Date 20/01/2020

Unit -2

Drug acting on autonomic nervous system (ANS) :-

Introduction:- ANS is a part of the nervous system that controls and regulates the internal organs with out any conscious by organism. It supplied the internal organ including the blood vessels, stomach instestine, lungs, kidney, blander (urinary bladder) Salivary gland and digestive gland.
The ANS control all the voluntary actions and helps to maintain the constancy of internal environmental ANS consist of two main divisions.

1) Sympathetic nervous system (SNS)
2) Parasympathetic Nervous system (PSNS)

→ Both these nervous system have opsative action
The SNS has catabolic effect like increse(↑) in
* blood pressure relexes of bronchial muscles contraction of arteries etc.
* PSNS has anabolic effect like conctraction of eye pupils desres(↓) in blood pressure, (↑)se in activity of the digestive system and (GIT) secrition.

Adrenergic drugs and neurotrans mitters

Adrenergic drugs are the agent which acts directly on the (SNS) and these drugs are also known as sypathominatic drugs as these agent mimies the actions of (SNS)
→ On stemilutation of SNS following responsence are produsced
1) Cardiac stimulation result in increasing heart rate and force of contreaction.

2) Stimulation of CNS (central nervous system)
3) Relaxation of bronical muscle
4) Increase in rate of glycogenolysis

Neurotransmetters

The neurotransmetters of the adrenergic system belongs to a ortho-dihydroxybenzene ring which attached to an amino ethyl side chain.
examples:- Epinephrine and non-epinephrine and DOPAmine are the principle neurotransmetters of adrenegric system

→ Neurotransmetters are the specific chemical agents which are responsible for transmisions of nerve impules across most of synapes.
- These neurotransmetters gets released only when the nerve imples proceudsed the responsnence at smoth cardiac, skelatan mussclurs, endocrine gland and post synaptic.
- These neurotransmetters process the synapes and enicipes the activity in another neuron by interaction with the post synaptic receptors.

Biosynthesis of neurotransmetters:-
The biosynthesis take place in adnereqic and dopaminergic neuron and CNS in sempatic neuron in the ANS.
- Various enzyme which are responsible for synthesis

1) Tyrosine hyroxylase
2) DOPA decarboxylase
3) Dhethanolamine-N-methyl transfrase.

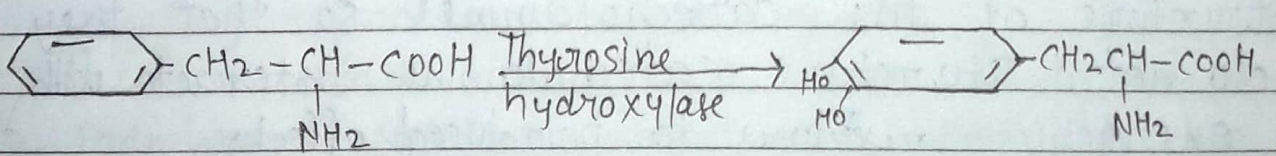
4) Dopamine - β - hydroxylase.

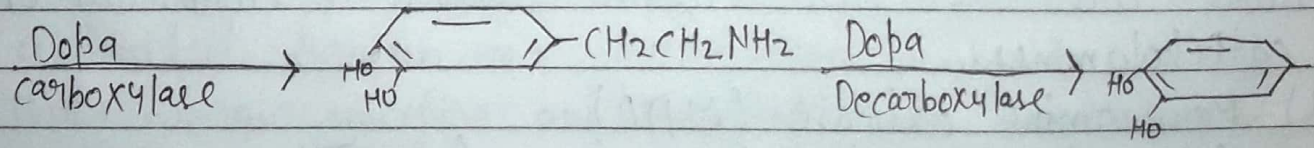
→ Various steps involved in the biosynthesis of adeneric neurotransmitters are follawes -

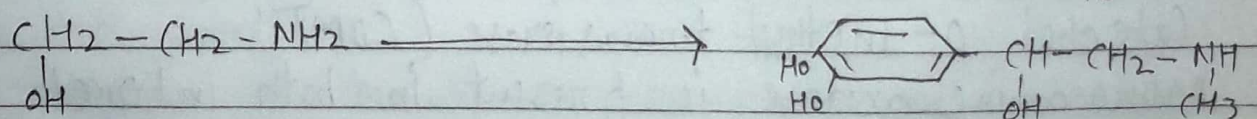
Phenylalanine $\xrightarrow[\text{in liver}]{\text{Hydroxylase}}$ Thyrosine

(i) L - tyrosine hydroxylated into 3,4 di-hydroxy Phenylalanine (DOPA) by the enzyme tyrosine hydroxylase
- This is the rate limiting the steps in the biosynthesis This steps take place in the cytoplasm and neurons.

(iii) DOPA decarboxylase causes decarboxylation of L-Dopa to from dopamine.
- This formation of dopamine take place in the cytoplasm of neuron.
- Dopamine from in the cytoplasma and than transported in the storage vessicles
- Where it gets hydroxylated by the enzyme dopamine β - hydroxylase to from not adenerenale.







Noradrenaline

DOPAMINE

Storage and release of neurotransmitters

The naraderenaline (Neurotransmitters) formed in the nerve ending remains stored in vesicals in the form of ATP complex.

→ Naraderenaline stored in vesicals diffeuses out in the cytoplasm

→ It forms methylated aderenaline than enters into chromaffin granules get stored

→ These neurotransmitters will released only

→ When there is increse in the permeability of the nerve ending membrane to calcium oins because of an action potaential

This process causes release of calcium ions

→ Which is term helps in fusion of the vesicals and resulting in exocytoxsis of the vesicals and release neurotransmitters.

Catabolism of catecholamines (neurotransmitters)

The actions of catecholamines can be termed through catabolism & metabolism transformation in this process the particular enzyme changes the structure of the catecholamines so that they do not sturcture catecholamine interact with energeric receptors to produced effects

There are two type enzyme involved in catabolism of catecholamines.

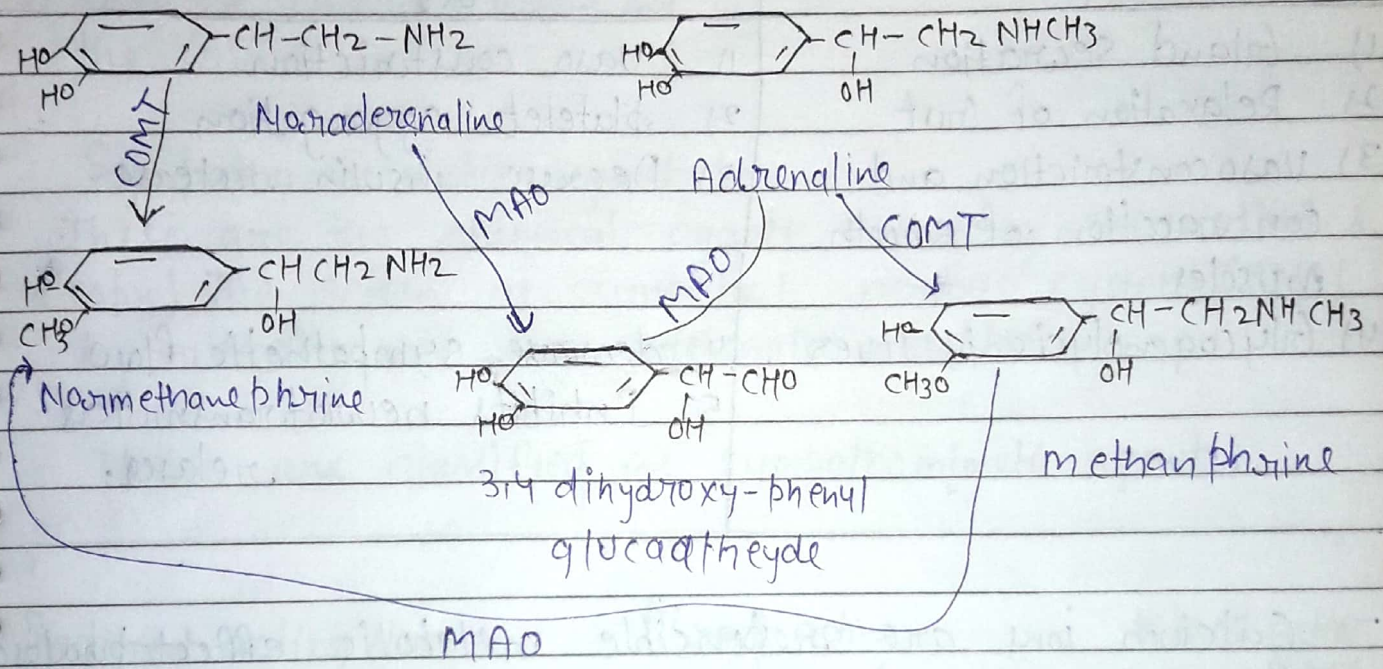
a) Monoamine oxidase (MAO)

b) Catechol O-methyl transferase (COMT)

→ Mono amine oxidase is present in both interact neurons and extra neurons.

→ There are two types of isoenzyme of monoamine oxidase are present in CNS and in peripheral tissue
→ COMT is a cytoplasmic enzyme and causes methylation of there hydroxyl group catchol ring of neurotransmitter with the help of isoenzyme and makes the neurotransmitters in active.

Catabolism can be summarised as :-



Adrenegic receptor :- Belongs to the class of ge-protein caupled receptor.
- These receptor blongs to a large family of cell membrane receptor. Which are liked to the carrier protein through the one or more GTP activated protein for producing responce.
- The adrenegic receptor are classified into two classes α and β receptor
- α receptor are mainly exitatory / activeness in nature.
- β receptor are inhibitory in nature.
- α receptor are categories into α_1 and α_2 receptor.

- α_1 receptor are present on post synatic sites of smoth muscles of blood vessels and gland cells
- α_2 receptors are present on pre and post synatic sites on the nerve terminal and in the CNS and Pachrac

Function of α_1 and α_2 receptors are as follows

α_1	α_2
1) Gland secration	1) Vaso constriction
2) Relaxation of Gut	2) Platelet aggregation
3) Vasoconstriction and contraction of smooth muscles	3) Decrese insulin release
4) Glycogenolysis in liver	4) decrease sympathetic flow
	5) Inhibits neurotransmitters relase.

- Calcium ions are responsible metabolic effect porodose by α reseptor α receptor stimulation result in increse in calcium ions up take by live cells and there is an increse transmembrane calcium ions fluxes in other tissue.
- β receptor are further some divided mto β_1 and β_2 receptor and β_3 receptor.
- β_1 receptor in present in cardiac tissue.
- β_2 receptor are present in smooth muscles and gland cells that is bronchi blood vessels, urthrus, liver, GIT, eyes.

→ β_3 present in adipose tissue and urinary bladder.

Function of B_1 and B_2 receptors are as follows:-

B_1	B_2
1) Increase force and rate contraction of heart mussels	1) Rexation of smooth mussels in the bronchi, uterac and arteries by supply skeletal mussule.
2) Dialates coronary blood vessels	2 linked with inhibit responnces
3) Rexatese smooth mussels in the GIT	

Sympatho mimetic agants:-
These are the chemical agants or drug which mimics (copy) the action of sympathoic nervous system (SNS) by reacting with the adrengic receptor.

These are classified as sympathomimetic agant

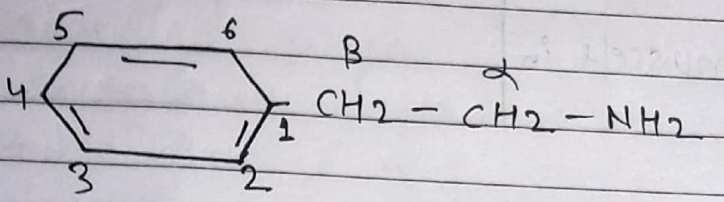
Indirect acting drug	Direct acting drug	Mixed action drug
• Hydroxyamphetamine	• Nor-epinephrine	• metarminol
• Pseudophedrine	• Epinepharine	• ephedrine
• Propyl hexedrine	• Dopamine	
	• Methyl Dopa	
	• turbutaline	
	• Salbutamol	

Structure activity relationship (SAR) of sympatho-mimetic agant

Sympathomimetic drug are considered derivative of β - phenyl ethyl amine.

Structurally substitution is possible on -

- An aromatic ring.
- Substitution on β carbon.
- Substitution on α carbon.
- Substitution on the amino group.

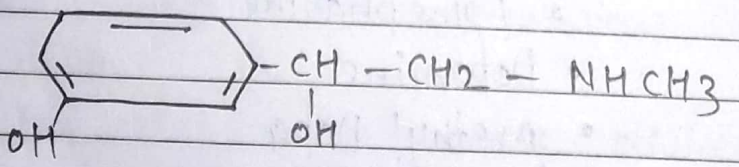


β - phenyl ethyl amine

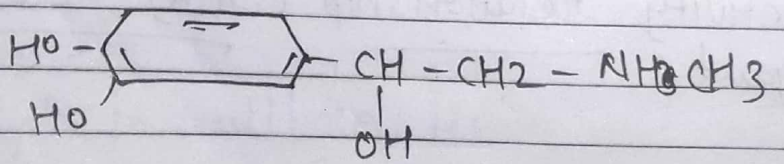
A) Substitution on the aromatic ring of β-phenyl-ethyl amine.

(i) The presence of OH group in the benzene ring at 3,4 positions gives maximum α and β activity.

→ If any of these OH group is absent the over all potency get decrease.



Phenylephrine
(less potent)

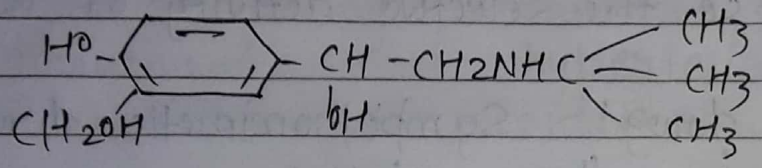


Adrenaline (more potent)

(ii) The presence of OH group at 3,5 position with substituents on the amino-nitrogen gives β_2 selective drug.

example :- orciprenaline, terbutaline relaxes bronchial muscles with out affect cardiac.

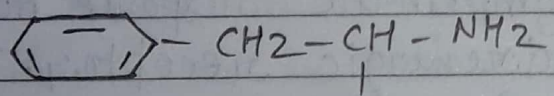
(iii) Drug having substitutents other then OH group have greater slectivity for aderegic receptor for ex:- salbutamol is β_2 selective receptor.



salbulamol (β_2 selective)

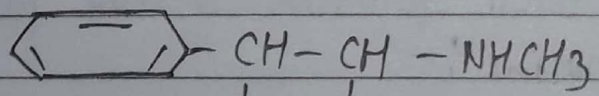
(iv) The unsubstits or Alkyl substituted adrenergic amino cross the blood, brain barrier and have more CNS Activity.

ex:- Amphetamine and ephidrine.

① 

Amphetamine

②



ephedrine

B) Substitution on the B- carbon
OH group on the B carbon use the central stimolate action of the drug.

C) Substitution on the α- carbon :-
Drug having substitution on the α carbon which blockes the metabolism of drug.

D) Substitution on the amino group :-
If the substitution on the amino group of any alkyl which use the selective activity of drug.

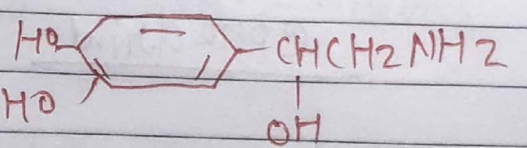
Sympathomimetic drug :- Sympathomimetic drug may be classified in three classes

- Direct acting drug
- Indirect action drug
- mixed action drug

1) Direct acting drug :- These agents produce a sympathatic responce by interacting direct with adrenergic receptor.
The action produced are of rabid & salt duration.
- The drug effect α and B both receptor
- Some drug of direct acting.

Nor- epinephrine :-

Structure :-



IUPAC Name :- 2 amino 3,4 dihydroxy phenyl 1 ethanol

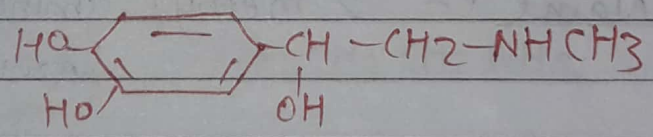
Machnism of action :- It is potent agonist at α receptor & has little or no effect on β receptor but has effect on B_1 receptor.
- It is less potent than adrenali.

Uses

→ It is used to reduce the absorption and to localised & effect of local anasthatic
→ It is given by intravenous infusion for the treatment of hypertesion.
- It has strong vasoconstraction properly.

Ebinephrine :-

Structure :-



IUPAC Name :- 3,4 dihydroxy phenyl 2 methyl amino 1 ethanol

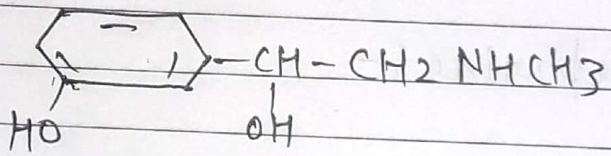
Machnism of action :- It is a direct acting drug
- It intract directly with α or B_1 and B_2 receptor
- It is highly potent among with all the directly drug.
- It isintctive when given by mouth as it under goes enzymatic degadation & first pass metabolism in liver

Uses

→ It act subcutaniously to produce vaso contraction
- It is mainly used in the emergency treatment of shock in the cardiopolmonary diease.
- It relexas bronchil musscles & is used in treatment of asthma.
- It is gerenally added to local anasthatic to decrese diffusion & to limit absarption.
- It is also used as in the farm of spray in acute allergic Rhinitis

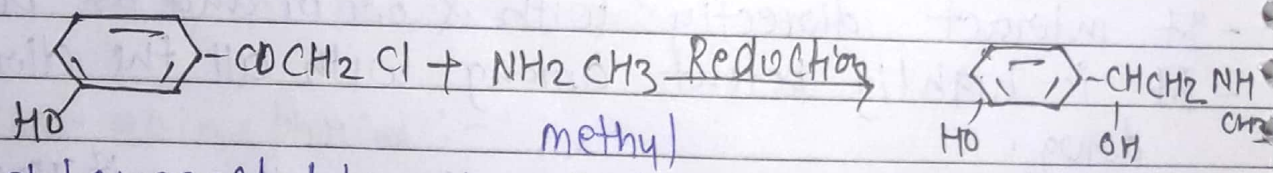
Phenylephrine

Structure



IUPAC Name :- 2 methyl amino 1ethanol 3 hydroxy phenyl

Synthesis :- It is a prepard by the reaction of meta choloro acetyl phenyl and methyl amine by the reduction of inter edite product formed.



m-chloroacetyl phenol | methyl amine | Phenylephrine

Machnism of action :- It is a selective α - agonist & has no action on the β - receptor activation of α_1 receptor causes vaso constraction of artioles & contraction of utraus.

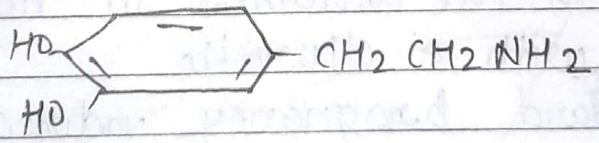
Uses

→ It is mainly used as a decongestant in a Rhinitis

- It is used as a pressor agent in the hypo- tensive circulatory failure or hypertensive
- Some time it is given in combination with local anasthatics to reduse their absorption.

Dopamine

Structure



IUPAC Name :- 4-(2 amino ethyl) benzene 1,2 diol

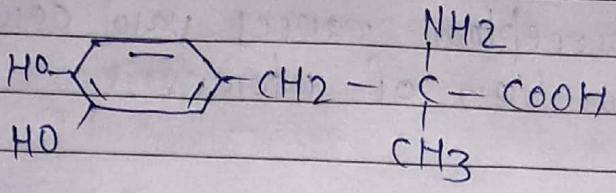
Machnism of action :- It intreact directly β adrenegic receptor & indirectly on α - adrenegic receptor

Use

- Dopamine is used as the treatment of Shock.
- It is used in several CHF where it increase blood pressure & orine out flow.
- It is used intravenously in myocardiac infarction septic shock & cardiac surgery.

Methyl dopa

Structure :-



IUPAC name :- 3,4 dihydroxy 2 methyl analine 2 oic acid

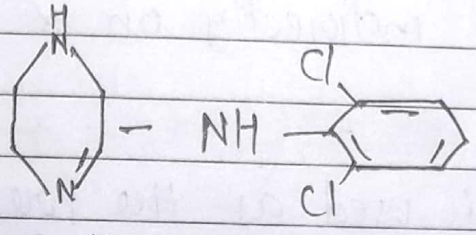
Machnism of action :- It is a competative inhibtor of enzyme dopa decarboxylase which result lower blood bressure & CNS effect like chxiety depression, methyl dopa is converted into α-methyl non-epinephrine by enzyme dopamine β-hydroxylase.

Use

- It is used in the treatment of hypertension in combination with a diuratic
- It is prefard bragnancy induced hypertension by given orally or intravenously.

Clonidine

Structure



IUPAC Name :- 2,6 dihydro phenyl amino 2-imidozoline.

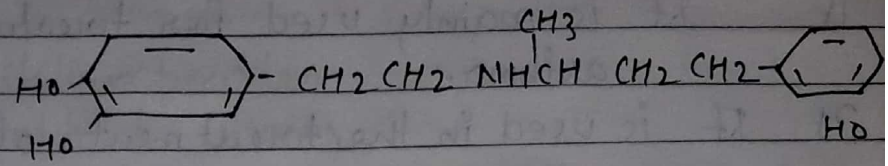
Machnism of action:- It is a centrally action α_2 receptor agonist & also imidazoline receptor agonist leading reduction in sympathatic out flow from CNS

Use

- Clonidine is given oor intravenously in treatment of all grades of hypertension
- It can be used in treatment of neurobsy chial onset in child hood.
- It may be used to associate system with long term used of alcohol nercotics, nicotine oor benzodi-zephines.

Dobutamine

Structure



IUPAC Name :- 4-hydroxy phenyl butan 2 amino ethyl benzene 1,2 diol

Machnism of action (MOA) :-

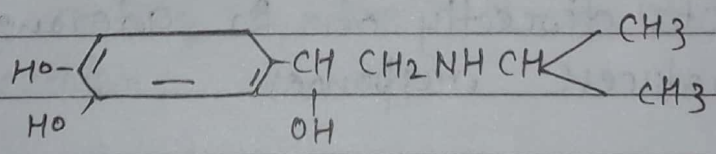
It directly stimulate B_1 receptor of (SNS) and α_1 receptor. It is dual acting drug.

Uses

→ In the treatment of CHF (congestive heart failure)
→ In the treatment of coronery artery dieases.

Isoproterenol (Isoprenaline)

Structure :-



IUPAC Name :- 3,4 dihydroxy phenyl 2 iso-propyl amino ethanol.

Machnism of action (MOA) :-

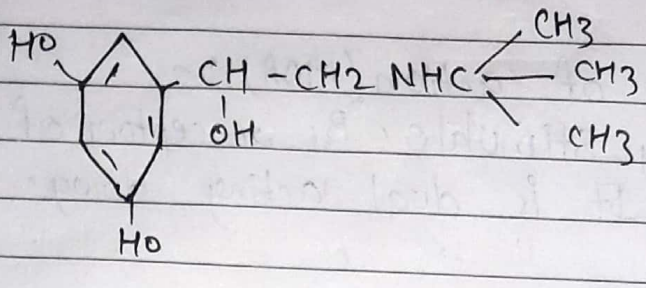
It acts on both B_1 and B_2 receptors on stimulating B_1 receptor increse cardiac out put and on stimulating of B_2 receptor increse Broncho dilation.

Uses

1) It is mainly used for treatment of bronchilal asthma.
2) It is used in the treatment of brady cardia.

Terbutaline

Structure



IUPAC Name :- 2 butyl amino 3,5 dihydroxi phenyl ethanol

Machnism of action :-

- It is selective to B_2 agonist
- It is much more affective than iso-prenyline.
- It acts directly on B_2 aderenqic receptor and broducers responces.

Properties

- It is a grey which ordorless, crystalline powder.
- It is freely soluble in water and also soluble in alcohol.

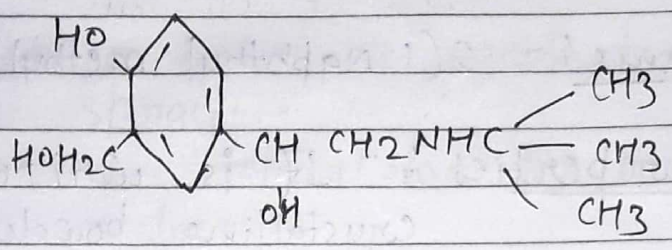
Uses

- When given only it is very affective as broncho dialater and is used in the treatment of asthma.
- It is also used as a arosol or inhasion.
- It is also used to arrest bre-matore lavour.

Salbutamol

- It is white crystalline powder
- It is slightly soluble in water
- It must be stored in a well close container and proceted from light.

Structure

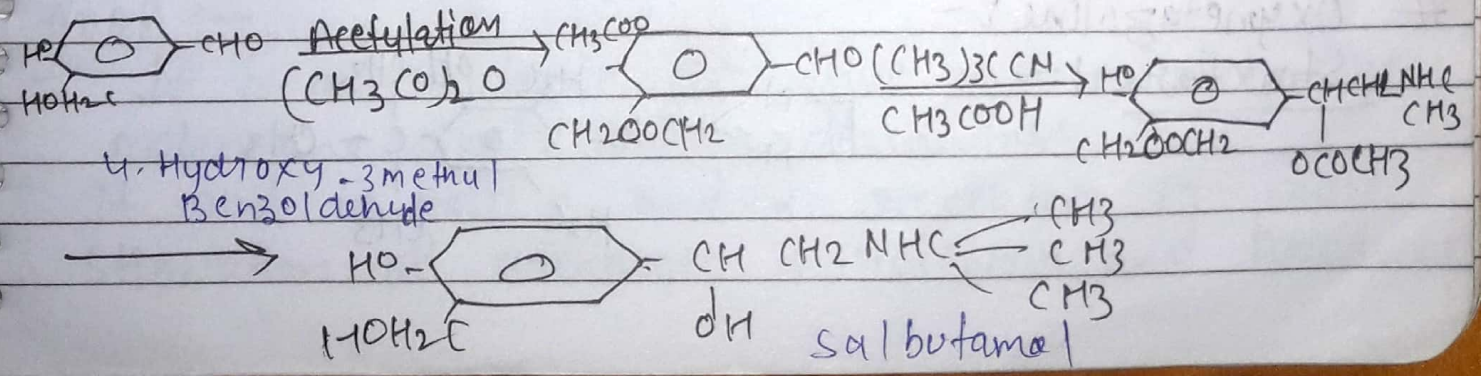


IUPAC Name:- 2 butyl amino 3,4 dihydroxy methyl phenyl ethanol.

Machnism of action:-
- It is a Strong B_2 adoreqic receptor B_2 agonist
- It is a directly acting symphotic drug having Strong action on B_2 receptor.

Synthesis

Salbutamol is prepard from 4-hydroxy 3-Hydroxy methyl benzul dehyde which is aceiyted in either with butyl synigite with acetic acid.

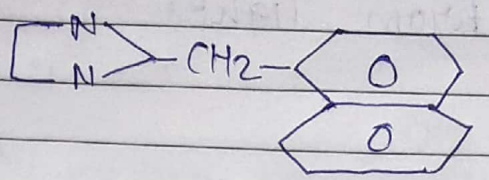


Uses

- It is used in the treatment of asthma.
- It is also used to arrest pre-mature labour.

Naphozoline

Structure :-



IUPAC Name :- 2(1 Naphthyl methyl) 2- imidazoline

Physical properties :- It is white or almost white crystalline powder.

It is freely soluble in water and must be stored in wall closed container protected from lite.

It is derivatives of imidazoline.

MOA :- It is a Pure full receptor stimulate but it is different from most of the other mimpato-mymetic amines as it diperance inspite of stimulating CNS

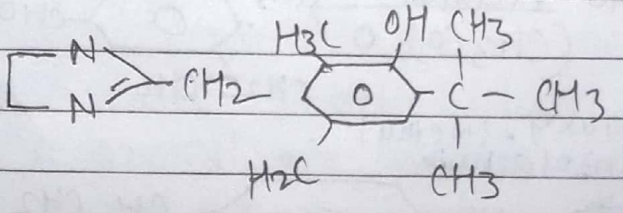
- It is a parical agonist of α_1 and α_2 receptor.

Use :- It is a vaso constrictor.

- It helps in reducing swalling and congestive on application to mucus membrane
- It is helps in the relife on rhinitis.

Oxymetazoline :-

Structure :-



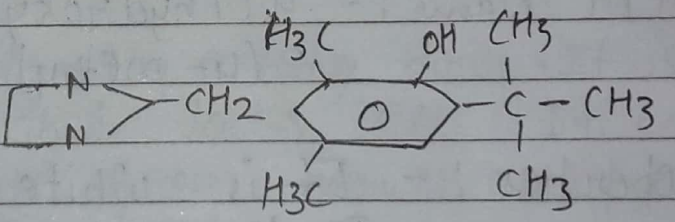
IUPAC Name :- 3-(4-5 dihydro 1-imididazole 2-yl) methyl 6(1,1 dimethyl ethyl) 2,4 dimethyl phenol

Properties :- It is a white crystalline powder
Freely soluble in water.

MOA :- It is a partical agonist at both α_2 selected agonist at α_1 receptor.

Use :-
- It is used as a topical decongestant in the form of Nasal spray.
- It is also used topical for the treatment of facial redness.
- It is used to treat nose bleading and redness of eye due to erotation.

Xylomelazoline :-
Structure :-



IUPAC Name :- 4 tertiary butyl 2.6 Dimethyle Benzyle 2 imidazolene.

Properties :- It is a white crystalline powder.
Soluble in water
- It should be stored in closed container protected from lite.

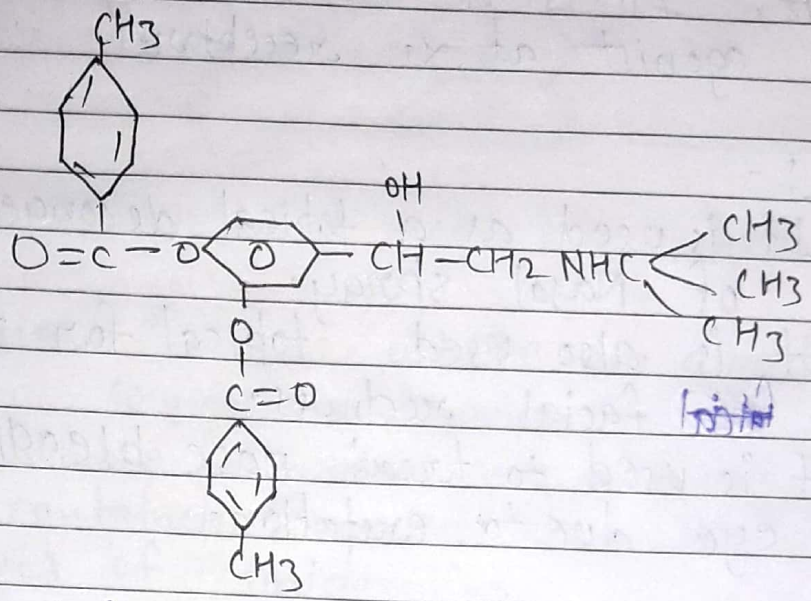
MOA :-
- It is an imidazole derivative and mimich the moleculame shape of aderenaline.
- It bind to both α_1 and α_2 receptor it cause stimulation of adienergic α receptor and produces

Conc of large in the nose.

Use :- It is used to treat symptoms of nasal congestion allargic.

- It solution has been used in the treatment of eye disorder.

* Bitolterol



IUPAC Name :- 4 (1 hydroxy - 2 - tertiary butyamino - 2 (4 - methyl benzoxyl) oxy - Phenyl) 4-methyl benzoate.

Properties :- It is white crystalline powder.
It is very soluble in water.

MOA :- It is a short action B_2 adeneregic receptor agonist

- It is direct acting sympathominatic many action of B_2 receptors.

Use :- It is broncolation and is used to treat asthma

- It is used to treat broncospasm associated with COPD (Chronic obstructive pulmonary dieases)

Indirect Acting drug :-

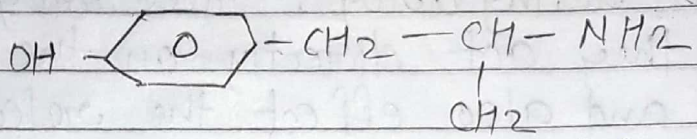
These drug produce there effect mainly by releasing noradrenaline from storage site in the sympathatic nerve to the effector organs

- The responce produce by these drug are similar to that of non adrenegic but have slower onset and longer diration of action.

Some of the drug which are indirectly acting are-

1) Hydroxy amphetamine

Structure



IUPAC Name :- 4-hydroxy α-methyl phenethylamine

Properties :- White crystalline powder.
Freely soluble in water.

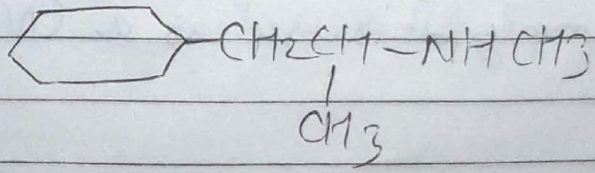
MOA :- It is an indirectly acting drug. It is a derivatives of that lacks CNS. It cause relexs of nor-aderenegic from nerves synapes and cause dilation of eye pupil.

Use :- It is used as an eye drops to dilate the eye pupil.

- It is used as a dignostic agent for testing damage of nerves of eye.
- It is used helps in indireating whether in eye is based on people responce or not

2) Propyl hexeridine :-

Structure

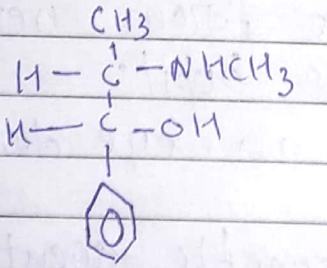


IUPAC Name :- 1 cyclo - hexyl - N- methyl propane - 2 - amine
MOA :- It is an indirect acting drug it's reverses the transporter from Dopamine storage and serotonin which leads to released of monoamine presynaptic vesicle which in term increase there.
Use :- It has sympathomimatic adrenergic vaso constriction and cycostimulant effect.
- It is used medicinal for relife of congestion due to allergies and renities.

mixed acting drug :- These drug as the name indicate they act directly on the both adrenergic receptor and also effect the release of nor-adrenergic. These drug acts both as directly and indirectly acting. Mixed acting drug are as follows.

Ephedrine :- It accures naturally ephedra and stimulate both α and β receptor that is acts both directly and indirectly.

Structure ⇒



IUPAC name → 2 methyl amino - 1 phenyl propane 1 ol.

MOA ⇒ It has α & β adrenergic activity It has high stimulating effect and the central nervous system. It has direct & indirect effect on adrenergic recep

Properties → white or colorless powder
→ Soluble in water.
→ Stored in well closed container
→ protected from light

Use → It is used as control bronchyl spasm in ashtma.
It is given orally It is used as a CNS stimulants.

Adrenergic Blocks

These are the drugs which blocks the effect of procedured by sympathominatic drug.
These are classified on the basis of their site of action

1) Alpha(α) adrenergic blockers
2) Beta (β) " "

1) Alpha (α) adrenegic blockers:-
These drug antagonises the effects proceduse by the drug acting on α receptors.

Alpha adrenegic drugs :-

- Non equilibrium type
  - β-halo alkyl amine
  - Phenoxy benzamine
- equilibrium type
  - Non selective
    - Ergot Alkaloids
      - Ergotamine
      - Ergotoxine
    - imidazoline
      - Phentolamine
    - Hydrogonated ergot Alkaloids
      - Dyhydro ergotamine
    - Miscellaneous
      - chlorpromazine
  - α_1-selective
    - Prazosin
    - Doxazosin
    - Alfuzosin
  - α_2 selectiv
    - Yohimbine

ISA → (Intrinsin sympathomimetic activity)

2) **β - adrenegic Blockers** :- These drug inhibits the actions of catholamine at the β - adrenegic receptors competetively

β - adrenegic drug

- Non selective ($B_1 + B_2$)
  - without ISA
    - Propranolol
    - Sotalol
    - Timolol
  - with ISA
    - Pindolol
  - with α-blocking property
    - labetalol
    - Carvedilol
- cardio selective
  - Metoprolol
  - Atenolol
  - Esmolol
  - Celiprolol

Generation wise classification

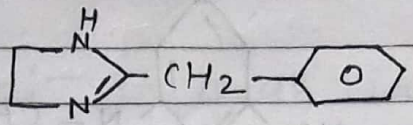
β - aderenegic Blocking

1) First generation
   * Non selective
   - Propranolol
   - Timolol
   - Sotalol
   - Pindolol
2) second gerenation
   * B_1 - or cardio selective
   - Metoprolol
   - Atenolol
   - Acebutolol
   - Bisoprolol
   - Esmolol
3) Third gerengretto
   * α - blocking
   - Labetalol
   - Carvedilol
   - celiprolol
   - Nebivolol
   - Betaxolol

α - adrenegic blockers

Tolazoline

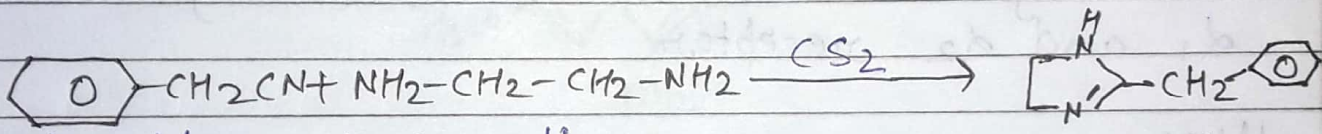
Structure



IUPAC Name :- 4,5 hydro 2-Phenyl methyl Imidazole

Properties :-
- White crystalline powder.
- Freely soluble in water.

Synthesis :- It is prepard by the reaction of Benzyl cyanide and ethylene diamine in the presence of carbondy sulphite (CS_2) it form tolazoline



Benzyl cyanide ethylene diamine Tolazoline

(MOA) :-
- It is a competative inhibitor of α receptor
- It's structure is similar to that of α-agonist
- It bind reversible with the α-receptor and blocks the effect of α-receptor's

Uses

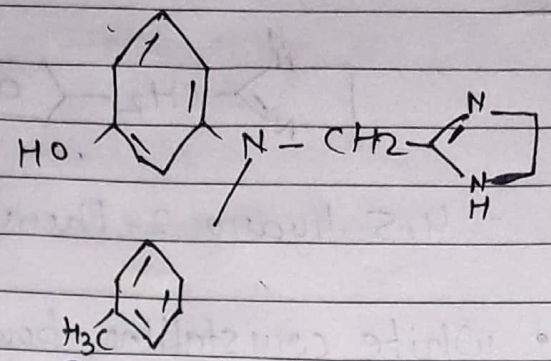
→ It is used in pulmonary, hyper tension

→ It has hastamine like effect and causes stimulation of gastric acid secration.

→ It is mainly used as vasodilator with direct vaso-dilatory action.

Phentolamine

Structure



IUPAC Name :- 3[2-Imidizoline-2methyl) 4-Toludino] Phenol

Properties :- It is a crystalline powder.
Freely soluble in water.

Machnism of action :- It is a competative α adenergic antagonist and has similar affinity for both α_1 and α_2 receptors

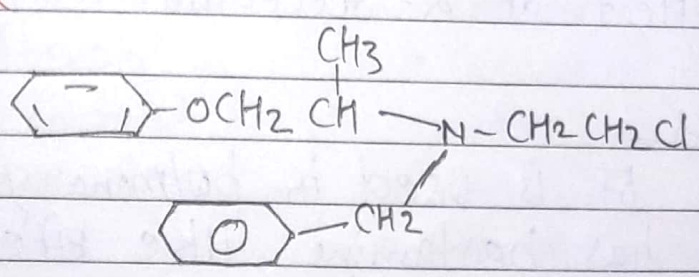
Uses

- It is used to control hypertensive condition in patient
- It is also used as a vaso dilatory as it inhibit vaso contractions

-

Phenoxy benzamine

Structure



IUPAC Name :- Benzyl 2-chloro ethyl 1 methyl 2-Phenoxy ethyl amine.

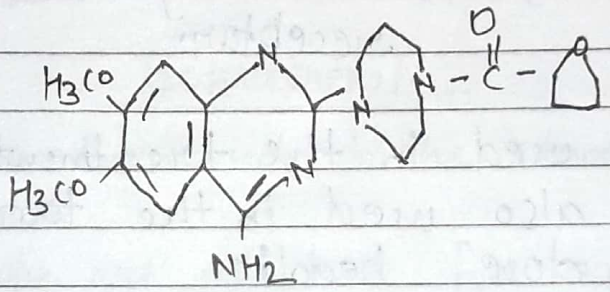
Properties — colourless crystalline compound
Soluble in alcohol, water & chloroform.

Machnism of action :- It is an irreversible α blockers and blocks both α_1 and α_2 receptor

Use :-
- It is used in the treatment of hypertension
- It is also used in the treatment of urinary retainsion.
- It is used as the treatment of peripheral vascular diseases

Prazosin

Structure :-



IUPAC Name :- 2(4-2 Furol] Piperazine-1-ethul]-6-7-dimethoxy quinazoline - 4 ylmine.

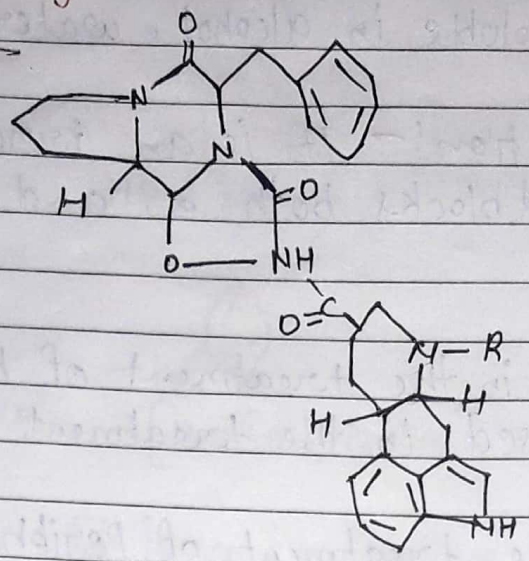
Properties :- Almost crystalline powder
Soluble in water

MOA :- It is an irreversible α blockers and blocks both α_1 and α_2 receptor

Uses :-
- It is used in the managment of hypertension
- " " " " " treatment of heart failure.

Dihydro - ergotamine :-

Structure



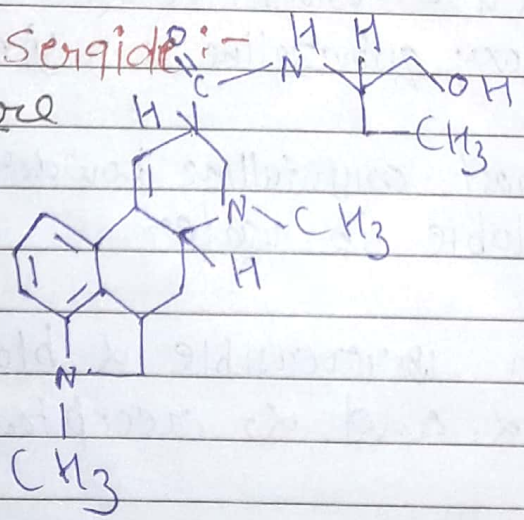
MOA :- It is an antagonist of α - adrenegic receptor.

Uses :-

- It is used in the treatment of migrane वेदेरा
- It is also used in the treatment of medication over dose headic
- It is used as vaso constraction.

Methyl Sergide :-

Structure



MOA :- It is an antagonist of α -adrenergic receptor
It is a potent secrotoxin antagonist

Use :- It is treatment of severa migrain.

SAR of β - Blockers :-

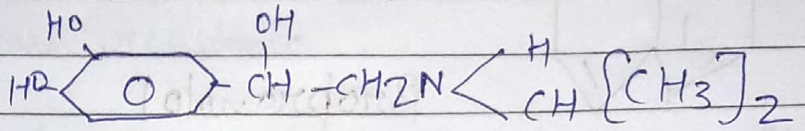
β - Blockers are classified according to structure into two classes

1) Aryl ethanol amine
2) Aryl oxy propanolamine :-

1) SAR of aryl ethanol amine :- Basic drug in this catagories

isoproterenol

Structure :-



isoproterenol

Various modifications have been made to the structure of isoproterenol these are

i) Phenoline OH groups are important for agonist activity Replacement of 4-OH group by other groups leads to removal of agonist activity and will make the compound antagonist.

ii) The two carbon site chain is required for the activity of compound.
It can not be decrese or increse that is two carbon chain must be there is should not be less than and more than two

iii) Phenyl ethyl, hydroxy groups when added to maintain the nitrogen these are responsible for β - blocker activity

iv) Cyclic alkyl substitution provide better p' cological activity than open chain substituents at nitrogen atom of amine.

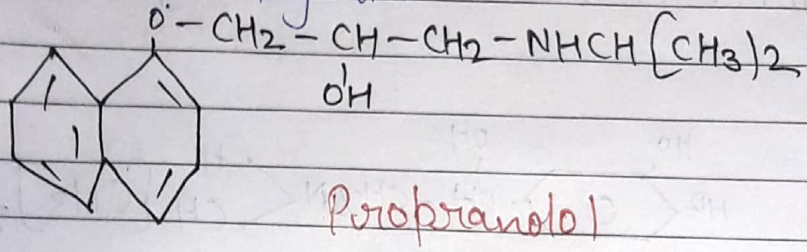
(v) Alpha (α) methyl substition decrese the activity.

(vi) Para -OH group on the phenyl ring can be replaced by methyl sulphonamide to increse the activity
CH_3SO_2NH

SAR of:-

(ii) Aryloxypropanolamine:-

The drug in this catagries is propanolol which is a potent β - antagonist



Propranolol

- Various modification have been made to under the activity of aryloxypropanol amine
- These are as follows

(i) The OCH_2 group is placed b/w the aromatic ring and the ethanol amino side chain which is assicial for the activity of compound

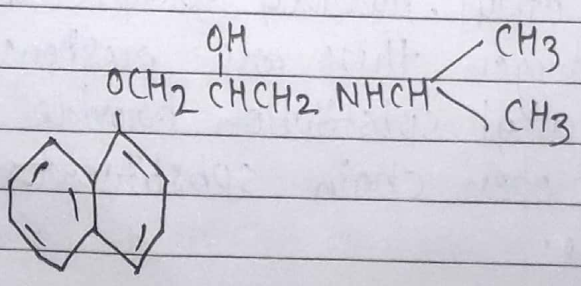
(ii) Most of the derivatives have substituted phenyl ring in place of napthaline ring.

(iii) Substitution of CH_3, OCH_3, NO_2 groups on the phenyl ring which leads the biological activity

Some of the β- Blockers are -

Propranolol :-

Structure :-



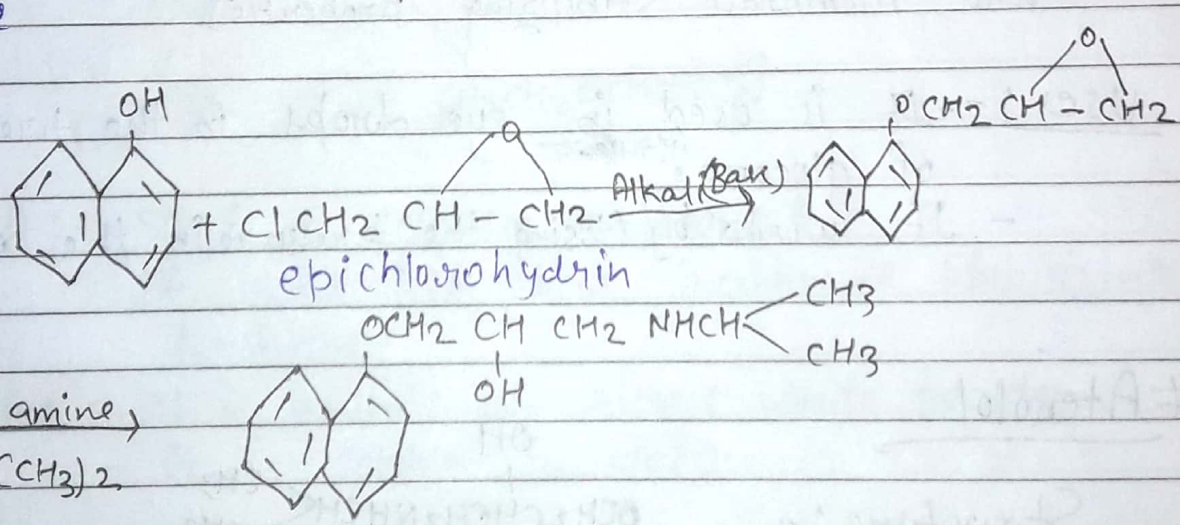
cardiac arrythmia → innregolar heart beat

IUPAC :- 1- Isopropyl amino 3 naphthoxy propan 2-ol

Properties :- It is a white or allmost white powder
It is soluble in water

Machnism of action :- It is a non cardio selective β - adrenergic Blocker. It has some membrane stabilizing property
It's machinsm of action may be due to —
(i) Decrese Resin Releas
(ii) Reduced cardiac outpot
(iii) Decrese Paripheral resistance

Synthesis :- It is prepard by treating α naphthol with epicholorohydrin in the presence of alkyl the intermediate formed is then treated with isopropyl amine



Isopropyl amine,
$NH_2CH(CH_3)_2$

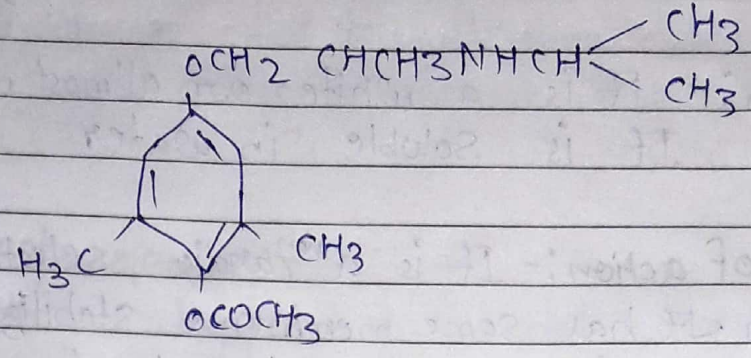
Propranolol

Uses :-
- In the treatment of hypertension.
- In the treatment of myocardial infraction.
- It is used in the treatment of cardiac arrythmia.

glucoma — मोतियाबिन्द

Metipranolol :-

Structure :-



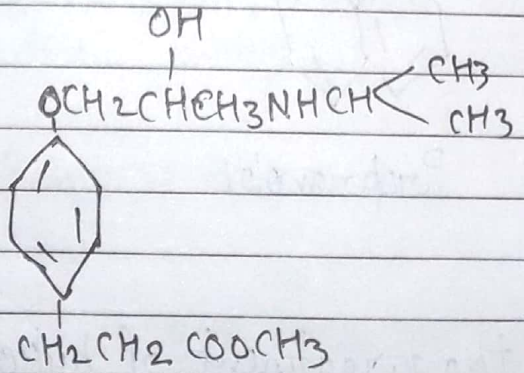
Properties - It is a white or almost white powder
- It is a soluble in water.

MOA :- It is a non cardio selective β - Blocker
It inhibit ISA (Intrinsic Sympathomimetic activity and membrane stibilizing properties

Uses :- It is used in eye drops in the treatment of glucoma (मोतियाबिन्द)
- It works by (↓)sing the pressure in the eye

Atenolol

Structure :-

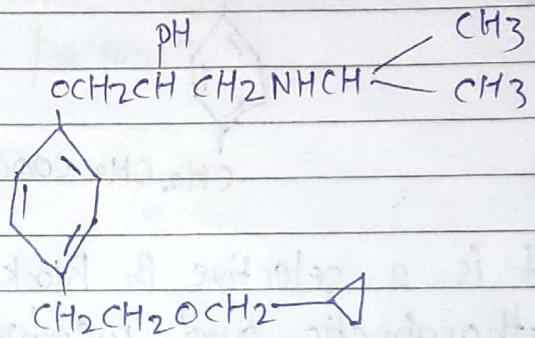


Properties :- White or almost white powder
- Soluble in wate

Machnism of action :- It is β_1 selective antagonist
It lacks ISA and membrane stabilizing properties

Uses :-
- It is used in the mangment of hypertension and anging pactaroise
- It is also used in the emergancy treatment of cardiac arrgelma
- It is used in the treatment of high blood pressure and help in prevent heart attack and kidney problems.

Betaxolol :-
Structure :-

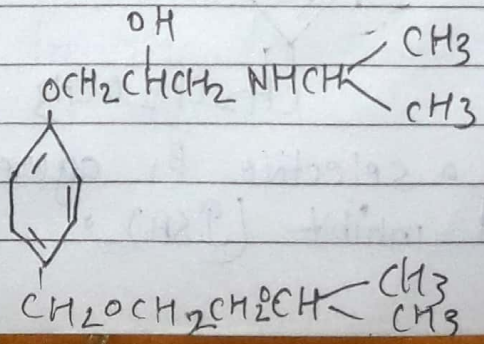


MOA :- It is β_1 selective antagonist
It lacks ISA and membrane stabilizing problems.

Properties :- - It is a white or almost white powder.
- It is soluble in water.

Uses :- Treatment of hypertension
- Eye drops in the management of glaucama.

Isoprolol
Structure :-

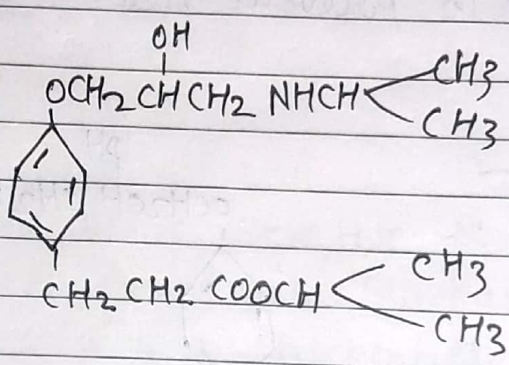


MOA It is β_1 selective antagonist. It is lacks ISA and membrane stabilizing problems.

Uses :- It is useful in treatment of high blood pressure
- Reduced the Activity of heart muscle.
- In the treatment of coronary artery diease.

Esmolol :-

Structure :-

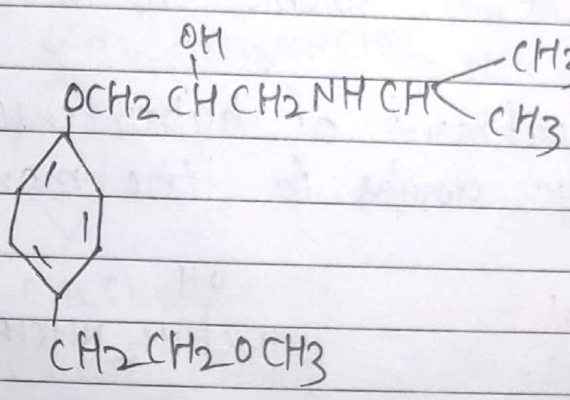


MOA :- It is a selective β_1 Blocker and lacks Intrinsic sympathomimetic and membrane stabilizing activity.

Uses :- In the treatment of soperventricular tachycardia.
- In the treatment of high blood pressure.
- In the treatment of myocardial Infaraction.

Metaprolol :-

Structure :-



MOA :- It is a selective β_1 adrenergic antagonist and inhibit (ISA).

- It has small or no membrane stabilizing activity.

Properties :-

- It is a white, crystalline powder or colourless crystals
- It is very soluble in water

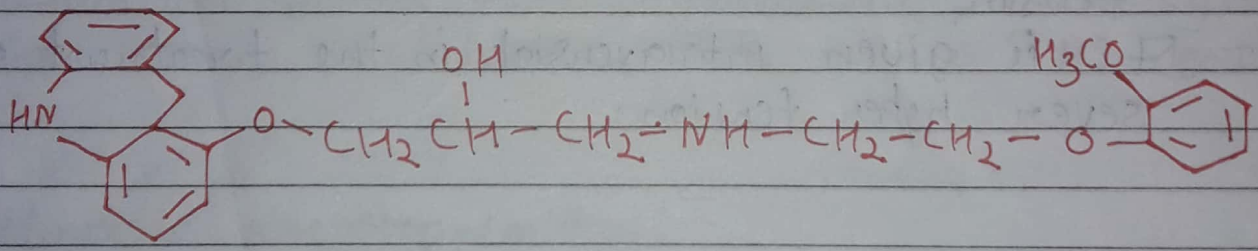
It is stored in well closed container & Proceted from light.

Use :-

- It is used orally in the treatment of hypertension
- It is also used in the managment of cardiac arrdhima & Angina pactaric

Carvedilol :-

Structure :-



MOA :- It is a non-selective β-Blocker It act on both α, and β Blocker.

Due to α, Blockage it relexes Blood vessel dilates tham and lowers blood pressure.

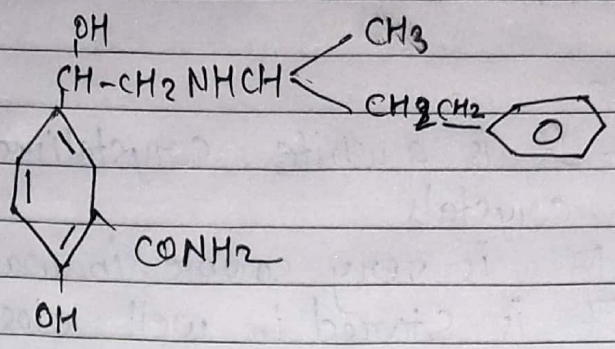
Uses :- It is useful in magament of CHF

It is useful in the treatment of hypertension.

and

Labetalol

Structure:-



MOA:- Labetalol is a non selective β Blocker and Act as a competative blocker on both α_1 and β Blocker

α_1 Blocker it use peripheral vascule resistance

Use:-

- It is given orally in the treatment of hyper-tension
- It is given intravensial in the treatment of sever hyper tension.