DRUGS ACTING ON ANS

AUTONOMIC NERVOUS SYSTEM

→ The ANS is a divison of the Peripheral Nervous System (PNS) that supplies smooth muscles and glands and that influence the function of internal organs.

→ The ANS is a control system that acts largely unconsciously and regulates bodily function such as Heart rate, digestion, respiratory right: pupillary response, urination, etc.

→ This system is a primary mechanism in control of the fight or flight respons.

→ Adrenergic ~~drugs~~ nervous system (sympathetic) is a group of organ and nerves in which adrenaline or noradrenaline are released as neurotransmitter.

→ Adrenergic nerve release neurotransmitter:- Nor-adrenaline, adrenaline, dopamine and produce their effect

→ Autonomic drugs can either inhibit or enhance the function of the parasympathetic and Sympathetic nervous System.

→ The type of drug can be used to treat a wide range of disease, such as glaucoma, Asthma,

Sympathomimetic Agents

Direct acting agent

Nor Epinephrine.
Epinephrine
phenylephrine
Dopamine
Terbutaline

Indirect acting agent.

→ Hydroxy amphetamine,
→ Pseudoephedrine

Agents with mixed mechanism – Ephedrine, Metaraminol

CLASSIFICATION OF ADRENERGIC DRUGS

(A) According to mode of action

(i) Directly acting – adrenaline, noradrenaline, dopamine, Isoprenaline.

(ii) Indirectly using – Amphetamine, Methamphetamine

(iii) By Both mechanism – Ephedrine, Metaraminol.

(B) According to receptor selectivity

(i) α_1 agonist – Methoxamine, phenylepenephrine.

(ii) α_2 agonist – clonidine, α-methyl nor-adrenaline

(iii) Both α_1-α_2 agonist – adrenaline, Noradrenaline

(iv) β_1-agonist – Prenalterol, dobutamine,

(v) β_2 agonist – Salbutamol, Terbutaline

(vi) Both β_1-β_2 agonist – Adrenaline, Isoproterenol

(v) Both α-β agonist – Adrenaline, Ephedrine

(C) According to chemical nature.

(i) Catecholamines – Adrenaline, Noradrenaline, dopamine, Isoprenaline.

(ii) Non-catecholamines – Ephedrine, Amphetamine, Metaraminol

(D) According to therapeutic effect

(i) Vasoconstrictor – Adrenaline, Noradrenaline, Ephedrine Metaraminol

(ii) Vasodilator – Dopamine, Isoprenaline

(iii) Bronchodilator – Salbutamol, terbutaline

(iv) CNS stimulant – Amphetamine, Methamphetamine

(v) Cardiac Stimulant – Adrenaline, Isoprenaline, Prenalterol.

(vi) Nasal decongestant : Ephedrine, Oxymethazoline

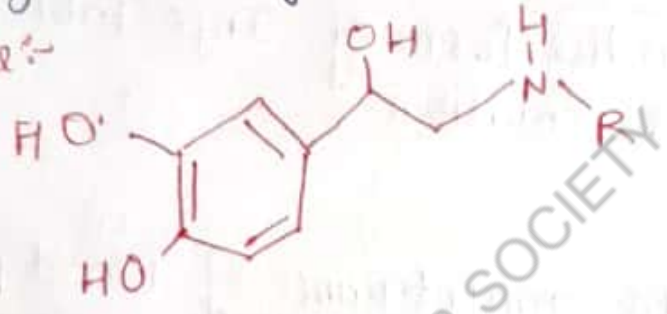
(vii) Uterine relaxants - Nylidrine, Salbutamol

NOR- EPINEPHRINE *

→ Nor-epinephrine (precursor of epinephrine) is a central and autonomic neurotransmitter secreted by adrenal medulla.

→ It acts as a major transmitter for the diffuse projection system which arises from the locus coeruleus of the brain and for the Postganglionic sympathetic fibres.

Structure:-



IUPAC name → 4 [(1R)-2-amino-1-Hydroxy ethyl] benzene-1, 2, diol

· Physical properties:-

Storage:- It is stable for 24 hours storage at 23°C and solutions that are not protected from light will retain only 90% of the initial conc after storage for 39 days at 4°C.

Dose- 0.01-0.1mg/kg/min injection

Category- Sympathomimetic drug

MOA → Nor-epinephrine acts on α- adrenergic receptor for peripheral vasoconstriction and on β-adrenergic receptor for causing inotropic stimulation of Heart and dilation of coronary arteries

Types of formulation:-

It is available in the form of Injectable solution and Intravenous solution.

Uses:-

(1) It is used in the maintenance of Blood pressure in acute hypotensive states arising due to surgical or non-surgical trauma, central vasomotor depression, and Haemorrhage.

Brand name:-

Levarterenol, Levophed, Noradeia, Vesine, Epinor

EPINEPHRINE

Epinephrine is a hormone neurotransmitter When it is produced in the body, it contract blood vessels, increase Heart rate, dilates air passage and contributes in the fight or flight response of the sympathetic nervous system

→ It is a catecholamine produced by the adrenal glands using phenylalanine and tyrosine (amino acid).

→ Stability → It stable in a syringe for at least 3hours

Storage → It should be stored in the carrier tube provided at a temp of 20-25°C. However, temperature excursions between 15-30°C are permitted.

Dose- 0.3-0.5 mg injection.

Uses:-

(1) It stimulate the Heart, increase Heart and Blood pressure, and relaxes the musculature of intestine and Bronchi.

(2) It is commonly used in acute allergic disorder and Histamine reactions.

MAO → It acts as a potent vasoconstrictor and cardiac stimulant. On its release or administration it produce (+ve) inotropic and chronotropic actions on the Hearts (mainly)

β_1 receptors) and cause vasoconstriction in many vascular beds (α receptor), thus the systolic blood pressure is increased.

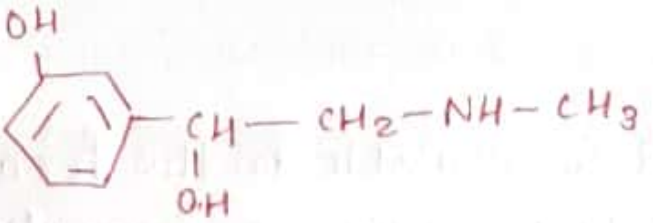
Brand name:- Adrenalin
Auvi-Q
Epinephrine sap-EMS
Epi pen 2-Pak
EPIsnap
Auvi-Q
Epinephrine snap V
Epipen JR - 2-Pak
Symjepi

PHENYLEPHRINE

→ Phenylephrine is sympathomimetic amine acting mostly on the α - adrenergic receptors.

→ It is a vasoconstrictor and used as a nasal decongestant and cardiotonic agent.

Structure:-



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

Physical properties;

(1) It occurs as white crystalline powder.
(2) It is odourless powder
(3) It has a bitter taste
(4) It is freely soluble in water

MOA → It acts as a selective α_1- adrenergic agonist. It acts as a vasoconstrictor and increase Blood pressure by increasing the total peripheral resistance

→ It constricts the ciliary body blood vessel and produce mydriasis, thereby reduce intra-ocular tension.

Storage:- It should store injection 10mg/ml at 20° to 25°C, excursions permitted to 15° to 30° protected from light. It should be store in carton until time of use.

Uses

(1) It is used for treating nasal congestion.
(2) Hypotension and shock.
(3) It is also used in hypotension during spinal anaesthesia.
(2)

Formulation:- It is available in the form of Capsules, Tablets, solutions, Granules.

Brand name:- Neo-Synephrine
Sudafed PE congestion
Biorphen
Suphedrine PE

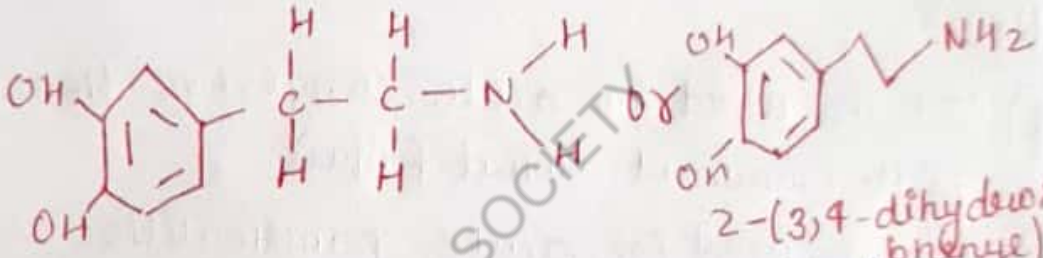
DOPAMINE

→ Dopamine (a central neuro-transmitter) is a metabolic precursor of nor-epinephrine and epinephrine.

→ It does not cross the the Blood Brain Barrier and thus has minimal effect on the CNS.

→ It acts on the receptors and produce a positive inotropic effect on Heart.

Structure:-



2-(3,4-dihydroxy phenyl) ethylamine

IUPAC → 4-(2-amino ethyl) benzene-1, 2,-idiol

→ Dopamine is a monoamine compound with positive inotropic activity

→ Dopamine is a naturally occuring catecholamines

→ It has a role as a cardiotonic drug, a-β eta adrenergic agonist

MOA:- Dopamine acts as a neuro transmitter in some area of the CNS.

→ It increases Heart rate and cardiac contractility through its positives chronotropic and inotropic effect on myo-cardium.

Physical Properties:-

Storage:- Dopamine HCl injection should be stored in such a way that is should avoiding contract with alkalies (including sodium bicarbonate) oxidising agent or iron salts.

Uses:-

(1) It is used in acute congestive Heart failure with imminent renal failure.

(2) It is used in acute pancreatitis

(3) It is used in septic shock and surgical shock.

Type of Formulation:- It is available in the form of injectable solution.

Brand name:- Intropin, Noradria, Vescue, Epinor

Dose- 0.01-0.1 mg/kg/min injection

Category→ Sympathomimetic drugs

TERBUTALINE

⇒ Terbutaline is a synthetic compound acting as a sympathomimetic amine. It is the most selective agent which stimulates β_2-adrenoreceptors.

⇒ Terbutaline is an ethanol amine derivative with Bronchodilating and tocolytic activities.

Physical properties

MOA:- Adenyl cyclase enzyme catalyses the conversion of ATP into cyclic-3'5. adenosine monophate (cAMP).

→ Terbutaline acts as by stimulating intracellular adenyl cyclase via β-adrenergic receptors, thus resulting in increased cAMP level.

→ The increased level of cAMP further relax the bronchial smooth muscles and inhibit the secretion of mediators of immediate Hypersensitivity from mast cell.

Storage:- It should be stored at Room temperature between 15°-30°C away from light and moisture.

It should not be stored in the moisture area.

Keep all medicines away from childrens and pets.

Uses:-

(1) It is used in breathlessness and wheezing arising from lungs problems (e.g- Asthma, chronic, Obstructive Pulmonary disease.

(2) Bronchitis and Emphysema.

Type of formulation- Powder
Solution.

Brand name- Brethine, Kazicof-TL
Bricanyl, Ascoril
Brethaire, Bricof EX

TERBUTALINE

⇒ Terbutaline is an ethanolamine deruvative with Bronchodilating and tocolytic activities.

⇒ Terbutaline is a synthetic compound acting as a sympathomimetic amine

→ It is most selective agent which stimulates β_2-adrenoreceptors.

Physical properties:-

(1) It is used as sulphate salt

(2) Terbutaline sulphate is a white to greyish white crystalline powder.

(3) It is odourless or with a faint odour of acetic acid.

(4) It has bitter taste.

(5) It is freely soluble in water

MOA:- Adenyl cyclase enzyme catalyses the conversion of ATP into cyclic-3's adenosine monophasphate (cAMP)

→ Terbutaline acts by stimulating Intracellular adenyl cyclase via β-adrenergic receptors, thus resulting in increased cAMP level

→ The increased level of cAMP further relax the bronchial smooth muscle and inhibit the secretion

of mediator of immediate Hypersensitivity reaction

Storage:- It should be store at 15°C - 30°C in air tight container protected from light

Uses:-

(1) It is used orally as a Bronchodilator in the treatment of Bronchial asthma.

(2) It is used in Breathlessness and wheezing arising from lung problems.
(e.g, Asthma, COPD, Bronchitis

Dose - 2.5 mg in tablet

category - Asthma

Formulation - Powder, solution

Brand name - Brethine, Bricanyl

SALBUTAMOL (ALBUTEROL) (15)

⇒ Salbutamol (INN) is also known as ALBUTEROL (USAN).

→ It is a short acting β_2- adrenergic receptor agonist in the treatment of Asthma and COPD (Chronic Obstructive Pulmonary disease)

→ The decomposition of salbutamol in aqueous solution obey first-order kinetic with respect to salbutamol sulphate.

→ The reaction rate increased with increasing drug conc^n and elevated temperature

Physical properties:

MOA:-

→ Salbutamol is a direct acting sympathomimetic agent. It acts as β_1-adrenergic agonist drug having a selective action on β_2-receptors

Storage:- It should be stored at Room temperature b/w 15-30°c and keep away from light and moisture

→ It is best to store the inhaler with the mouthpiece down.

→ The canister should not be puncture or exposed to high Heat or Open flame

Dose- 2-4 mg of Tablet, Nebulizer and inhalant

Category- Bronchodilators

Formulation - Aerosol, Solution, Tablet

Brand name - Ventrolin, Bronko, Atromir
Asthalin, Bronosol, Proair
Budesal, salbu, Xopenex.

Uses:-

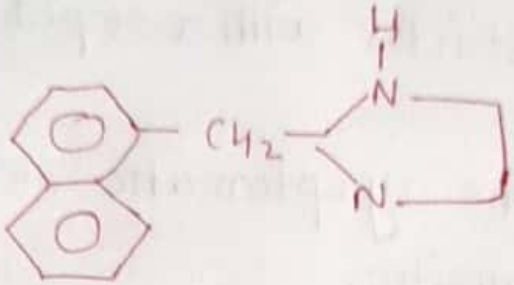
(1) It is used in Bronhial Asthma
(2) It is used in Peripheral vascular disease.
(3) It is used in the treatment (prevention) of premature labour.

NEPHAZOLINE

→ Nephazoline acts on ocular arterioles through its rapid sympathomimetic vasoconstrictor action

→ It decrease the congestion of conjunctiva and is present in many OTC eye drop

Structure



IUPAC name – 2-(naphthalen-1-ylmethyl)-4,5-dihydro-1H-imidazole

Physical properties :-

(1) It occurs as white or almost white, ~~odourless~~ crystalline powder.

(2) It is odourless powder.

(3) It is sparingly soluble in water and soluble in alcohol.

(4) It is practically insoluble in ether.

(5) A 1% solution in water has PH - 5 - 6.5

MOA → It acts on α- adrenergic receptors present in the arterioles of nasal mucosa through its sympathomimetic action

Storage:-

The dropper should be stored upright at Room temperature between 20-25°C and keep away from moisture and sunlight.

Uses:-

(1) It is a vasconstrictor with a rapid and prolonged action.

(2) It is used for the symptomatic relief of Rhinitis and sinusitis.

(3) It is a decongestant that relieve redness, puffiness and itchy / watering eye due to cold, allergies or eye irritation.

Category- Nasal decongestant, Sympathomimetic

Dose- 1 drop of opthalmic or nasal drops

Formulation:- Opthalmic gel forming soln, Solution

Brand name- Privine, Allendrop,
Napzol, Fenx
celosN, Freydex

TETRAHYDROZOLINE

⇒ Tetrahydrozoline also known as Tetryzoline (member of imidazolines and carboxamides).

⇒ Tetrahydrozoline HCl is an α- adrenergic agonist

⇒ It is used as a decongestant to relieve redness in the eye caused by minor irritants e.g- smog dust or smoke etc

Physical properties:-

(1) It occurs as white solid powder

(2) It is odourless powder

(3) It is freely soluble in water and alcohol.

(4) It is very slightly soluble in chloroform and practically insoluble in ether

Mechanism of Action:-

→ Adrenergic receptors are G-protein coupled receptor (GPCR) that regulate vascular tone.
i.e- Vasoconstriction is caused by the stimulation of α1 adrenergic receptor.

Storage :-

→ It should be keep container tightly closed in a dry and well- ventilated place.

→ The bottle should be tightly closed when it is not in use.

Uses :-

(1) It is used for the symptomatic relief of Rhinitis and sinusitis

(2) It is used as a vasoconstrictor by narrowing swollen blood vessel in the eye for reducing eye redness.

(3) Its opthalmic preparation (for the eye) are used for providing temporary relief from minor eye redness, swelling or draining caused by minor irritant.

Dose - 1-2 drops, Opthalmic solution, Nasal drops

Formulation - Opthalmic solution

Category - sympathomimetic, Nasal decongestant

Brand name - Tyzine Nasal
Visine Original
Colirio Ousan

HYDROXY AMPHETAMINE (Oxamphetamine)

→ Hydroxyamphetamine occurs as Hydrobromide salt derived from amphetamine.

It is a powerful vasoconstrictor which stimulates the α- receptors but lacks any CNS activity.

Physical properties:-

(1) HAT HCl occurs as white crystalline powder.

(2) It is freely soluble in water and alcohol.

(3) It is practically insoluble in ether

(4) Solution in water have a PH of about 5

(5)

MOA:- It is an indirect acting sympathomimetic agent.

→ It causes mydriasis by releasing nor-epinephrine from adrenergic nerve terminals.

Storage- It should be stored between 20°c and 25°c

It should be protected from light and sunlight.

Uses:- (1) It is used in children having Hyperkinetic syndrome.

It is used as an anorexiant for treating obesity.

It is used as a mydriatic agent for diagnosing opthalmic nerve lesions.

Formulation- solution, Hydroxy Hydrobromide Opthalmic Soln.

Brand name- Paremyd

Category → dilation of pupil. **Dose-** 1-2 drops

PSEUDOEPHEDRINE

⇒ It is a α and β adrienergic agonist and a sympathomimetic agent which also increase norepinephrine release

⇒ It is structurally similar to ephedrine, and relieves nasal and sinus congestion

⇒ It also relieves otalgia related to air travel, in adults

Physical properties :

(1) It is used as Hydrochloride and sulphate

(2) Hydrochloride salt is a white, crystalline material

(3) It is freely soluble in water while sulphate salt is soluble in water

MOA :-

⇒ It is directly act on α- adrenergic and β-adrenergic receptors (to a lesser degree)

⇒ It causes vasoconstriction by directly acting on α- adrenergic receptor in the Respiratory tract mucosa

→ It stimulate β_2- adrienergic receptors and relax the bronchial smooth muscles

Storage:- It should be stored in well-closed and light resistant container

Uses:-

(1) It is used in vasomotor rhinitis, and nasal, sinus and eustachin tube congestion

(2) It is also used as a first line therapy in priapism

(3) It is used as an adjunct in allergic rhinitis, croup, sinusitis, otitic media and tracheobrachitis.

Formulation - Syrup, Tablet

Brand name - Sudafed congestion, Altiva-D
Sudo Chest, Anticold
Sudofed 12-Hour, Acticold, Belrin-D
Sudafed Children nasal Decongestant

Category - Nasal decongestant.

Agents with mixed Mechanism

⇒ Some sympathomimetic agent (e.g- Ephedrine, Metaraminol and pseudoephedrine) have a mixed action.

⇒ They act by releasing a neurotransmitter and also have a direct-agonist activity.

→ Amongst the adrenergic agonists, epinephrine and nor-epinephrine are the least specific.

→ Both α- and β receptors can be stimulated by nor-epinephrine and epinephrine but due to the difference in their structural chemical, nor-epinephrine has more pronounced effect at α-receptors while epinephrine has more pronounced effect at β-receptors.

Also, the potency of both these drug is different from each other.

The drugs studied below are

Ephedrine

Metaraminol.

EPHEDRINE

→ Ephedrine acts as as agonist on α- receptor as well as on β- receptor.

→ It also increase the release of nor- epinephrine from the sympathetic neurons

→ It is a mixed acting sympathetic drug.

→ The structure of ephedrine involves two asymmetrical carbon atoms

→ The clinically used form of ephedrine are l- ephedrine and racemic ephedrine only.

Physical properties:-

(1) It consist of fine crystaline powder.

(2) It is a odourless crystalline powder.

(3)

MOA → It is a sympathomimetic amine which acts by indirectly stimulating the adrenergic receptor system and also by increasing nor-epinepherine activity at the post synaptic α- and β- receptors

→ It acts on the CNS partially because it does not cross the BBB (Blood Brain Barrier) efficiently.

Storage:- This medication should be stored at Room temperature between 15° and 25°C.

Uses

(1) Ephedrine and its salts are used in the allergic disorders, colds, Hypotensive conditions and narcolepsy through oral, i.v, i.m and topical route

(2) It is applied locally for nasal decongestion as it constricts the nasal mucosa
It also cause dilation of the pupil or Bronchi.
It is used in asthma, Hay fever and urticaria

(3) It is used for stimulation, appetite suppresion, decongestion, as a conc^{n} aid and for treating Hypotension related to anaesthesia

Type of Formulation :-

(1) Tablet
(2) Capsule

Brand name :-

Akovaz
Bronkaid
Corphedra
Emerphed
Primatene
Rezipres

METAR-AMINOL

→ Metaraminol (or araamine) is structurally similar to phenylephrine with the only difference that it is a primary (and not secondary) amine.

→ It is directly acts on α- adrenergic receptors and has mixed mechanism of action.

Physical properties:-

(1) Metaraminol tartrate occurs as an odourless or almost odourless, white crystalline powder.

(2) It is freely soluble in water and sparingly soluble in alcohol.

(3) It is practically insoluble in chloroform and ether.

(4) The 5% solution in water PH of 3.2-4.5

(5) The B.P injection is sterilized by filtration.

MOA → Metaraminol through its peripheral vaso-constriction action increase systemic B.P (Both systolic and diastolic) by agonising α_1- adrenergic receptor.

Storage:- It should be stored between 2-8°C for 24-48 hours in an I.V infusion.

→ It should not be stored above 25°C.

Dose- 5-10mg injection

Category- Used for prevention and treatment of
Used acute Hypotensive state occuring with spinal anaesthesia priapism.

Formulation – solution.

Brand name- Aramine

ALPHA- ADRENERGIC ANTAGONIST (30)

Adrenergic antagonist

→ Adrienergic antagonist prievent the response of effector cells to both sympathetic nerve activity or sympathomimetic drugs by their blocking action on the adrenoreceptors.

CLASSIFICATION

→ These drugs are broadly sub-divided into two groups.

(1) Alpha adrienergic receptor Blocking agent
(2) Beta- adrienergic receptor blocking agent

Alpha adrienergic Receptor Blocking agent :-

→ They usually produce a generalized peripheral vasodilation by inhibiting the effect of various agonists on the α- receptors

→ They reverse the action of adrenaline on Blood Pressure and opposite the action of noradrenaline

Example- Tolazoline, Phenoxy benzamine, Phentolamine, Prazosin, Doxazosin.

TOLAZOLINE

⇒ Tolazaline is a member of the class of imidazole that is 4,5-dihydro-H-imidazole substituted by a benzyl group. It has a role as an alpha-adrenergic antagonist.

Physical properties :-

(1) It occurs as a white to off white odourless crystalline powder.
(2) Its taste is bitter.
(3) It is very soluble in water.
(4) The solution for injection are steilized by autodaving or by filtration.

MOA → It cause vasodilation by directly acting on the peripheral vascular smooth muscle and indirectly by releasing endogenous histamine.

→ It blocks α-adrenergic receptor moderately and agonises histamine.

→ It reduce pulmonary arterial pressure and vascular resistance.

Dose - 25-50mg / ml injection

Category - Vasodilator agent, Anti-Hypertensive agent

Storage- It should be store in air-tight containers protected from light.

Uses :-

(1) It is used to increase blood flow in peripheral vasospastic conditions like- Ranaud's Syndrome, childblains, frostbite etc.

(2) It has also been used as 10% w/v in solution eye drop in the treatment of opthalmic condition.

(3) It is given orally. It has also been given by subcutaneous, i.m, i.v, or slow intra-arterial injections.

Brand name:- Tolazoline, Benzazolin, Tolazolina cloridrato, Priscol.

PHENTOLAMINE

⇒ The group attached to the imidazoline ring decides whether it will be an agonist or an antagonist.

⇒ Two imidazoline α- antagonists used therapeutically are tolazine (Priscoline) and Phentolamine (Regitine). Both of them are competitive (reversible) blocking agent.

Physical properties:

① It occurs as a white or off white crystalline Powder. T

② It is a odourless powder.

(3) It is freely soluble in water and alcohol.

(4) It is slightly soluble in chloroform.

Storage:- It should be stored in air-tight containers protected from light. Injection should be stored at 15-30°C.

Category – Vasodilation

Dose - 5 mg injection

Use-(1) It is an alpha adrenoreceptor blocking agent and it also has a direct action on vascular smooth muscle.

(2) It is used to prevent paroxymal Hypertension in patients with Phaeochromocytome.

(3) It is also used as prophylactic against catecholamine induced hypertensive crisis during surgery in those patient

(4) It has also been employed for differential diagnosis of phaeochroma cytoma

Brand name - Phentosol
Fentanor
Fentosol
Rogitine

PHENOXYBENZAMINE

⇒ Phenoxy benzamine is a synthetic, dibenzamine alpha (α) adrenergic antagonist with antihypertensive and vasodilatory properties.

Physical properties:-

(1) It is a white crystalline powder.
(2) It occurs as odourless powder.
(3) Its taste has tasteless
(4) It is very slightly soluble in water.

MOA → Phenoxybenzamine wide blood vessels and relaxes muscles by blocking α- receptor. Blood pressure reduce due to widened blood vessels.

~~Uses~~; Storage: It should be store at 25°C, excursion Permitted to 15°-30°C.

Dose - 20-40 mg Capsule and Injection
Category - Pheochromocytoma
Use - (1) It is a powerful alpha adrenoreceptor blocking agent with prolonged duration of action.
(2) It is used to control Hypertension by Phaeochromocytom in the treatment of Peripheral vascular disease.

Brand name:- Fenoxene, Fenoben, Dibenzyline.

PRAZOSIN

⇒ Prazosin is derived from quinazoline and it is highly specific antagonist of α_1- receptor.

Physical properties:-

① It occurs as white to tan coloured powder.

② It is odourless powder.

③ It is slightly soluble in water and isotonic with saline.

④ It is practically insoluble in chloroform and acetone.

Storage:- It should be stored in well- closed container, and light resistant container 15- 30°C

MOA → Prazosin inhibit the post-synaptic α_1- adreno- receptors present on vascular smooth muscle.

→ It can also be used alone or with β- blockers for pre-operative management of the signs and symptoms of Pheochromocytoma.

Category- Relax the Blood vessels

Dose- 5mg Tablet, capsule

Use- ① It is used in the treatment of all grades of Hypertension often in conjunction with a diuretic and other Hypertensive agent

Brand name- Prazovin-X, Minipress XL, GITS, Prazopress, Czopress XL, Prazocip-1

BETA - ADRENERGIC BLOCKERS

→ These usually inhibit the action of catecholamines at Beta adrienergic receptor sites. completely.

→ These agents normally reduce the cardiac activity, by preventing B- adrienoreceptor stimulation

→ They are used in the treatment of angina- pectoris, cardiac arrhythmia and also in control and treatment of Hypertension.

Example- Propanolol, Practolol, Esmolol, Labetolol, Carvedilol, Atenolol, Metroprolol, Acebutolol

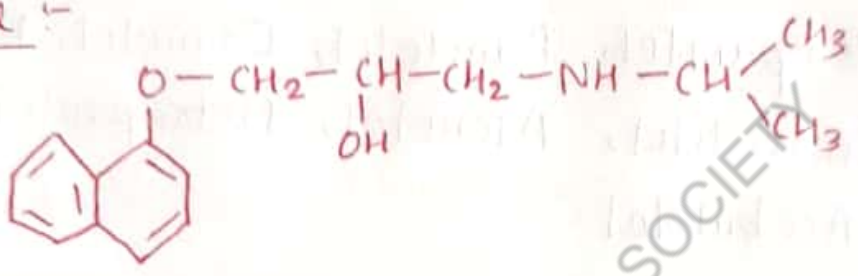
PROPRANOLOL

⇒ Propranolol is a synthetic, non-selective Beta-adrenergic receptor blockers with anti-angina, anti-arrhythmic, anti-Hypertensive properties.

Physical properties :-

① It occurs as white odourless powder
② It has bitter taste
(3) It is soluble in water.
(4) Solution are more stable at PH 3

Structure :-



IUPAC name:- 1-Isopropylamino-3-naphthyloxy-Propan-2-ol

Storage:- It should be store at controlled room temperature 20° to 25°C

Dose - 80 mg Tablet once a day

Category - Anti-Hypertensive agent.

MOA (Mechanism of Action) :-

→ Propanolol acts as a competitor to sympathomimetic neuro-transmitter such as catecholamine to bind at β1-adrenergic receptors in the Heart, therefore, inhibiting sympathetic stimulation.
→ It reduce the resting Heart rate, cardiac output, systolic and diastolic B.P.

Uses :-

(1) It was the first Beta Blocker to get into clinical use.

(2) It is used in the treatment of cardiac arrhythmia.

(3) It is also used to improve the tolerance to exercise in patient with angina pectoris.

(4) It is also used in the treatment of High Blood Pressure, usually in combination with a thiazide diuretic.

(5) Propanolol is usually given by mouth. It has also been employed for some symptoms of anxiety and Migraine.

Official Preparation :-

(1) Propanolol Hydrochloride B.P. I.P

(2) Propanolol Injection B.P

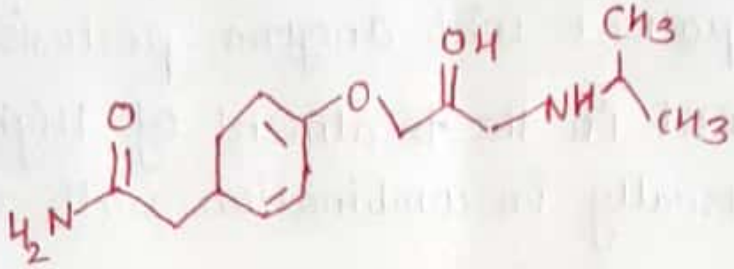
(3) Propanolol Tablet B.P. I.P

Brand name :- Ciplar-La
Probeta-SR
Alprom-plus
Betacap
Norten.

ATENOLOL

⇒ Atenolol is a cardioselective Beta-Blocker that is widely used in the treatment of Hypertension and angina pectoris.

Structure:-



IUPAC → 2-[4-[2-Hydroxy-3(propan-2-ylamino) propoxy] Phenyl] acetamide.

Physical properties:-

(1) It occurs as white colour powder
(2) It is odourless powder
(3) It has a bitter taste
(4) It is slightly soluble in water.
(5) It is very soluble in dilute solutions of acetic acid.

Storage Mechanism of Action:-

→ Atenolol is a competitior of sympathomimetic neurotransmitter (catecholamines) in binding at B1-adrenergic receptor in the Heart and vascular smooth muscle. therefore inhibiting sympathetic stimulation.

Storage- It should be store this drug at Room temperature between 20°c and 25°c.
Keep the medication tightly closed and in a light-resistant container.
It should be stored away from moisture.

CARVEDILOL :-

→ Carvedilol is a member of class of Carbazoles with an adrenergic antagonist, non-selective Beta and alpha 1 receptor blocking properties which helps in the management of congestive Heart Failure.

Physical properties :-

1. It occurs as a off white crystalline powder.
2. It is odourless powder.
3. Its taste is bitter.
4. It is sparingly soluble in water

Storage :- It should be stored at 20-25°C. Keep the tablet in a dry place and away from Light (moisture).

Uses :-

(1) It is used in the treatment of Hypertension.
(2) It is used as adjunct in symptomatic treatment of congestive cardiac failure.

Formulation :- Tablet

Dose - 10mg/day Tablet

Category - Anti-Hypertensive agent

Brand name - Compres
Cadmos,
Carloc
Cevas

Dose- 50mg Tablet

Category- Anti-Hypertensive agent

Official preparation:

(1) Practolol B.P

(2) Practolol Injection B.P, I.P

Brand name- Tenormin, Betacard, Tenolol, Hipres.

CHOLINERGIC DRUGS AND RELATED AGENTS

⇒ Cholinergic drugs are a category of pharmaceutical agents that act upon the neuro-transmitter acetylcholine, the primary neuro-transmitter within the parasympathetic Nervous System.

→ Acetylcholine is released from post ganglionic Parasympathetic nerve to produce action resembling those of muscarine e.g (cardiac inhibition, Peripheral vasodilation, contraction of pupil, increased salivation, increased peristalsis, contraction of muscles of urinary bladder) and to those of nicotine. e.g (stimulation of skeletal muscles, the adrenal medulla and autonomic ganglia).

→ Ach is rapidly destroyed by cholinesterase enzyme at or near the site of liberation.

→ The cholinergic drugs are compounds that stimulate the parasympathetic system and imitate the actions of acetylcholine. These drugs are also called as parasympathomimetics or Cholinomimetics.

Classification

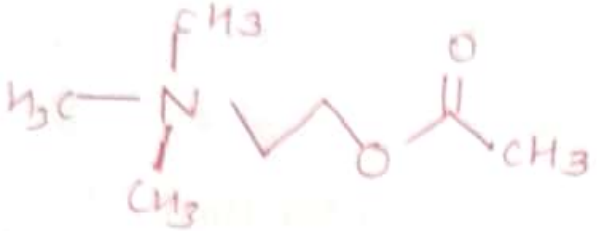
- Direct acting agent
  - → Acetylcholine
  - → Carbachol
  - → Bethanechol, Methacholine
  - Pilocarpine
- Anti-cholinesterase agent
  - → Neostigmine
  - → Tacrine HCl
  - → Pralidoxime Chloride
  - → Echothiopate Iodine
  - → Edrophonium chloride

ACETYLCHOLINE

⇒ Acetylcholine is an ester of acetic acid and choline, which acts as neurotransmitter.

It has a role as a vasodilator agent, a muscarinic agonist, a hormone and a neurotransmitter.

Structure :-



IUPAC → 2- Acetoxy - N, N, N - trimethylethanaminium

Physical properties:-

1. It occurs as white crystalline powder
2. It is very soluble in water freely soluble in alcohol.
3. It is practically insoluble in ether.
4. It is decomposed by Hot water.
5. It is incompatible with alkalis.

Storage - It is stored in air - tight container protecting from freezing and store between 3° to 7°C

Dose - 20 mg powder for injection

Category - Miosis during ocular surgery

Uses:

1. It is a powerful parasympathomimetic agent but its action is transient as it is rapidly destroyed by cholinesterase.

(2) It is used as miotic in cataract surigery to constrict the pupil.

(3) It may be used in penetrating Kerato plasty and in simple iridectomy.

(4) It has also been used in a wide variety of condition such as -

→ trophic ulcers
→ Gangrene
→ Post-operative distension
→ Paralytic ileus

Brand name :- Miochol-E,
Miochol,
Miochol Plus

CARBACHOL

⇒ Carbachol is an ammonium salt and a carbamate ester. It has a role as a nicotinic acetylcholine receptor agonist, a muscarinic agonist, a non-narcotic analgesic and a cardiotonic drug

Physical properties:-

(1) It occurs as white or faintly yellow micros
(2) It is odourless powder
(3) It has a faint amine like odour
(4) It is very soluble in water and sparingly soluble in alcohol
(5) It is practically insoluble in chloroform and ether
(6) Solutions in water are neutral to litmus

Storage:- It should be store in air-tight container and store in refrigerator at 4°c

Dose - 0.5 ml opthalmic solution

Category - Glaucoma

Use (1) It is used to lower intraocular pressure in glaucoma
(2) It has also been used in the treatment of post operative intestinal atomy and urinary retention
(3) It has also stop supraventricular paroxysmal tachy-cardia

Brand name - Miostat, Isopto, Carbochol, Carbastat, Carbyl

PILOCARPINE

→ Pilocarpine is a natural alkaloid extracted from plants of the genus Pilocarpus, with cholinergic agonist activity.

→ It is a para-sympathomimetic agent with primary the muscarinic effect of acetylcholine

→ Physical properties

1. It occurs as viscous, colourless oily liquid.
2. It is hygroscopic in nature
3. It is soluble in water.
4. It occurs as odourless powder.
5. It has faintly bitter taste.
6. It found also as a nitrate form and it is white crystalline powder.
7. Pilocarpine nitrate is freely soluble in water.

Storage → It should be store at a temperature not exceeding 8°C in airtight container and light resistant container

Uses:

1. Pilocarpine salts are used as solution (1-4%) to exert an action on the eye to cause miosis
2. It is used to retard intraocular pressure in glaucoma.
3. It is used to prevent or break adhesion of iris with lens or cornea

④ It is also used to antagonise the effect of shorts acting mydriatic and cycloplegic action of atropine (48)

Dose- 5mg for tablet and ophthalmic eye drop

Category- Xerostamia, Sjogrens syndrome

Brand name - Andre Carpine,
Carpinol.
Locarp GEL
Pilocar

CHOLINESTERASE INHIBITORS

⇒ Anti-cholinesterase agent or Cholinesterase inhibitors. are also known as Indirect Acting cholinergic agonists.

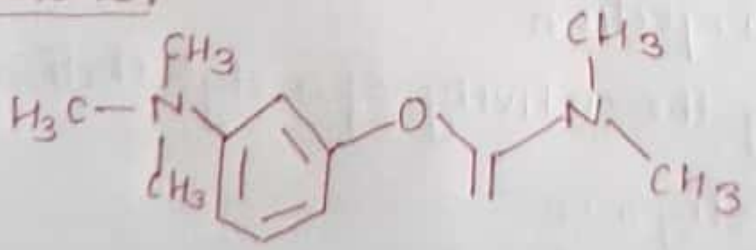
⇒ They inhibit the acetylcholinesterase inactive at nerve ending and produce effect similar to excitation of cholinergic system by increasing availability of Acetylcholine at these site

⇒ Example- Neostigmine, Pyridostigmine, Physostigmine, Edrophonium chloride.

NEOSTIGMINE BROMIDE

⇒ Neostigmine is a parasympathomimetic agent that acts as a reversible acetylcholinesterase inhibitors

Structure:-



IUPAC:- 3-[dimethylcarbamoyloxy) phenyl]-Trimethyl-azanium.

Physical properties:-

(1) It occurs as odourless white crystalline powder
(2) It is slightly Hygroscopic powder
(3) It has a bitter taste
(4) It is very soluble in water.
(5) Solutions are sterilized by autoclaving
(6) Solutions are neutral to litmus

Storage:- It should be stored in air-tight containers protected from light

Uses:-

(1) It is used orally in the treatment of Myasthenia Gravis.
(2) It is used in injection in the treatment of paralytic ileus and post operative urinary retention
(3) It is used for reversal of neuro-muscular block caused by muscle relaxant

Dose- 0.5 mg/ml injection

Category - Blocking the activity of acetyl cholinesterase

Brand name - Tilstigmin
Prostigmin
Myostigmin
Stimim.

EDROPHONIUM CHLORIDE

⇒ Edrophonium is a cholinesterase inhibitor. It is a quarternary ammonium ion and a member of phenols

Physical properties :-

1. It occurs as a white crystalline powder
2. It is odourless powder.
3. It is very soluble in water and freely soluble in alcohol.
4. It is practically insoluble in chloroform and ether.
5. A 10% solution in water has a PH of 4 to 5
6. solutions for injection are sterilized by autoclaving.

Storage :- It should be store in well-closed container protected from light.

Uses :-

1. It is used in the diagnosis of myasthenia gravis

Dose - 0.1-0.2 ml injection

category - Myasthenia Gravis

Brand name - Reversol, Tensilon, Enlon

TACRINE HCL

⇒ Tacrine is an oral acetylcholinesterase inhibitor previously used for therapy of Alzheimer disease.

→ Uses

(1) It has been used to prolong the action of sux methonium and to antagonise competitive muscle relaxant

(2) It has also been used as a Respiratory Stimulant usually in conjunction with opioid analgesics.

Storage:- It should be stored at controlled Room temperature 15°–30°C.

Dose- 40mg/day Tablets

Category- Alzheimer disease

Brand name- Cognex

PRALIDOXIME CHLORIDE

⇒ Pralidoxime is a pyridinium salt, it has a role as a cholinesterase reactivator and a cholinergic drug.

Physical properties:-

1. It occurs as white or pale yellow crystalline powder
2. It is a odourless powder.
3. It is freely soluble in water.
4. A 2.87% solution in water is iso-osmotic with serum.

Storage:- It should be store at room-temperature between 20°C and 25°C.

Uses:-

1. It is used as adjunct to atropine in the treatment of poisoning by certain cholinesterase inhibitors.
2. It has been reported effective in poisoning by some organophorus insecticide and miotics
3. It is effective in relieving paralysis of respiratory muscles

Dose- 1000mg-2000mg injection

Category- Antidote to treat poisoning

Brand name- Clopam, Lyphe, Aldopam, Adipam. Nispam.

ECHOTHIOPATE IODIDE

⇒ An irreversible acetylcholinesterase inhibitor, its iodide salt is used an ocular antihypertensive in the treatment of open-angle glaucoma.

Physical properties :-

(1) It occurs as white crystalline Hygroscopic Powder with an alliaceous odour.

(2) It is freely soluble in water and soluble in alcohol and practically insoluble in chloroform and ether.

(3) A solution in water has a PH of about 4.

Storage :- As per B.P specification it should be stored at a temperature between 2° and 8°c

→ It should be store in air-tight container protected from light.

Uses :

(1) It is mainly used in the treatment of open angle glaucoma.

Dose - 0.125% soln once or twice daily opthalmic soln

Category - Open angle glaucoma

Brand name - phospholine Iodide, Echodide.