamine.

Adrenergic Antagonists:

Tolazoline



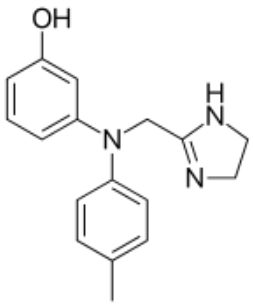
2-Benzyl-4, 5-dihydro-1H-imidazol



Use:

1. In the treatment of acute or chronic vascular hypertension.
2. It is used in the treatment of peripheral vasospasm.
3. Used to cause dilation of the blood vessels.

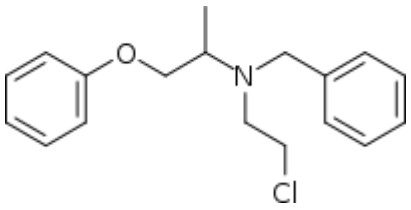
Phentolamine



3-[(4, 5-Dihydro-1H-imidazol-2-ylmethyl)(4-methylphenyl)amino] phenol

Use: It is used for the treatment of hypertension in patients with Pheo-chromo-cytoma. (Tumor of the chromaffin cells of the adrenal medulla)

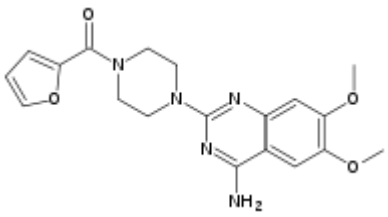
Phenoxybenzamine



N-(2-chloroethyl)-N-(1-methyl- 2-phenoxyethyl) Benzyl amine

Use: It is used for the treatment of hypertension in patients with Pheo-chromo-cytoma. (Tumor of the chromaffin cells of the adrenal medulla)

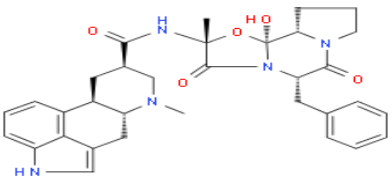
Prazosin



[4-(4-Amino-6, 7-dimethoxy-2-quinazolinyl)-1-piperazinyl](2-furyl) methanone

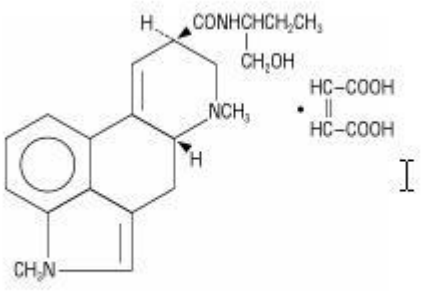
Use: Prazosin is also useful in treating urinary hesitancy associated with prostatic hyperplasia, blocking alpha-1 receptors, which control constriction of both the prostate and urethra. Although not a first line choice for either hypertension or prostatic hyperplasia, it is a choice for patients who present with both problems concomitantly. The antihypertensive characteristics of prazosin make it a second-line choice for the treatment of high blood pressure

Dihydroergotamine



(5'α,10α)-5'-Benzyl-12'-hydroxy-2'-méthyl-3',6',18-trioxo-9,10-dihydroergotaman

Methysergide



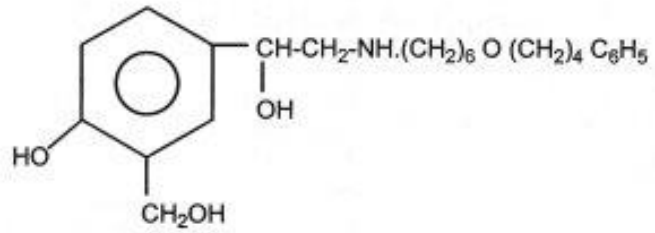
$C_{21}H_{27}N_3O_2 \cdot C_4H_4O_4$ Mol. wt. 469.54

ergoline-8-carboxamide, 9,10-didehydro-N-[1-(hydroxymethyl)propyl]-1,6-dimethyl-, (8ß)-, (Z)-2-butenedioate (1:1)

USE

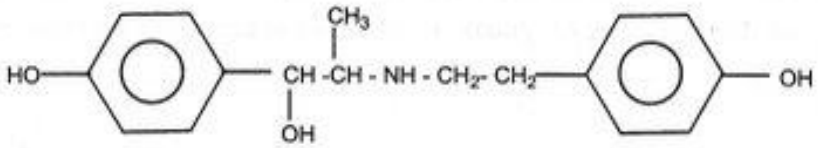
used exclusively to treat episodic and chronic migraine and for episodic and chronic cluster headaches

. Salmeterol



±) -4- Hydroxy - α' - {[(6- (4-phenyl butoxy) hexyl] amino methyl} -m- xylene -α,α'

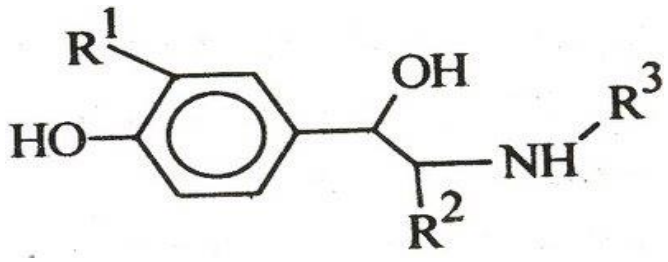
Ritodrine



Erythro-p-hydroxy-α-{1-[(p-hydroxy phenyl ethyl) amino]-ethyl} benzyl alcol

SAR for Adrenergic Agonists

General structure



SAR for sympathomimetic drugs are discussed in the following category.

A). Substitution in the Phenyl ring system

The receptor selectivity of the drugs depends on the substituent at aromatic ring , a,b- Carbon and Amino group.

The maximal sympathomimetic activity shown by substitution of hydroxyl group in M and P position of aromatic ring.

The amino group should be separated from the aromatic ring by two carbon atoms for optimal activity.

The naturally occurring Nor Adrenaline has 3',4'-dihydroxy benzene ring active at both a and b-Adrenergic receptors.

The dihydroxy substitution at 3',4' position(Ex-Metaproterinol) gives good oral activity and selectivity for b2-Adrenergic receptors.

Ther substituents like3'-hydroxy methyl (albuterol), 3'- trifluoro methyl, 4' amino, 5' chloro (Mebuterol) have good oral activity.

One hydrogen bonding group is essential at the 4' position for beta activity and 3'- OH substitution for Alpha activity.

B). Substitutions at Nitrogen (Amino group)

The presence of amino group is important for direct agonist activity.

Primary and secondary amines are more potent direct acting agonist than tertiary amine.

Size in alkyl group of nitrogen increases, a-recptor agonist activity decreses and beta-receptor agonist activity increases (Ex-Isoproterenol).

N-substitution also provides selectivity for different b-receptor sub types. Large t-butyl group have selectivity to b2 receptor (Ex-Colterol). Ritordrine with large P-Hydroxy phenyl ethyl substitution is a aelective b2 agonist .

Nitrogen in the part of heterocyclic ring such as imidazoline possess anti hypertensive property.

C). Substitutions on Carbon in the side chain

There are two carbon atoms a and b to nitrogen function. Small alkyl groups such as methyl or ethyl present in the a-carbon, an ethyl group at this position diminish the a-activity for more than b-activity.

The presence of a-alkyl group increases the duration of action by making the compound resistant to metabolic deamination by MAO.

Maximal direct activity in a-methyl nor adrenaline in the erythro enantiomers.
b- carbon has hydroxyl group in the (R) absolute configuration for maximal direct activity.

Mechanism of Action

1. For Directly acting Sympathomimetics

They act through complexation with specific receptors. For the activation of b-receptor phenolic hydroxy group in meta position of aromatic group and an alcoholic hydroxyl group in b-position of side chain and an amine with bulky group.

2. For InDirectly acting Sympathomimetics

They act either by releasing catecholamines mainly norepinephrine from storage granules in the sympathetic nerve terminals or through inhibition of nor adrenaline uptake at the neuronal membrane.

3. Sympathomimetics of Mixed action

They act by both mechanisms described above.

MED.CHEM, BPH 4.2

Prof. (Dr.) S.N.DAS, Principal, GCP, Sambalpur

CHOLINERGIC NEUROTRANSMITTERS
(CHOLINERGIC DRUGS AND RELATED AGENTS)

The Peripheral Nervous System (PNS) consists of Cranial and spinal nerves and act as a communication line between CNS (brain, spinal cord and retina) and rest of the body. The PNS is divided into two parts

1. ANS (Autonomic nervous system)
2. SNS (Somatic nervous system)

The ANS has two divisions (i) Adrenergic (Sympathetic) and (ii) Cholinergic (Parasympathetic).

Acetyl-choline serves as a neuro transmitter at both sympathetic and parasympathetic pre ganglionic nerve endings. Cholinergic agents are drugs that either directly or indirectly produce effect similar to acetyl choline (Ach).

Cholinergic receptors

There are two types of cholinergic receptors on the basis of their ability to be bound by the naturally occurring alkaloids nicotine and muscarines are called **nicotinic receptors and muscarinic receptor.**

muscarinic receptor:

Muscarinic receptors are characterised through their interaction with muscarine, a water-soluble toxin derived from the mushroom ***Amanita muscaria*** that causes substantial activation of the peripheral sympathetic nervous system. Acetyl choline when binds to muscarinic receptors it causes conformational change in the receptor,causes activation of an intracellular G-Protein which catalyses intracellular events.

Muscarinic receptors are of five subtypes

1. M_1: Present in autonomic ganglia, gastric gland and in the CNS. It causes depolarisation, histamine release, acid secretion, affect learning, memory and motor function.
2. **M_2:** These are called cardiac muscarinic receptors because they are located in atria and conducting tissue of the heart. Their stimulation causes a decrease in the strength and rate of cardiac muscle contraction. M2 receptor activate K+ channels to cause hyper polarization of cardiac cells, resulting in bradycardia.
3. **M_3** receptors: These are referred to as “glandular” Muscarinic receptor, are located in exocrine glands and smooth muscles. Glandular secretions from lacrimal, salivary, bronchial, pancreatic and mucosal cells in GI tract are characteristics of M_3 receptor stimulations.
4. **M_4** receptors: They are present in tracheal smooth muscle, when stimulated inhibit the release of acetyl choline.
5. **M_5** receptors:

Nicotinic receptor

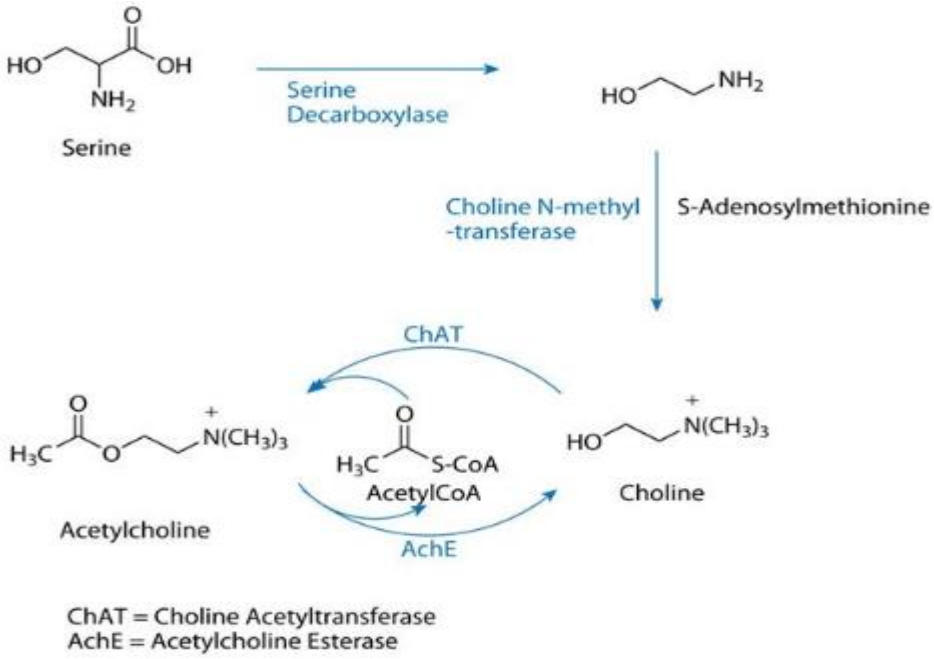
Nicotinic receptors are coupled directly to ion channels and mediate very rapid responses when activated by acetyl choline. These receptors are selectively activated by nicotine and blocked by tubocurarine or hexamethonium. These belongs to ligand -gate ion channel receptors and acetyl choline serve as a gate keeper by interacting with the receptor to modulate passage of ions, principally K + and Na + through the channel. Their activation causes opening of the channel and rapid flow of cation resulting depolarization and generation of action potential. Sub types
Theyare

N1 nicotinic receptors - These are present in neuromuscular junction. They are blocked by succinyl choline, d – tubocurarine and decamethonium and stimulated by phenyl trimethyl ammonium.

N2 nicotinic receptors - These are found in autonomic ganglia. They are blocked by hexamethonium and trimethaphan but stimulated by tetra methyl ammonium and diethyl 4-phenyl piperazinium.(DMPP)

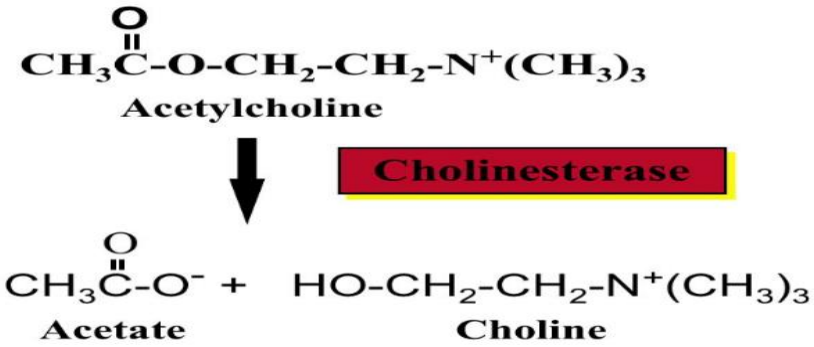
Biosynthesis of acetylcholine

Synthesis of acetyl-choline is done by cholinergic neurons. Acetyl-choline is synthesized by choline and Acetyl coenzyme A. Choline is synthesized in the liver by reaction between serine and ethanol-amine.



Catabolism of acetylcholine:

After release and producing action, effect of acetyl-choline can be terminated by the help of enzymatic hydrolysis. Cholin-esterases(Acetyl-choline-esterase, AChE) rapidly hydrolysis Ach into choline and acetic acid. It only causes hydrolysis of the Ach which is released from cholinergic nerve terminals.



Parasympathomimetic agents

These are the compounds which mimic the actions of acetyl-choline, which is the majour neurotransmitter causes the nerve stimulation

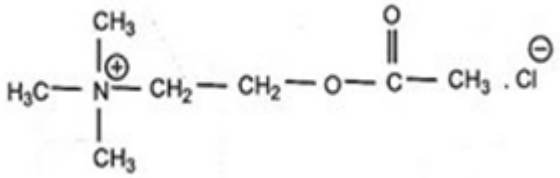
CLASSIFICATION

1.Directly acting Cholinergic drugs : These drugs bind to the nicotinic or muscarinic receptors and cause excitation of cholinergic system.
A) Cho line Esters – Acetyl choline, Carbochol, Bethanechol, Methacholine.
B) Alkaloids - Pilocarpine
2.Indirectly acting Cholinergic drugs (Anti choline esterase)
A) Reversible Direct acting: – Physostigmine, Neostigmine, Pyridostigmine, Endrophonium chloride, Ambinonium chloride. Tacrine hydrochloride
B) Irreversible Indirect acting – Parathione, Malathion

3.Cholinesterase reactivator: Pralidoxime chloride,

Direct acting agents:

Acetylcholine



2-Acetoxy-N, N, N-trimethyl ethan-aminium chloride.

2-Acetoxy ethyl-1-trimethyl ammonium chloride.

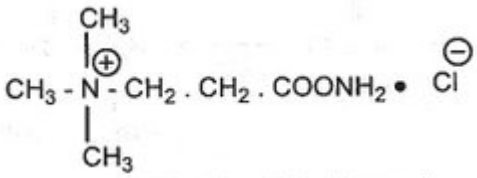
Properties: It is white or almost white crystalline powder. It is slightly soluble in water, freely soluble in alcohol and hygroscopic in nature.

Mechanism of Action: It is a direct acting quaternary ammonium cholinergic drugs, it act on muscarinic receptor.Its action is due to its destruction by choline-esterase.

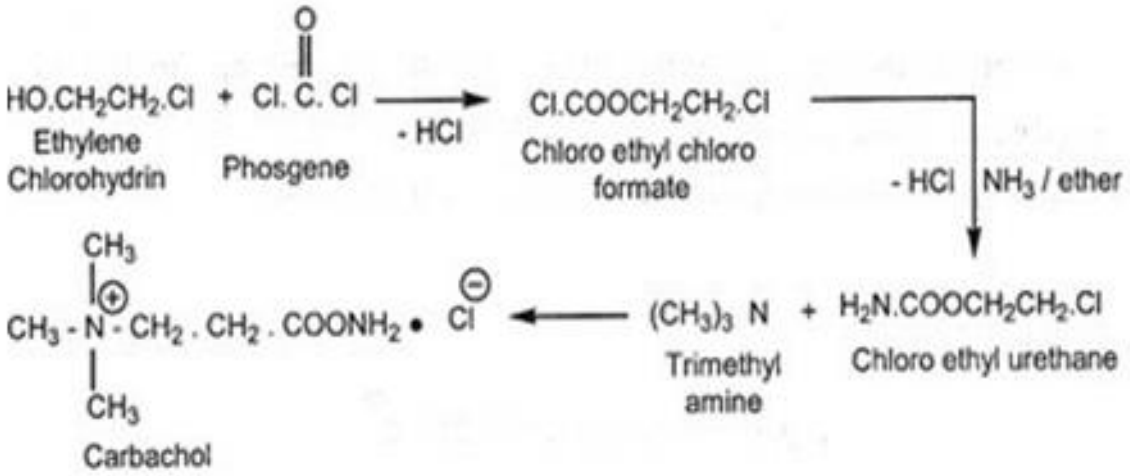
Use:

1. It is widely used as an eye drop to cause miosis (Excess contraction of Pupil) during surgery.
2. It also used as a vasodilator and cardiac depressant, a stimulant of the vagus (each of the teeth pair of cranial nerves, supplying the heart, lungs, upper digestive tract.)
3. It has a tonic (tonic sensory receptor) action on smooth muscle.

Carbachol



Synthesis



2-Carbamoyl-oxy-N, N, N-trimethyl-ethyl-ammonium chloride.

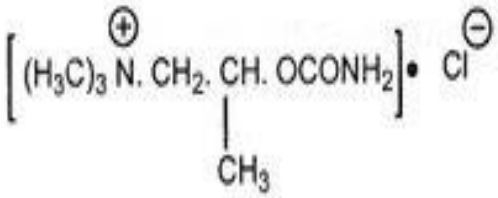
Properties: It is a white powder. freely soluble in water, slightly soluble in alcohol, practically insoluble in chloroform and ether.

Mechanism of Action: It is a quaternary ammonium cholinergic drugs, it possesses both muscarinic and nicotinic action of acetyl-choline.

Use:

1. It is widely used as an alternative to pilocarpine in the management of Glaucoma.
2. It has also been used for the treatment of decreased gastro-intestinal motility.
3. It is widely used as an eye drop to cause miosis (Excess contraction of Pupil) during surgery.

BethanecholChloride

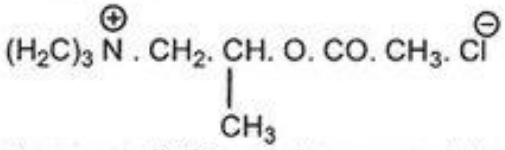


2- [(Amino carbonyl) oxy] N,N,N trimethyl propanaminium chloride

Use:

1. It is used to stimulate GIT and urinary bladder after surgery.
2. It is also used in the relief of urinary retention.

Methacholine



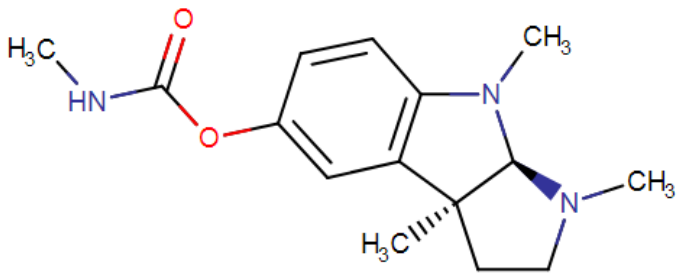
(2- Acetoxypropyl) trimethyl propanaminium chloride

Use:

1. It is used for diagnose asthma.
2. It is also used as a diagnostic agent for belladonna poisoning.
3. It is widely used as a diagnostic agent for bronchial hyper activity.

Indirect acting/ Cholinesterase inhibitors (Reversible & Irreversible):

Physostigmine

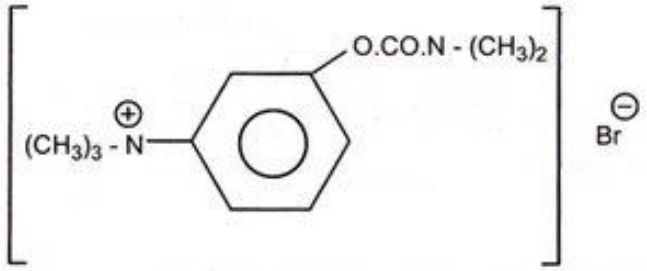


1,3a,8-Trimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indol-5-yl methyl carbamate

Use:

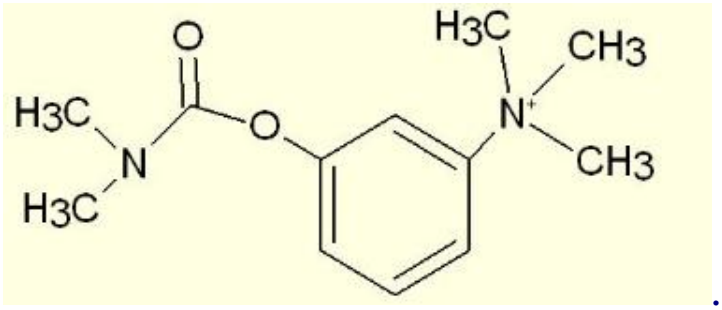
1. It is used to treat glaucoma.
2. To treat poisoning with anti-cholinergic drugs and tricyclic antidepressant drugs.
3. To treat neurologic disorder.
4. It is also used to treat post operative over-sedation.

Neostigmine Bromide



3 - {[(Dimethylamino) carbonyl] oxy} - N,N,N - trimethyl benzeneammonium bromide

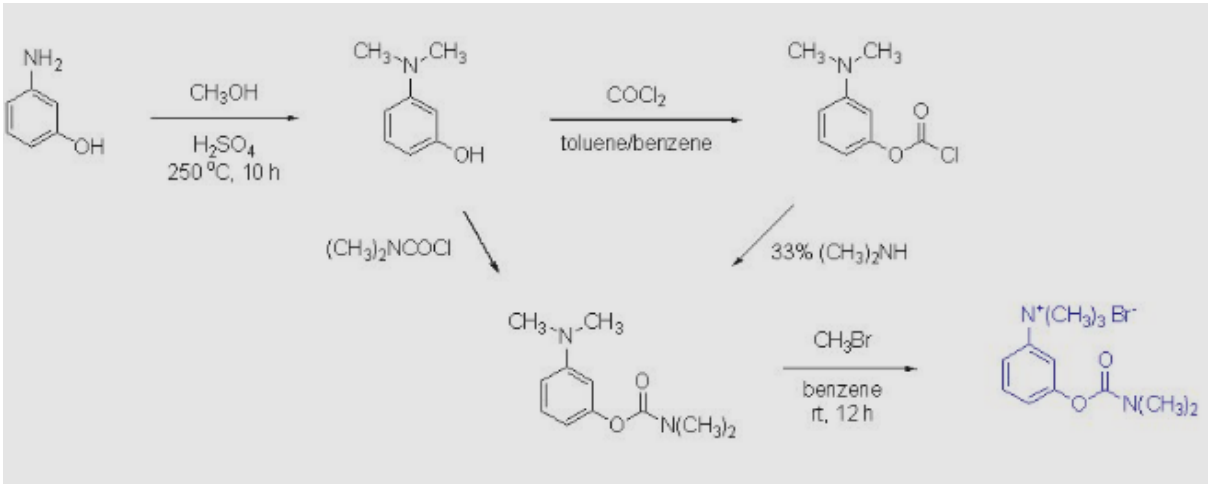
OR



. Br

3-(dimethyl carbamoyl oxy) - N, N, N- trimethyl anilinium bromide.

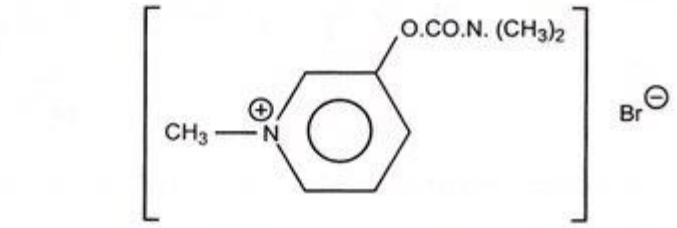
Synthesis



Use:

1. It is used to treat Myasthenia gravis (Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs. The name myasthenia gravis, which is Latin and Greek in origin, means "grave, or serious, muscle weakness.")
2. To treat paralytic ileus. (Obstruction of the intestine due to paralysis of the intestinal muscles.)
3. To treat post-operative urinary retention.
4. To promote expulsion of intestinal flatus (gas in stomach or intestine) before radiography of kidney.
5. Used as a muscular relaxation.
6. Methyl sulphate salt is used as diagnostic agent for Myasthenia gravis.

Pyridostigmine Bromide

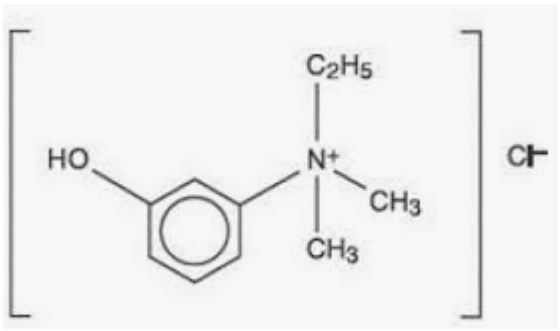


3 - {(Dimethylamino)carbonyl]oxy} -1 - methyl-pyridinium bromide.

Use:

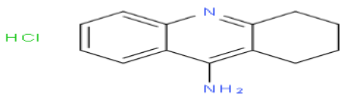
1. It is used to treat Myasthenia gravis (Myasthenia gravis is a chronic autoimmune neuromuscular disease that causes weakness in the skeletal muscles, which are responsible for breathing and moving parts of the body, including the arms and legs. The name myasthenia gravis, which is Latin and Greek in origin, means "grave, or serious, muscle weakness.")
2. To treat paralytic ileus. (Obstruction of the intestine due to paralysis of the intestinal muscles.)
3. To treat post-operative urinary retention

Edrophonium chloride



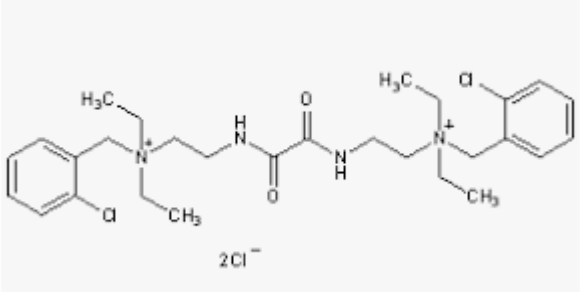
Benzenaminium, N-ethyl-3-hydroxy-N,N-dimethyl-, chloride

Tacrine hydrochloride

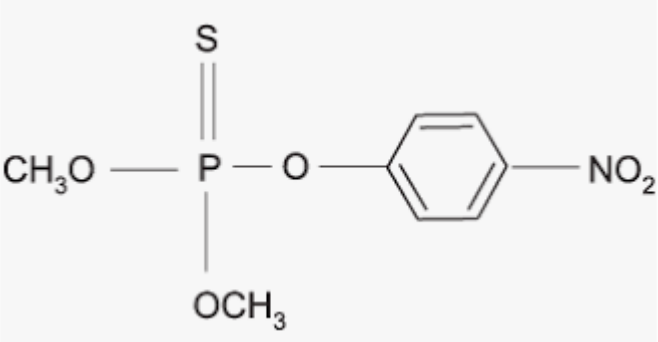


1,2,3,4-Tetrahydro-9-acridinamine hydrochloride

Ambenonium chloride



Parathione



Malathion