

# ANTI-ANGINALS

## ➤ **Definition:**

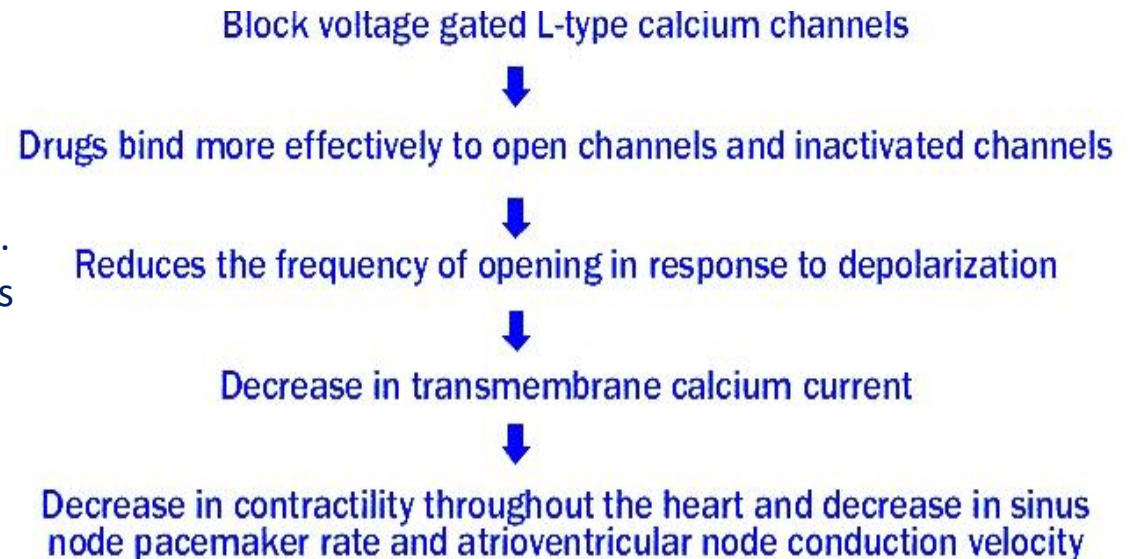
- Anti-anginal Drugs: A drug used in the treatment of angina pectoris.
- Angina pectoris:
  1. angina pectoris is a medical term for chest pain or discomfort to coronary heart disease. It occurs when the heart muscles don't get as much blood as it needs.
  2. This usually happens one or more of the hearts arteries is narrowed or blocked, also called ischemia.

## ➤ **Classification:**

### 1. Vasodilators:

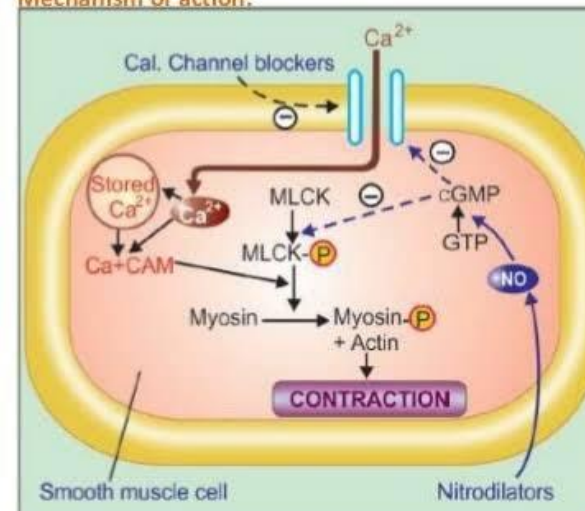
- **Organic nitrites:** amyl nitrites, Isosobridedinitrate, nitroglycerine
  - **Calcium channel blockers:** verapamil, nifedipine, amlodipine
  - **Potassium channel openers:** Nicorandil.
- ### 2. Beta adrenoreceptor:
- atenolol, metaprolol, nadolol, propranolol
- ### 3. Metabolic modifiers:
- Ranolazine, Trimetazidine

## ❖ **Mechanism of action**



## Nitrates/ Organic Nitrates

Mechanism of action:



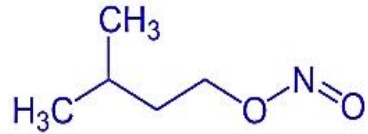
Mechanism of vascular smooth muscle relaxant action of nitrodilators like glyceryl trinitrate and calcium channel blockers

- (- - ->) Inhibition
- CAM—Calmodulin;
- NO—Nitric oxide
- MLCK—Myosin light chain kinase
- MLCK-P—Phosphorylated MLCK
- GTP—Guanosine triphosphate;
- cGMP—Cyclic guanosine monophosphate

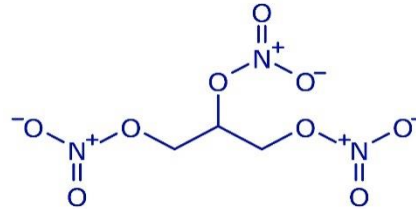
## ❖ Structures

### ➤ Vasodilators:

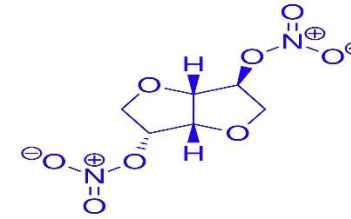
#### 1. Organic nitrites:



Amvl nitrite

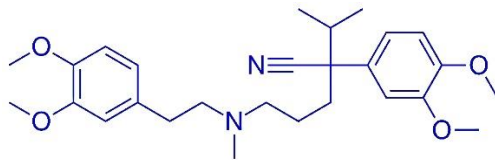


Nitro glycerin

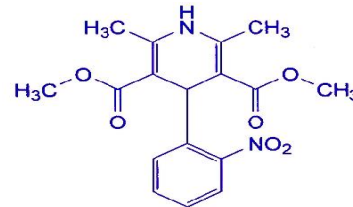


Isosobridedinitrate

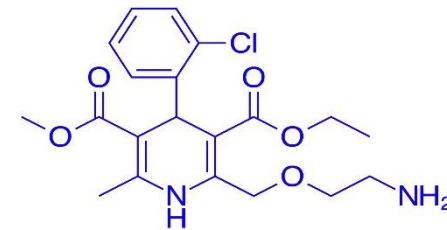
#### 2. Calcium channel blockers:



Verapamil

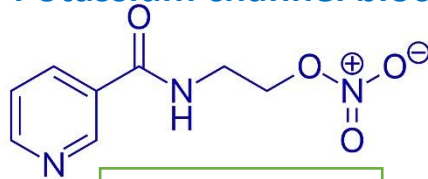


Nifedipine



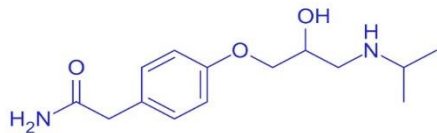
Amlodipine

#### 3. Potassium channel blockers:

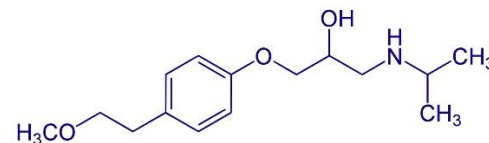


Nicorandil

### ➤ Beta adrenoreceptor



Atenolol



Metoprolol

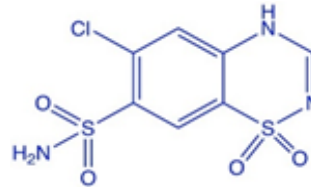
# DIURETICS

## Contents:

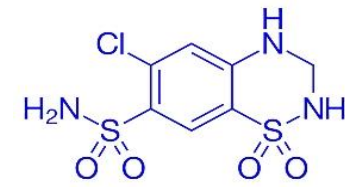
- Definition
  - Classification
  - Structures
  - SAR
  - Mechanism of action
1. **Definition:** A type of drug that causes the kidney to make more urine. Diuretics help the body get rid of extra fluid and salt.
  2. **Classification:**
    - Thiazides: Chlorothiazide, Hydrochlorothiazide, Hydro flumethiazide, Dichlorphenamide
    - Loop Diuretics: Furosemide, Bumetanide, Ethacrynic acid
    - Carbonic anhydrase inhibitors: Acetazolamide, Methazolamide, Dichlorphenamide.
    - Potassium sparing Diuretics: Spironolactone, Triamterene, Amiloride.
    - Osmotic Diuretics: Mannitol

## Structures:

### ➤ Thiazides:

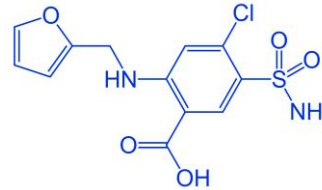


Chlorothiazide

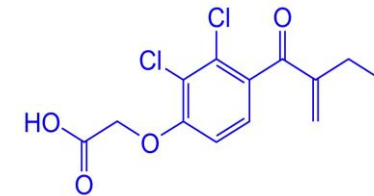


Hydrochlorothiazide

### ➤ Loop diuretics

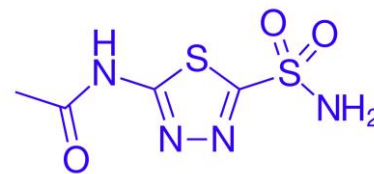


Furosemide

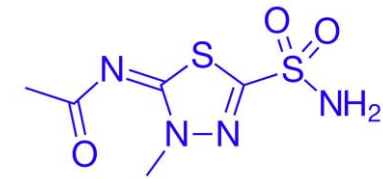


Ethacrynic acid

### ➤ Carbonic anhydrase inhibitor

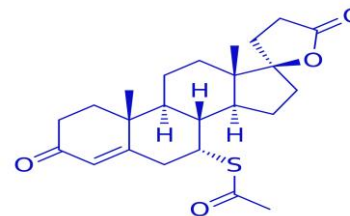


Acetazolamide



Methazolamide

### ➤ Potassium sparing diuretics

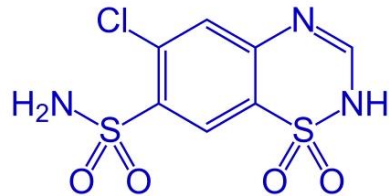


Spironolactone



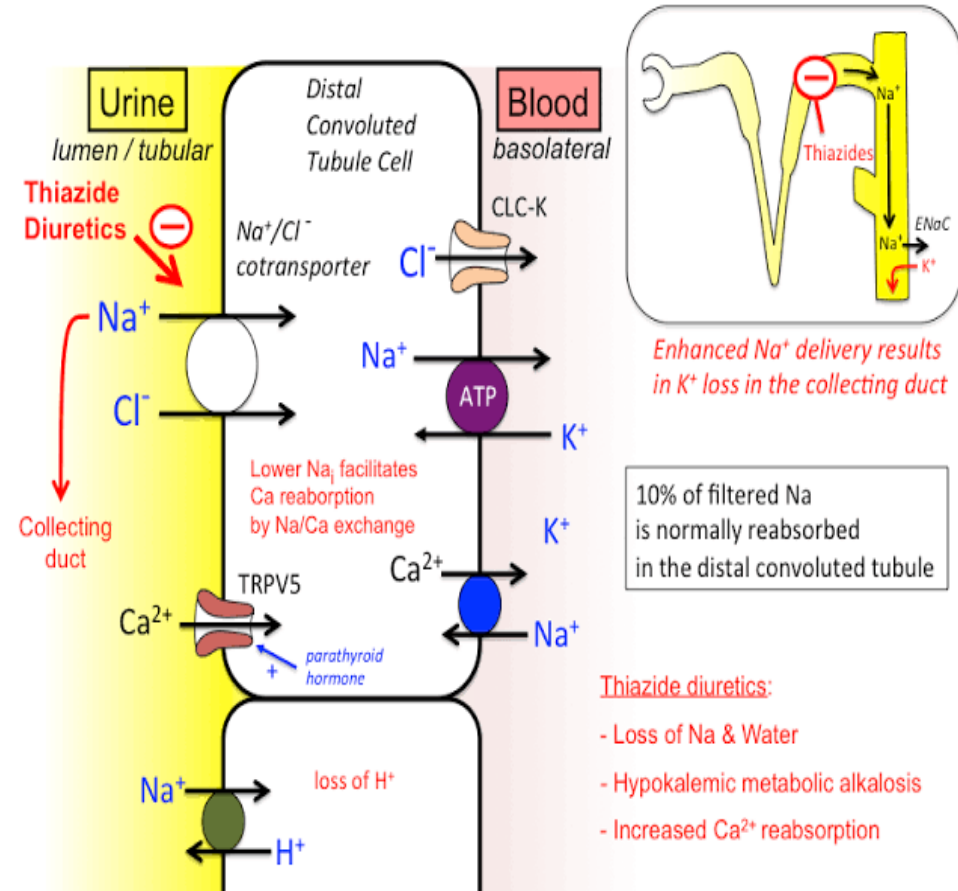
Amiloride

## ➤ SAR OF Thiazide



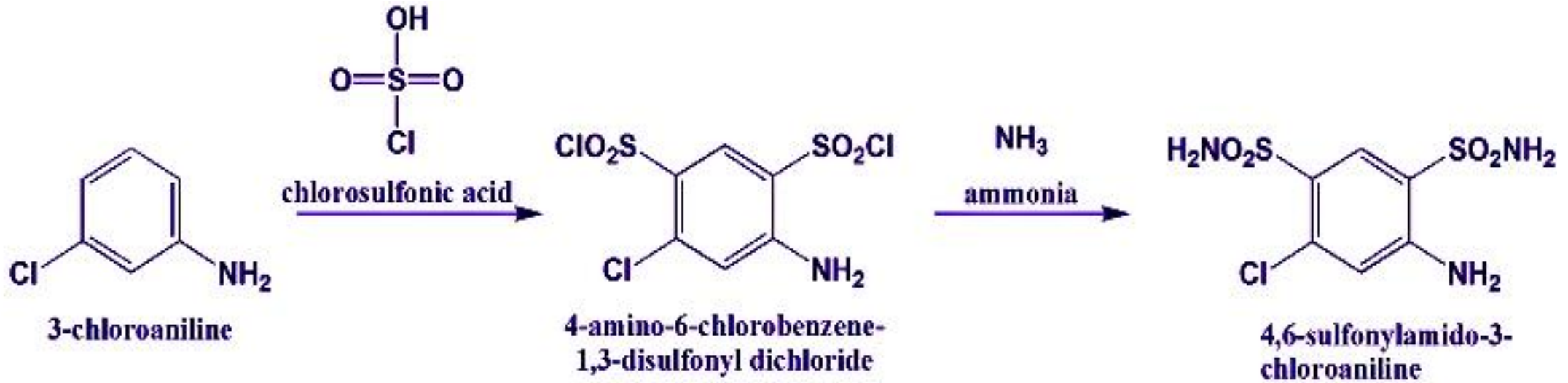
1. The 2 positions can tolerate small alkyl groups at CH3.
2. Substitution in the position 3 determine the potency and duration of action of the thiazide.
3. Saturation of C-N Bond between 3 and 4 position of the benzothiladiazine-1,1dioxide nucleus increase the potency of these diuretics approximately 3-10-fold.
4. Substitution of 6 position with an activating group is essential for the diuretic's activity.
5. The best substitution induces the Cl, Br, Cf3 & NO2 group.

## ➤ Mechanism of action



❖ Method of synthesis

➤ Synthesis of chlorothiazide



# ANTIHYPERTENSIVE DRUGS

## ❖ Contents :

- Definition
- Classification
- Structures
- SAR, Mechanism of action
- Method of synthesis

## ❖ Definition:

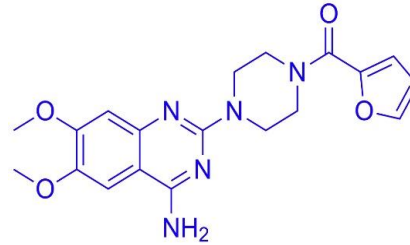
Antihypertensive Drugs: Antihypertensive are a class of drugs that are **used to treat hypertension (high blood pressure)**.

## ❖ Classification:

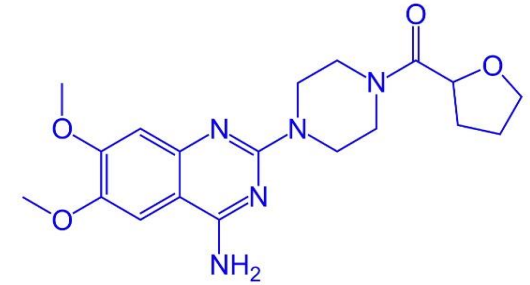
- Alpha Blockers : Prazosin ,Terazosin
- Beta Blockers : Propranolol,Atenolol
- ACE inhibitors: Captopril,Lisinopril, Enalapril,Quinapril.
- Angiotensin II receptor antagonist: Losartan, Telmisartan, valsartan.
- Misc. Class: Methyldopate hydrochloride, Clonidine hydrochloride, Guanethidine monosulphate, Reserpine

## ❖ Structures

### ➤ Alpha blockers

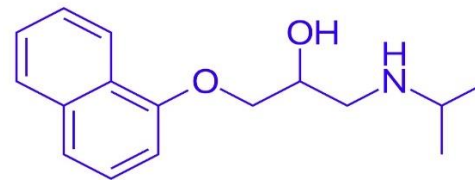


Prazosin

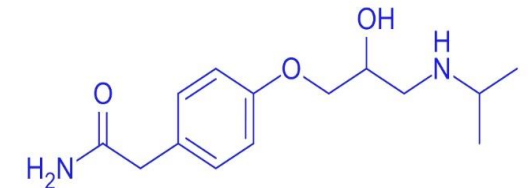


Terazosin

### ➤ Beta blockers

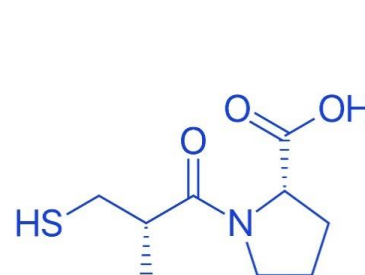


Propranolol

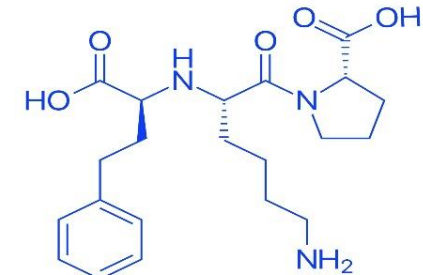


Atenolol

### ➤ ACE inhibitors

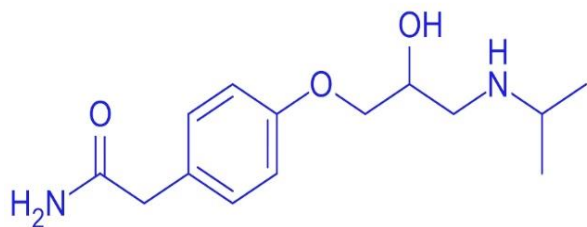


Captopril



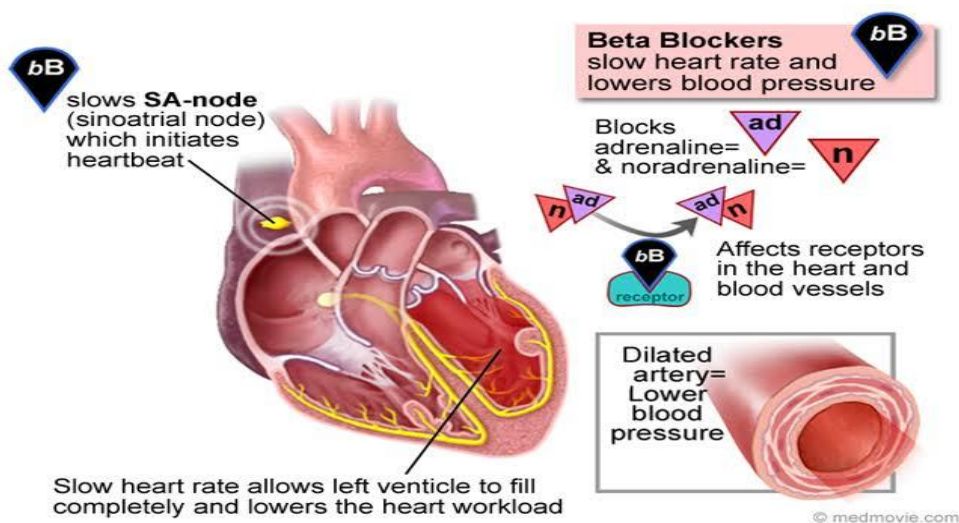
Lisinopril

## ❖ SAR of atenolol



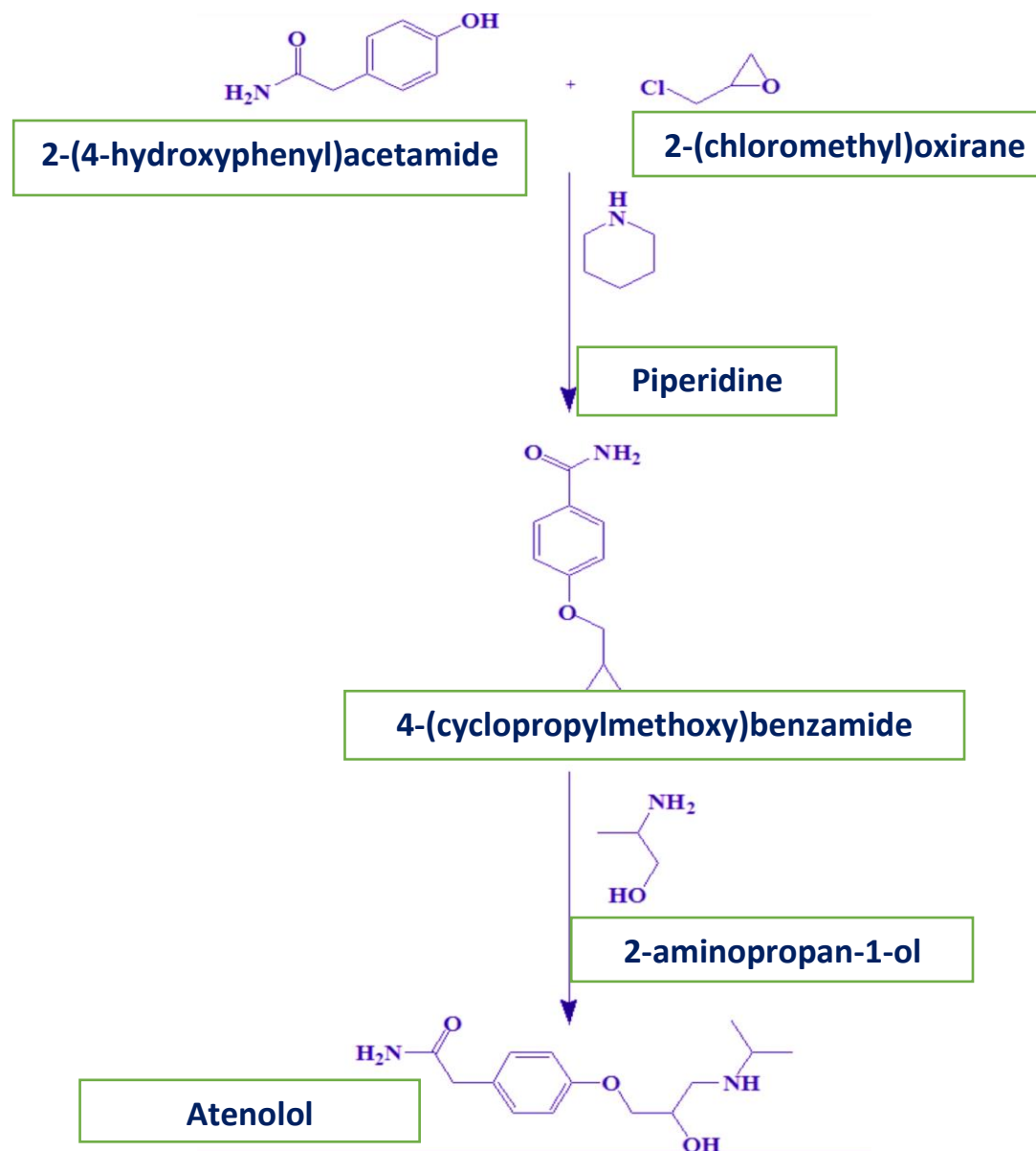
Atenolol

1. Increasing the chain length of the sidechain prevents appropriate binding of the required functional group to the same receptors side.
2. Side chain of aryloxpropanolamines can adopt a conformation that places the hydroxyl and amine groups into approximately the same position in space.
3. Aryloxpropaloamines permits a close overlap with the aryethanamine side chain.
4. Aryloxypropanolamines are more potent than aryloxethanolamines.

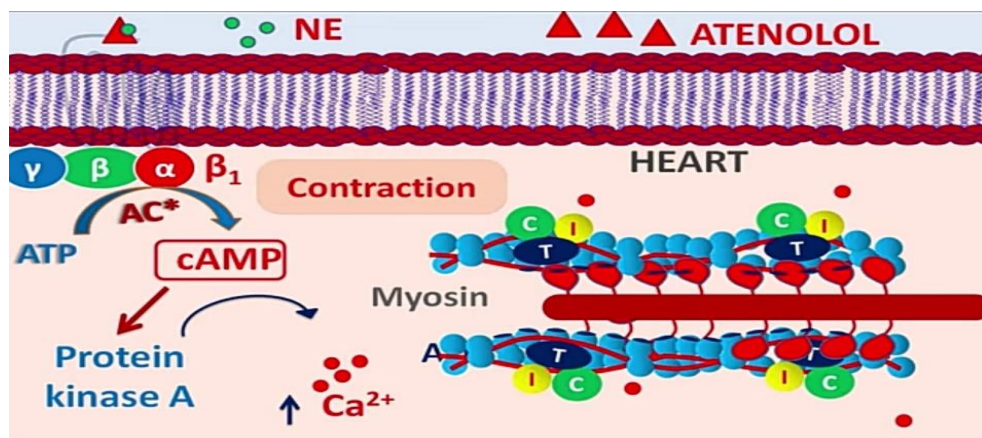


## ❖ Method of synthesis

1. 2-(4hydroxyphenyl)acetamide reacts with 2-(chloromethyl)oxirane in presence of piperidine to give 4-(cyclopropylmethoxy)benzamide.
2. Later compound reacts with 2-aminopropan1-ol to give atenolol



## ❖ Mechanism of action



1. Beta blockers work by blocking the effect of hormone epinephrine, also known as adrenaline.
2. Beta blockers cause the heart to beat more slowly and with less force, which lowers blood pressure.
3. Beta blockers also help widen veins and arteries to improve blood flow.
4. Atenolol is used in treating angina.

## ❖ Therapeutic uses:

Atenolol is used for treatment of:

- Angina
- Hypertension
- Reduce attack of death after a heart attack

### Reference:

1. Wilson and Griswold's organic medicinal and pharmaceutical chemistry
2. Foye's principles of medicinal chemistry

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