

# ANTI-HISTAMINIC AGENTS

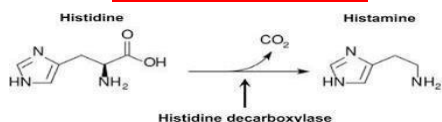
## ➤ HISTAMINE

- Chemical messengers generated in mast cell.
- Itself act as a autacoid.

## ➤ LOCATION

- In the blood basophils.
- Mucosal cells of GIT track.
- In the hypothalamus.

## ➤ BIOSYNTHESIS



## HISTAMINE RECEPTOR LOCATION

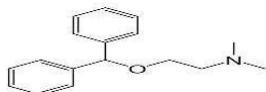
- **H1 RECEPTOR**
  - Smooth muscle
  - Ganglionic cells
- **H2 RECEPTOR**
  - Gastric gland
  - Uterus
- **H3 RECEPTOR**
  - Brain

## CLASSIFICATION OF ANTIHISTAMINE

### H1 RECEPTOR ANTAGONIST -

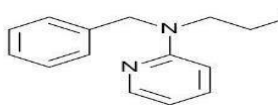
#### a) Amino alkyl ethers

##### 1) Diphenhydramine



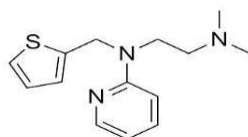
#### b) Ethyl diamines

##### 1. Triplanamine hydrochloride



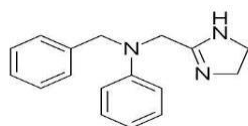
#### c) Thiopene derivative

##### 1. Methapyrilene hydrochloride



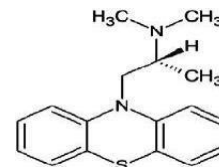
#### d) Cyclic basic chain analogue

##### 1. Antazoline Hydrochloride



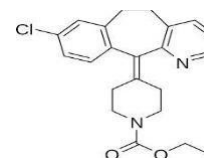
#### e) Phenothiazine hydrochloride

##### 1. Promethazine hydrochloride



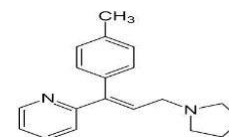
#### f) Second generation of non-sedating anti-histamine

##### 1. Loratidine



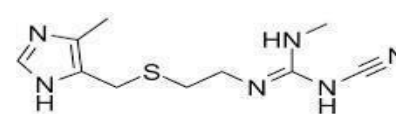
#### g) Miscellaneous agent

##### 1. Triprolidine hydrochloride



#### H2 RECEPTOR ANTAGONIST

##### 1. Cimetidine

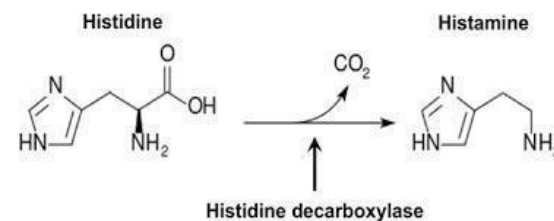


## STRUCTURAL RELATIONSHIP. ACTIVITY



- These are characterized by presence of OXYGEN atom.
- Most compounds in this series are simple N, N -dimethyl ethanolamine derivative.
- Most amino alkyl ethers are optically active.
- The drugs in this groups possess significant anticholinergic activity.
- This amino alkyl ethers have to penetrate the BBB and occupy central H1 receptor.

## Biosynthesis:-



- **Histamine synthesized by decarboxylation Of amino acid histidine.**
- **Histamine is present in storage granules Of mast cells.**
- **It is synthesized from amino acid tryptophan and degraded primarily by MOA and to a small extent by a dehydrogenase.**

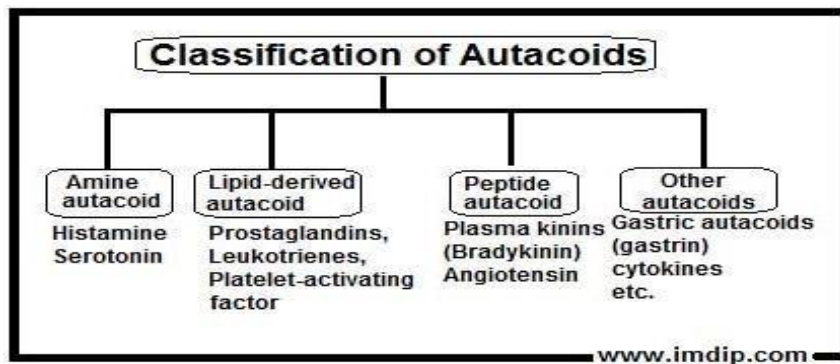
## • AUTOCOID:

### DEFINATION:-

Autocoids = Auto + Akos. This is a Greek word. Auto means automatic and Akos means healing material.

Autocoids are biological factors which act like local hormones, have a brief duration, act near the sites of synthesis, and are not blood borne.

### CLASSIFICATION :-



### PROSTAGLANDINS :-

- Prostaglandins are unsaturated fatty acid derivatives. They act on the tissue in which they are synthesized and are metabolized into inactive products at the site of action.

### SAR :-

- It contains an -OH group at the 15<sup>th</sup> position.
- It contains trans double bonds.
- It contains a 20 fatty acid chain containing a cyclopentane ring.
- Methyl ester, Sulphonamide, and Hydroxyl group.

### THERAPEUTIC USES :-

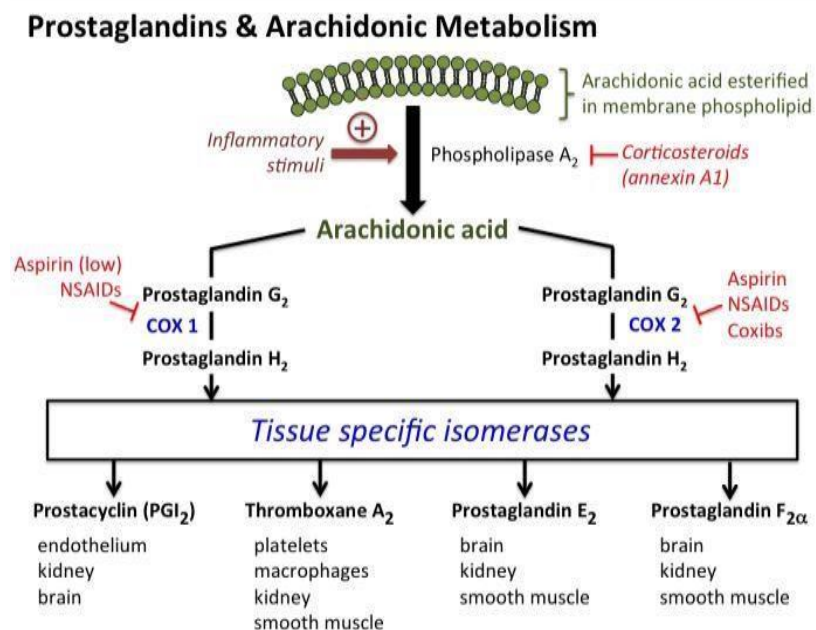
- Pregnancy termination
- Peptic ulcer
- Abortion
- Conception
- Menstruation
- Parturition

### PROSTANOIDS :-

- Prostanoids are a family of lipid mediators generated by the action of cyclooxygenase on unsaturated fatty acids.

- Prostanoids are produced when arachidonic acid is released from the plasma membrane of injured cells.
- Prostanoids are a subclass of eicosanoids. Following two products are available for this:
  - 1) Prostanoid acid
  - 2) Cloprostenol Sodium

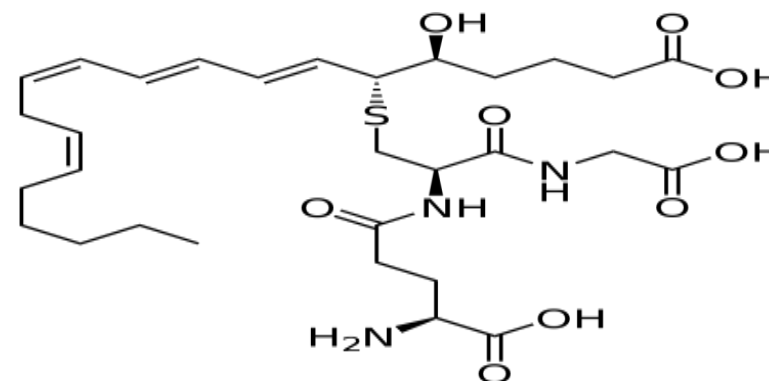
## PROSTAGLANDIN AND ARCHIDONIC METABOLISM :-



## LEUKKOTRIENS :-

Leukotrienes are a group of biologically active compounds isolated from leukocytes. Leukotrienes are a family of biologically active molecules, formed by leukocytes.

Eg. Platelets possess only 12-lipoxygenase while leukocytes show both 12-lipoxygenase and 5-lipoxygenase.



## THERAPEUTIC USES:-

- To prevent breathing problem i.e asthma
- To prevent allergies (allergic rhinitis)
- Exercise induced asthma

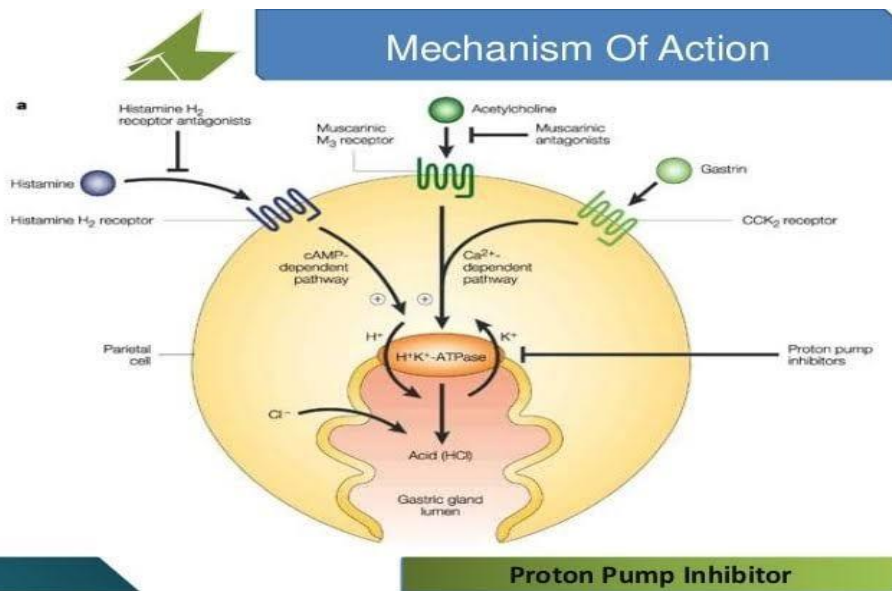
## SIDE EFFECTS :-

- Vomiting
- Water diarrhea
- Uterine bleeding
- Diarrhea
- Ear Infection
- Headache
- Nausea
- Fever

## GASTRIC PROTON PUMP INHIBITORS

### Introduction:-

Proton Pump Inhibitors are a group of drugs whose main action is a pronounced & long lasting reduction of gastric acid production.



### Mechanism of action:-

PPIs are administered as inactive prodrugs.

Converted into active form thiophillics

sulphonamide cation in the parietal cell .

The sulphonamide reacts with the H<sup>+</sup>/K<sup>+</sup> ATPase (Proton pump) forms a covalent disulfide linkage.

Irreversible inactivation of proton pump.

Counter transport of H<sup>+</sup>/K<sup>+</sup> ions via Proton pump is blocked.

No secretion of H<sup>+</sup> by Parietal cell .

Clinically used PPIs :- 1) Omeprazole

Adverse Effects of PPIS :-

1) Diarrhea. 2) Headache

Therapeutic Uses:-

1) Gastro esophageal reflux disease.



# DRUG SYNTHESIS

## Promethazine HCL

### Structure =

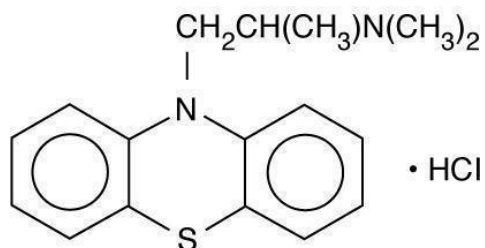
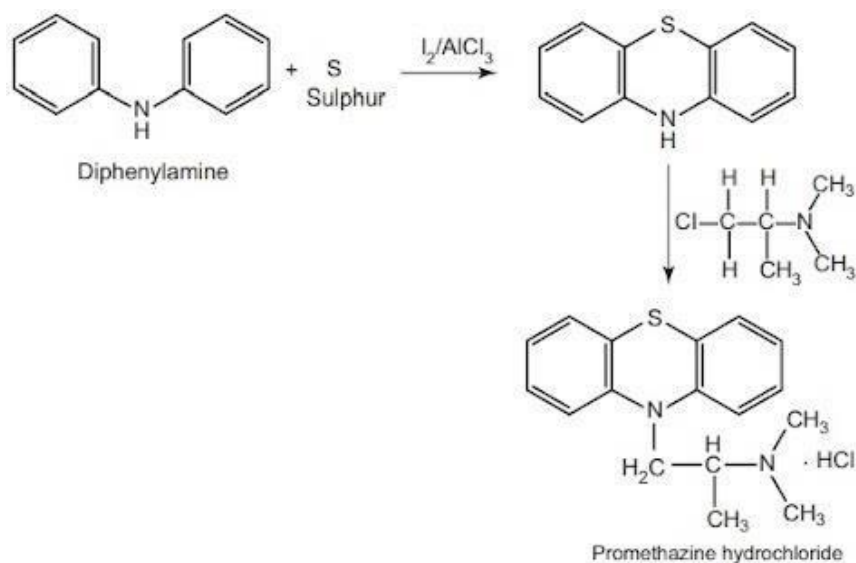


Fig. Promethazine HCL

### IUPAC Name =

10- [ 2-(dimethylamine)propyl Phenothiazine mono hydrochloride

### Synthesis =



## Diphenylhydramine HCL

### Structure =

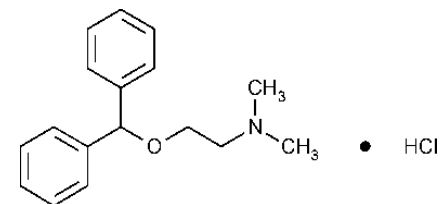
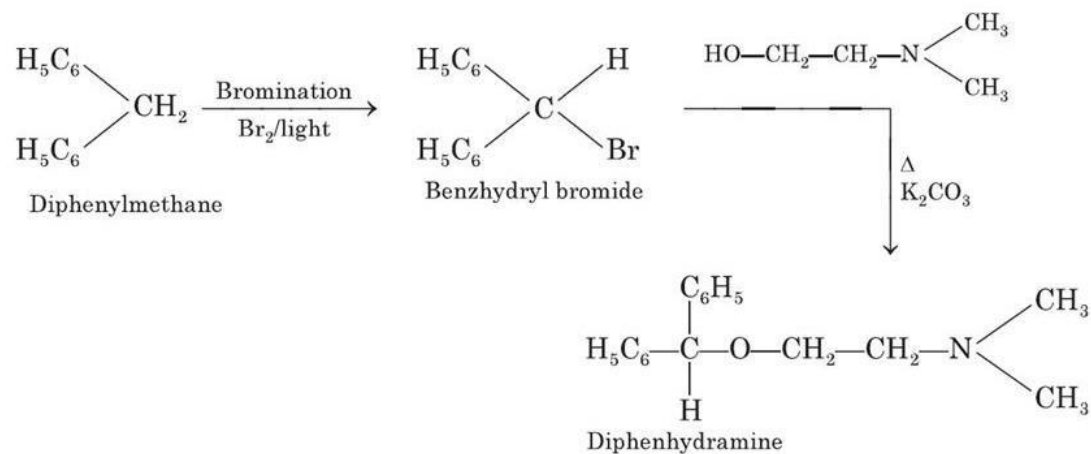


Fig. Diphenylhydramine HCL

### IUPAC Name =

2 - (Diphenylmethoxy ) - N , N - dimethyl- ethyl amine hydrochloride

### Synthesis =



## Ranitidine

### Structure =

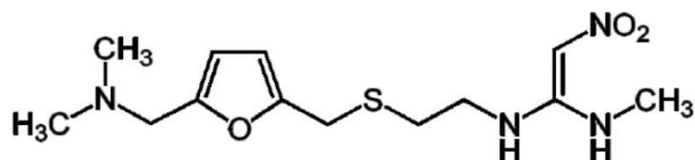
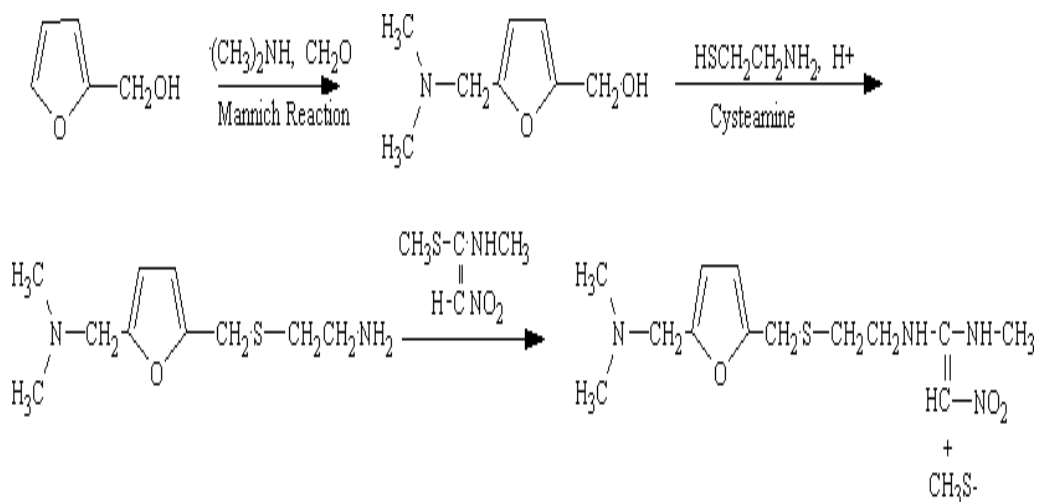


Fig. Ranitidine

### IUPAC NAME =

Dimethyl – [ 5 – [ 2 – ( 1 - methyl amino - 2 – nitro vinyl amino )  
ethyl thiomethyl) fur furyl ] amine

### Synthesis =



## Certirizine

### Structure =

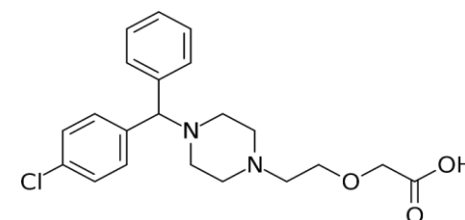
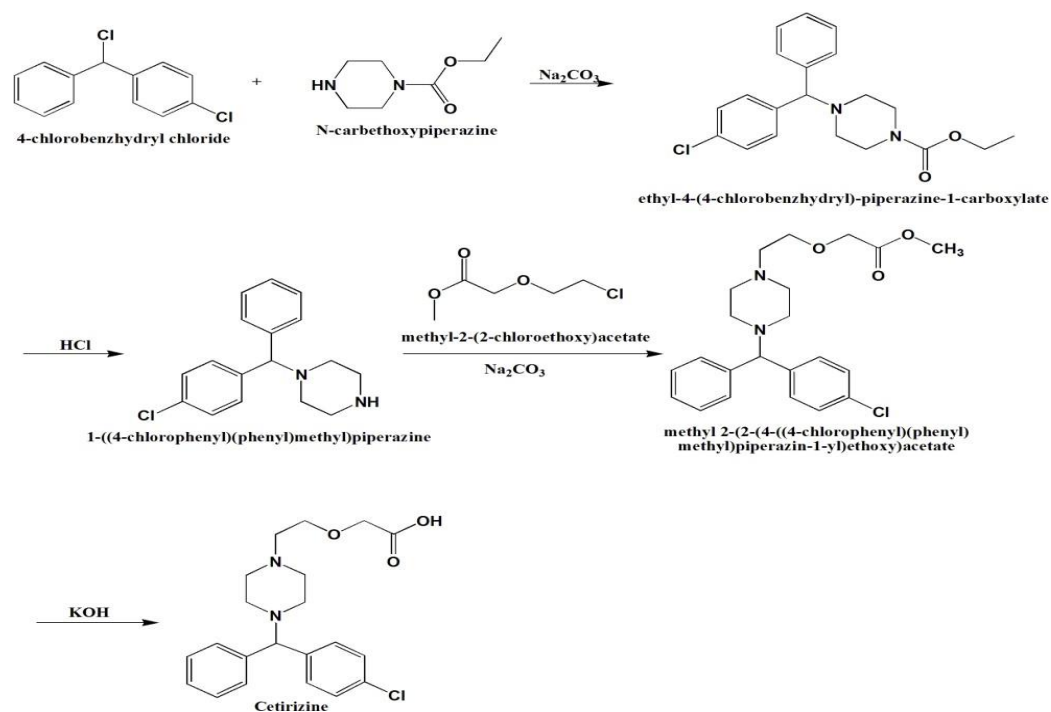


Fig. Cetirizine

### IUPAC NAME =

(RS)-2-[2-[4-[(4-Chlorophenyl) phenyl methyl] piperazin-1-yl]ethoxy]acetic acid dihydrochloride

### Synthesis =



### **REFERENCE :**

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- ❑ Textbook of medicinal chemistry by Nirali prakashan Dr. SSKadam K R mahadip pg no71-79
  - wilson and givold's textbook of organic chemistry and p'chemistry twelfth edition , page no 654 to 662
- ❑ Textbook of William. o. foye principle of medicinal chemistry , third edition , page no. 383 to 393
- ❑ Dr.S.S kadam ,.K.R.Mahadik Textbook of medicinal
- ❑ Chemistry by nirali prakshan Page No.15.7-15.70

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