

ADRENERGIC BLOCKER


↳ Block the action of Sympathetic action by antagonising α & β receptor

I. α -blocker

(a) Non Selective -

- ↳ Phenoxybenzane - **irreversible**
- ↳ phentolamine
- ↳ Tolazoline
- ↳ Dihydro ergotamine
- ↳ Dihydro ergotoxine

(b) α_1 blocker - "zosin"

- BV ←
- ↳ Prazosin
 - ↳ Terazosin
 - ↳ Doxazosin
 - ↳ Tamsulosin
 - ↳ Alfuzosin
 - ↳ Silodosin
- bladder Trigen 
BPH

(c) α_2 blocker

- ↳ ~~Yohin~~ Yohimbine
- ↳ Rauwolfscine
- ↳ Gdazexon
- ↳ mianserin

II $\alpha\beta$ blocker - Labetalol, carvedilol - "CL" Central debrary "3rd generation"

III β blocker = "lol"

(a) Non Selective β blocker = "PRO Pim Tim"

- ↳ Propranolol
- ↳ Pindolol - ISA = First Generation
- ↳ Timolol

(b) β_1 (Cardio selective) blocker - New β -Blocker Acting **Exclusively** 3rd At Myo Cardium

- Nebivolol ^{3rd}
- celiprolol

- ISA
- Betaxolol
 - Bisoprolol
 - Acebutolol
 - Esmolol
 - Atenolol
 - metoprolol

(c) β_2 blocker - Butoxamine

- 2nd generation

ADRENERGIC ANTAGONIST (SYMPATHOLYTIC AGENTS)

The drugs which block the action of Adrenaline/Noradrenaline by antagonising adreno receptors (α and β receptors)

1. Alfa (α)-Blockers

Tolazoline, Phentolamine, Phenoxybenzamine, Dihydroergotamine
 Prazosin, Methylsergide (5HT_{2A} Antagonist)

2. Beta (β) Blockers \rightarrow SAR of β -blockers

Propranolol, Metoprolol, Atenolol, Betaxolol, Bisoprolol, Esmolol, Metoprolol, Labetolol, Carvedilol

Alfa Blockers

a) Non-Selective α blockers

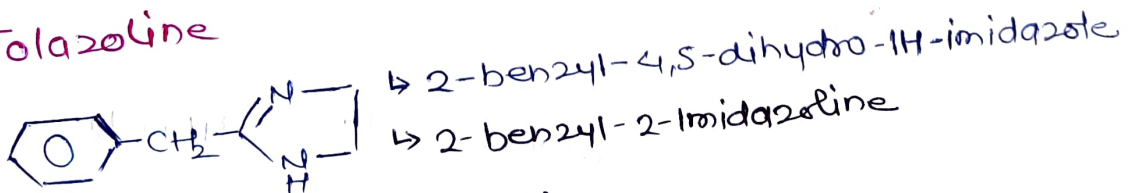
- # Haloalkylamine \rightarrow Phenoxybenzamine
- # Imidazolines \rightarrow Phentolamine, Tolazoline
- # Ergot derivative \rightarrow Dihydroergotamine

b) Selective α_1 blocker

- # ~~Quinazolinamines~~
- # Quinazolinamines - Prazosin, Terazosin

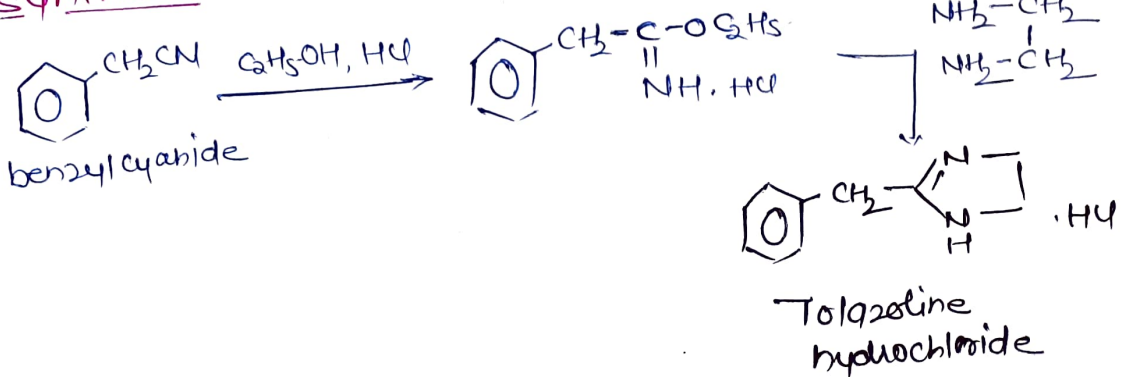
c) α_2 blockers - Yohimbine, Idazoxan

① Tolazoline



MOA: \rightarrow α_1 & α_2 receptor blocking

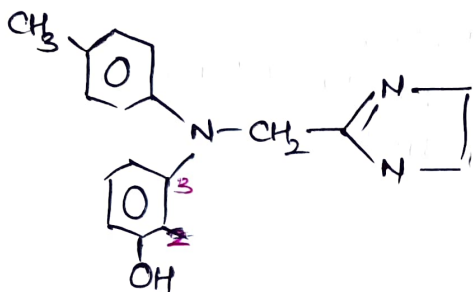
Synthesis



Uses of Tolazidine ; - Vasodilator

- # Persistent pulmonary hypertension in newborn
- # Raynaud's disease
- # Cerebral vascular accidents
- # Antihypertensive agents
- # It may reflex sympathomimetic action on heart

② Phentolamine



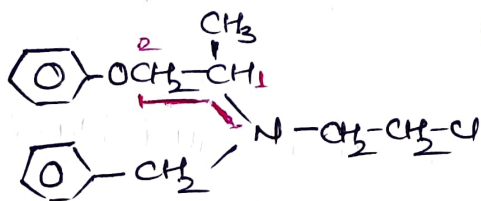
3 - [N-(2-imidazolin-2-yl methyl)
-p-toluidino] phenol

2 - [N-(4-methylphenyl)-N-(3-hydroxyphenyl)-amino
methyl]-imidazoline

MOA - α_1 & α_2 blocker, short duration

- USES -
- # To control hypertension in patient with Pheochromocytoma
 - # Also use intra-operative management of Pheochromocytoma
 - # Control hypertension due to clonidine with

③ Phenoxybenzamine



N-benzyl-N-(2-chloroethyl)-1-methyl
-2-phenoxy-ethylamine

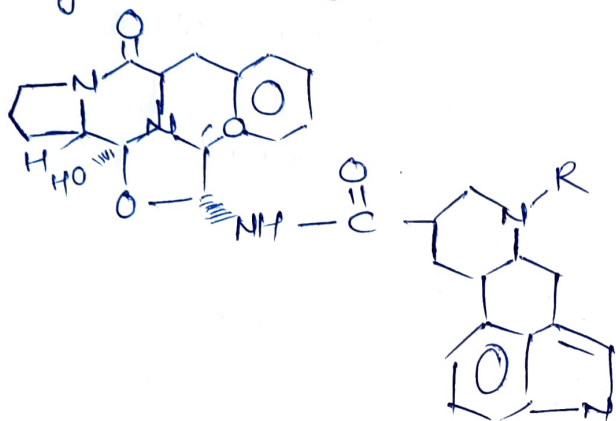
MOA - block the α_1 & α_2 receptor \rightarrow \downarrow TPR & \uparrow NorAd release

- USES -
- # treatment of pheochromocytoma
 - # Raynaud's syndrome
 - # ~~by~~ treatment of urinary retention

④ Dihydroergotamine

Hydrogenated are generally α_1 blocker

Natural alkaloid - Ergotamine & Ergotaxin - show partial agonist & antagonist of α receptors

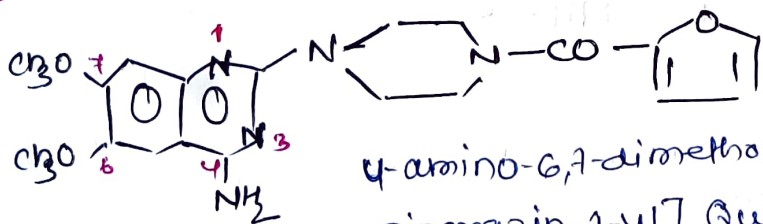


(5 α)-9,10-dihydro-12'-hydroxy-2'-methyl-5'-(phenyl/methyl)-ergotamine-3',6',8'-trione

MOA = block α receptor

Uses - # treatment of migraine & Headach
Combination with heparin in prophylaxis of post-operative deep vein thrombosis

⑤ Prazosin



4-amino-6,7-dimethoxy-2-[4-(2-furoyl)-piperazin-1-yl] Quinazoline

MOA - Selective α_1 blocker \rightarrow \downarrow TPR

Uses - # Antihypertensive agent

Raynaud's Syndrome

used as an adjuvant in the symptomatic treatment of urinary obstruction caused by prostatic hypertrophy

β-Blockers

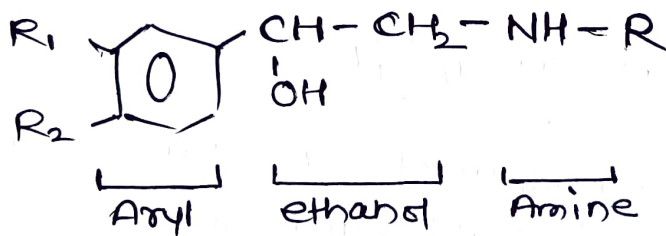
- Ⓐ Non Selective α & β blocker - Labetalol, Carvedilol
- Ⓑ Non-Selective β-blocker → Propranolol, pindolol
- Ⓒ Cardioselective β₁ blocker → Atenolol, Metoprolol, Esmolol, Bisoprolol
- Ⓓ β₂ blocker = Butoxamine

SAR OF β-Blockers

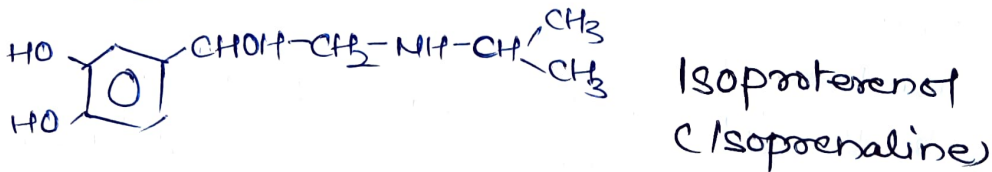
According to structure β-blockers classified into two classes

1. Arylethanamines - Sotalol, Labetalol
- * 2. Aryloxypropanamine - Propranolol, Atenolol, Metoprolol, Acebutalol, etc

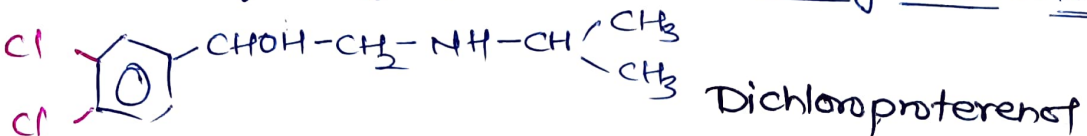
Arylethanamine



Substitution of -OH group at R₁ & R₂ with bulky alkyl group at NH-R show Agonist Activity

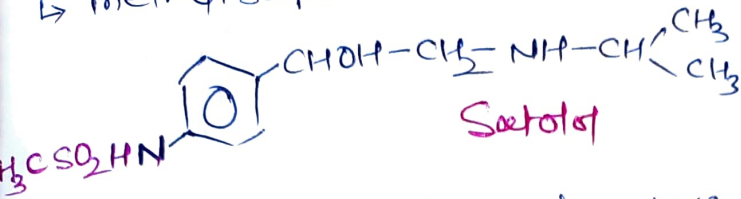


Substitution of -Cl group at R₁ & R₂ → Antagonistic Activity

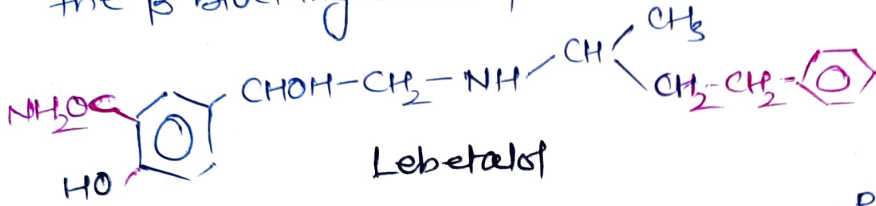


-OH group at benzene ring must for agonist replacing with other shows antagonistic action

Sulfonamide
 ↳ methyl sulfonamide at 4-position - enhance β blocking action



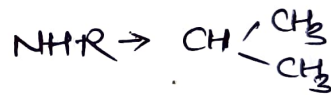
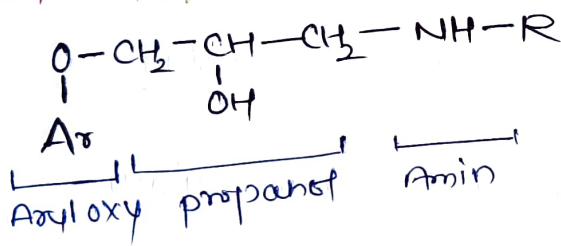
↳ Phenyl ethyl, hydroxyphenyl ethyl group added to 'N' maintain the β -blocking activity



↳ N,N-disubstitution - inactive $-N \begin{matrix} \diagup R \\ \diagdown R \end{matrix}$

↳ α -methyl substitution \rightarrow \downarrow Activity $-CH \begin{matrix} | \\ CH_3 \end{matrix} -NHR$

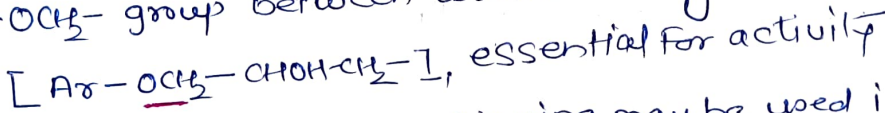
Aryloxypropranolamine



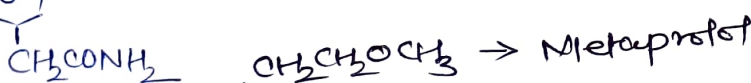
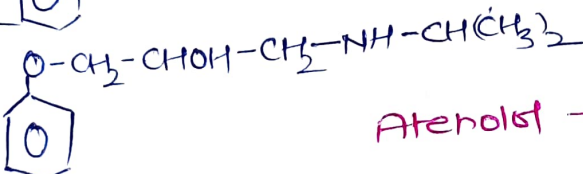
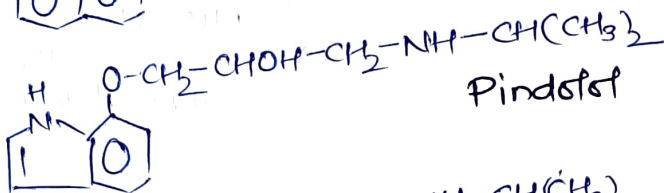
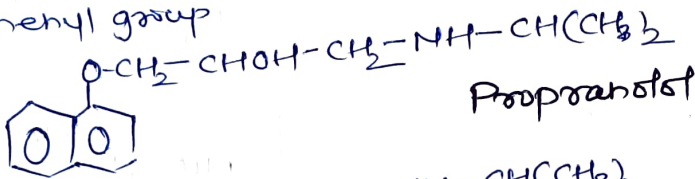
More potent than aryl ethanolamine

Various modifications may alter the overall activity these are as follow \rightarrow

$-OCH_2-$ group between aromatic ring & ethanolamine

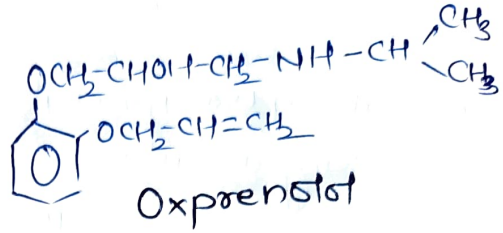
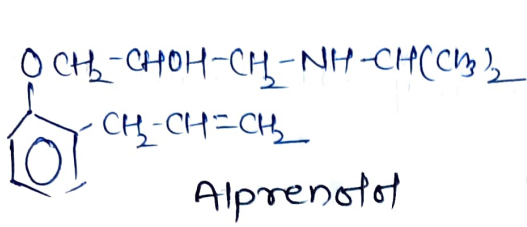


Different types of aromatic ring may be used in place of phenyl group

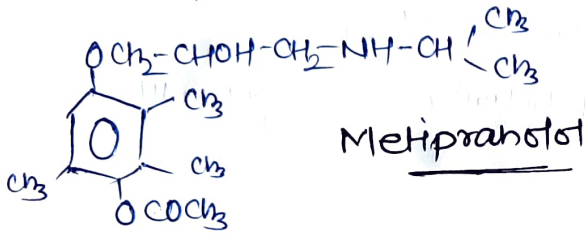


Non Selective β blocker

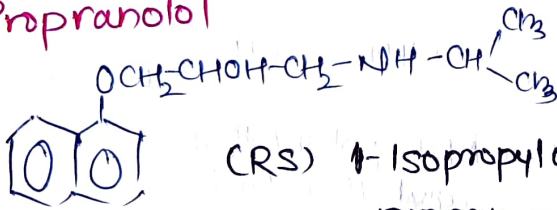
Alkenyl & alkenyloxy groups when present in ortho position on phenyl ring gives good β -antagonist activity



Substitution of $-CH_3$, $-OCH_3$, $-NO_2$ group on phenyl ring generally done at 2, & 3 position, at 4 position is less favoured.



1. Propranolol



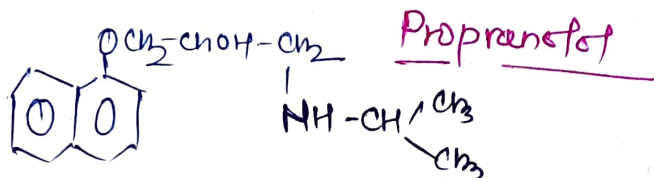
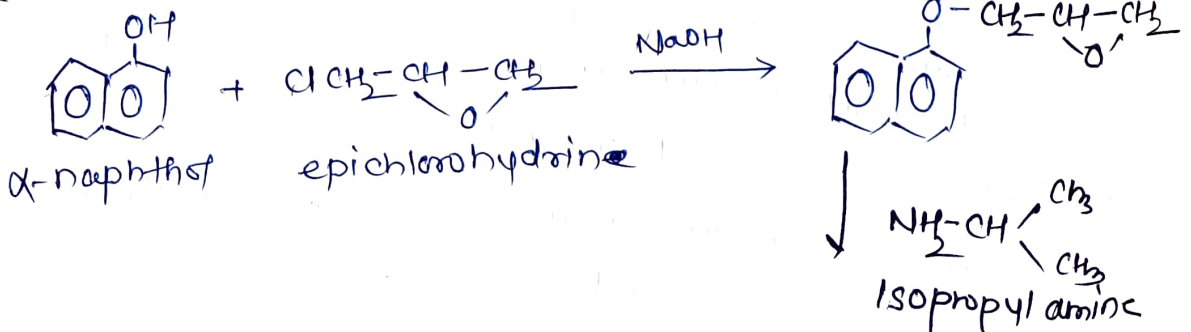
(-) form more potent

(RS) 1-Isopropylamino-3-(1-naphthylloxy)-propan-2-ol

MOA = blocking the β_1 & β_2 activity

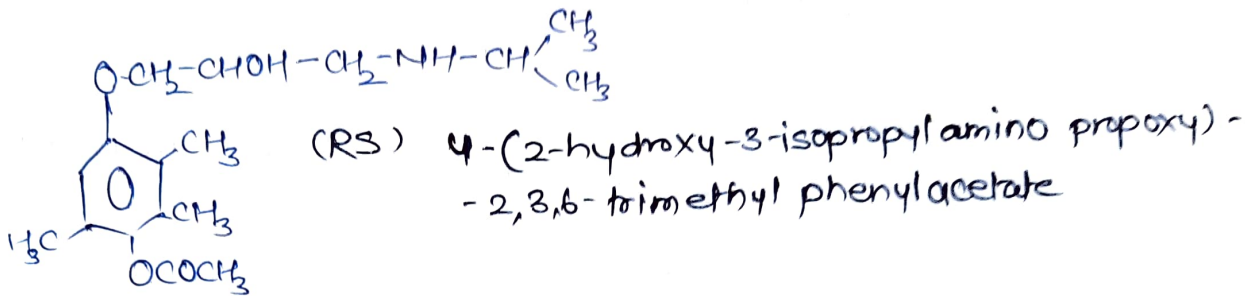
- ↳ ↓ Myocardial activity & O_2 demand, ↓ Renin release
- ↳ Also have mem. stabilizing property

Synthesis - from α -naphthol



- Uses - # Hypertension
 # Cardiac arrhythmia
 # Myocardial infarction

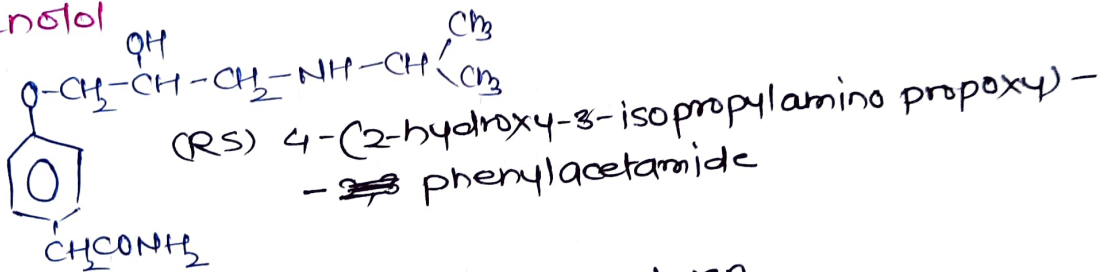
2. Metipranolol



MOA :> Non Selective β blocker without ISA
 → also has mem. stabilizing property

- Uses - # Eye drops in treatment of Glaucoma
 # ↓ IOP

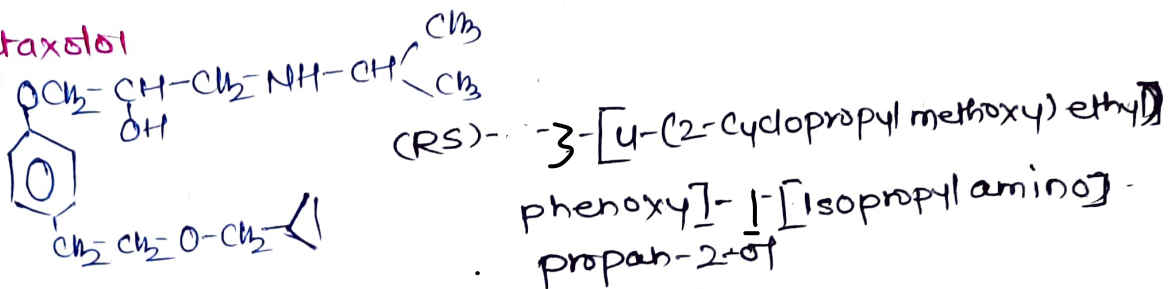
3. Atenolol



MOA = Selective β_1 blocker without ISA

- Uses = # Hypertension
 # Angina pectoris
 # Cardiac arrhythmia
 # management of symptoms of alcohol withdrawal.

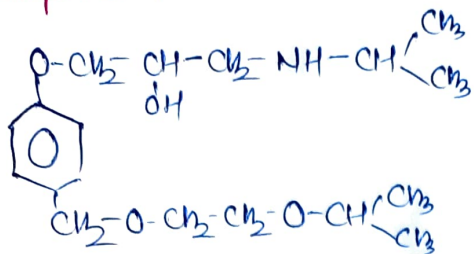
4. Betaxolol



MOA - Selective β_1 blocker without ISA

- Uses - # Hypertension # eyedrops in Glaucoma
 # Neuroprotector in glaucoma treatment

5. Bisoprolol



(RS)-3-[4-((2-isopropoxy ethoxy) methyl) phenoxy]-1-isopropyl amino-propan-2-ol

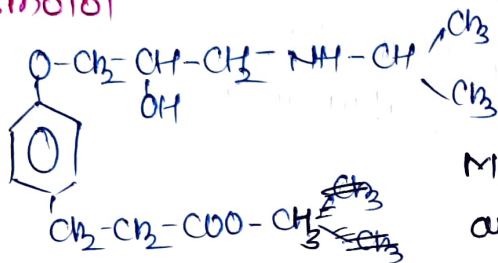
MOA - Selective β_1 blocker without ISA

Uses - # Hypertension

Management in Cardiac ischemia

used to treat coronary heart disease, arrhythmia, & myocardial infarction

6. Esmolol



Methyl-3-[4-(2-hydroxy-3-isopropyl amino) propoxy-phenyl] propionate

MOA = β_1 blocker without ISA

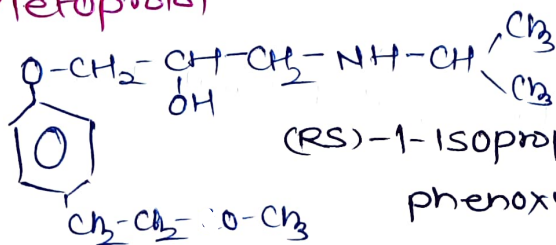
Uses - # used in Supraventricular tachycardia

Management of atrial fibrillation

Hypertension

early treatment of myocardial infarction

7. Metoprolol



(RS)-1-isopropylamino-3-[4-(2-methoxy ethyl) phenoxy]-propan-2-ol

MOA - β_1 blocker without ISA

Uses - # Hypertension

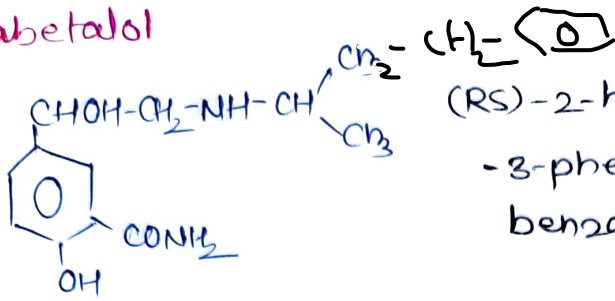
cardiac arrhythmia & Angina pectoris

early management of acute myocardial infarction

heart failure

used as an adjuvant in the treatment of hyperthyroidism

8. Labetalol

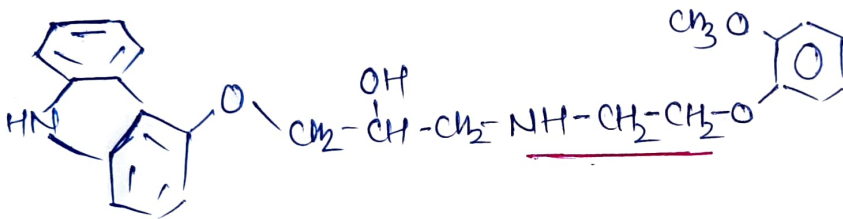


(RS)-2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenylpropylamino)ethyl]benzamide

MOA - Non selective - α_1 & β blocker, with ISA
 $\rightarrow \alpha_1$ blocking $\rightarrow \downarrow$ TPR

Use - # Hypertension
 # pregnancy-induced hypertension
 #

9. Carvedilol



N-[3-(9H-carbazol-4-yl-oxyl)-2-hydroxypropyl]-2-(2-methoxyphenoxy)ethylamine

MOA - α_1 & β -blocker

Uses - # management of CHF
 # Hypertension
 #

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