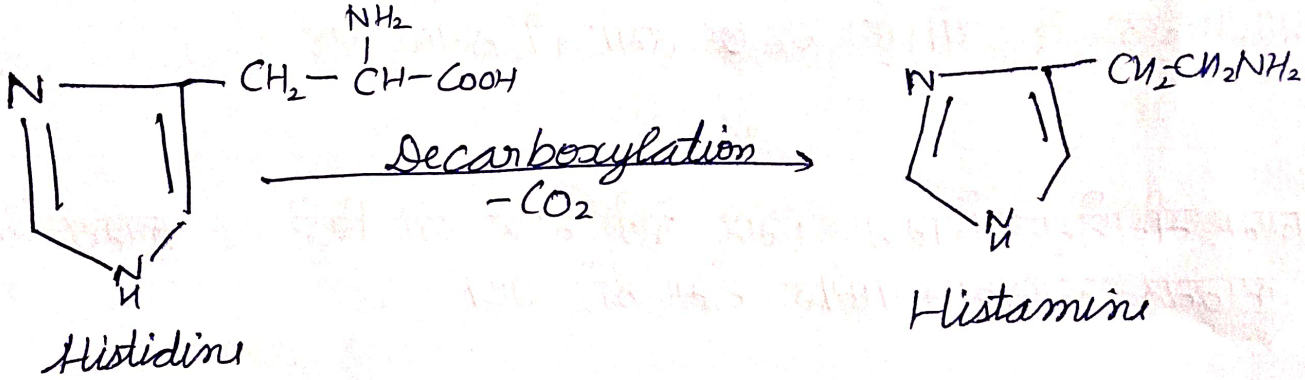
#ANTIHISTAMINIC AGENTS

Histamine :- Histamine is a naturally produced α-Amino acid derivative.

→ it Synthesized from histidine (Amino Acid) by loss of Carboxyl group through decarboxylation.



Histidine Histamine

☆ Release of histamine gives rise to a number of Physiological actions which Activates by the histaminic receptors.

☆ Mild release of histamines in body lead to allergic reactions

☆ Histamine release can be blocked by using Antihistaminic agents.

* Histamine is present in high concentration in lungs leads to Vasoconstriction etc.

* Antihistaminics are widely used in palliative treatment of allergic conditions like hay fever, urticaria, conjuctivitis, nasal discharge, mild Asthma etc.

→ A few antihistaminics possess antiemetic (Stop vomiting) action.

→ Most common side Effect of antihistaminics is Sedation followed by Drowsiness, impaired alertness etc

Classification of Antihistaminics

Histamine H_1-Receptor Antagonists

- **Aminoalkylethers**
  Example - Diphenhydramine HCl, Bromodiphenhydramine HCl, Dimenhydrinate, Doxylamine Succinate; Diphenylpyraline HCl
- **Ethylenediamines**
  Example - Mepyramine Maleate, Tripelennamine HCl, Thonzylamine HCl, Zolamine HCl
- **Thiophene Derivative**
  Example - Methapyrilene HCl, Methaphenilene HCl, Chlorothen HCl etc
- **Cyclic Basic Chain Analogue**
  Example - Piperazine Derivative, Cyclizine HCl, Chlorcyclizine HCl, Meclizine HCl, Buclizine HCl, Piperidine Derivative etc
- **Phenothiazine Derivatives**
  Example - Promethazine HCl, Trimeprazine Tartrate etc

Second generation Non Sedating Antihistamines

Examples
- Terfenadine
- Astemizol
- Loratadine
- Acrivastine

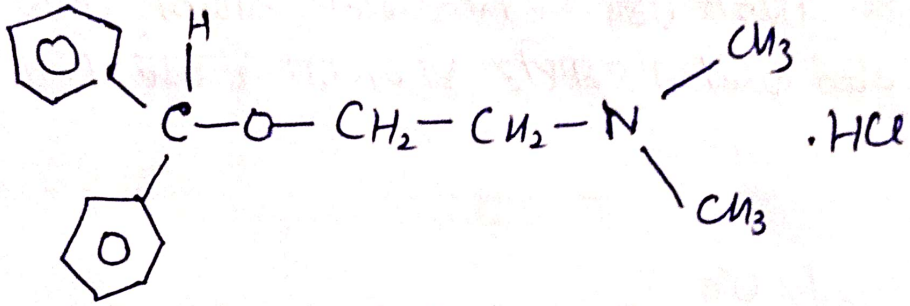
Miscellaneous

Examples
- Phenindamine Tartrate
- Triprolidine HCl
- Chlorpheniramine Maleate
- Cyproheptadine HCl

H_1 Receptor Agonist Blockers (Antagonists)

① Alkylethers (Aminoalkylethers)

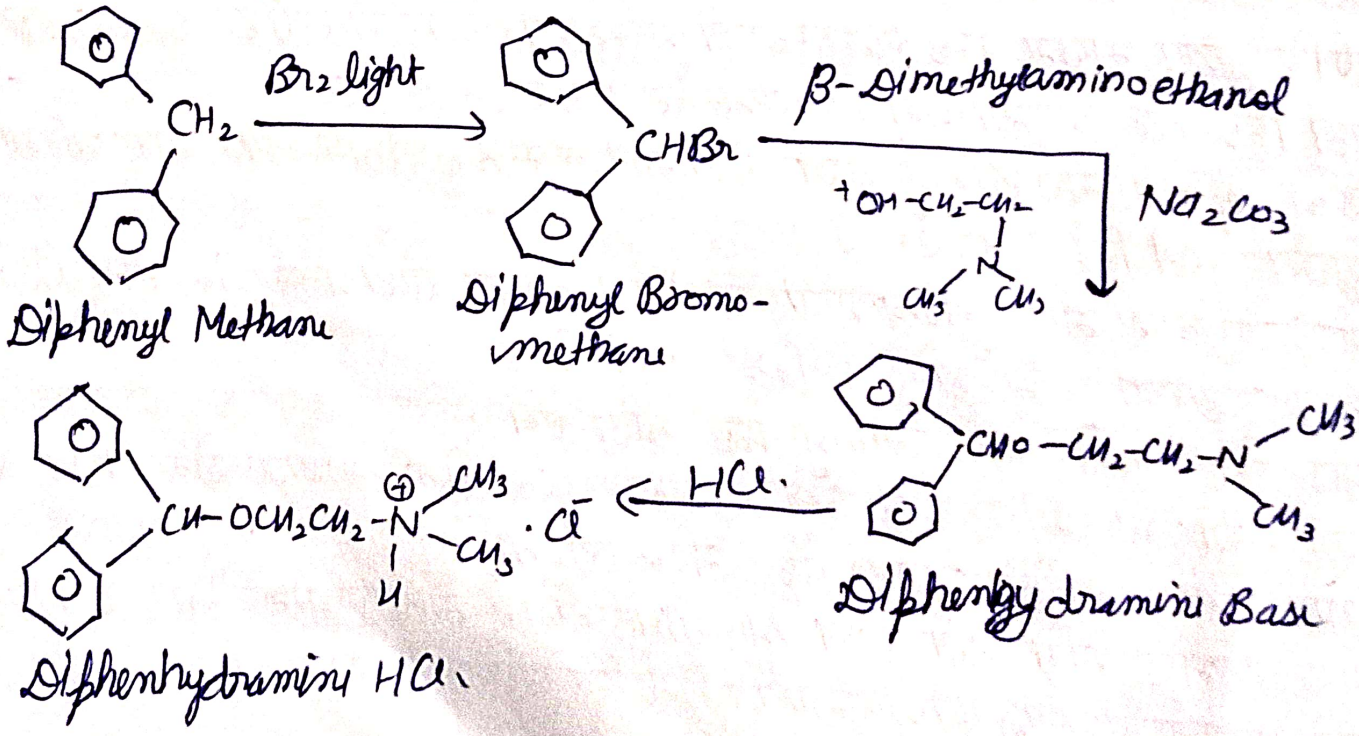
★ Diphenhydramine HCl



2-(Diphenylmethoxy)-N,N-dimethylethylamine HCl /

Ethanamine, 2-(diphenylmethoxy)-N,N-dimethyl, Hydrochloride.

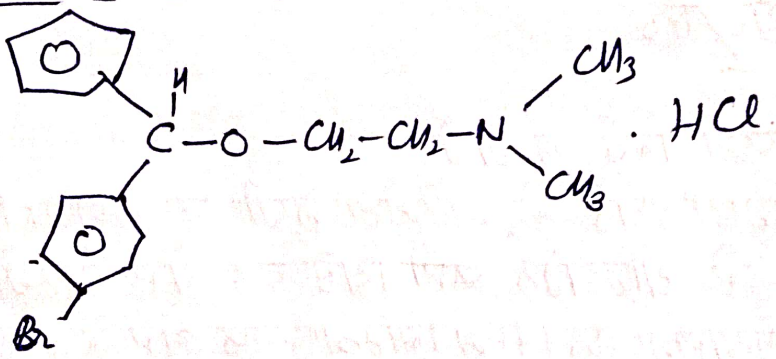
Synthesis :-



→ Diphenhydramine is frequently used in mild, local allergic reactions due to insect bite. It also used as sedative, antiemetic and anti-tussive.

Dose - 25-50 mg, adult, oral dose 3 to 4 times a day maximum 400 mg daily.
→ topical to skin 2% Cream 3 or 4 time a day

★ Bromo diphenhydramine HCl :-

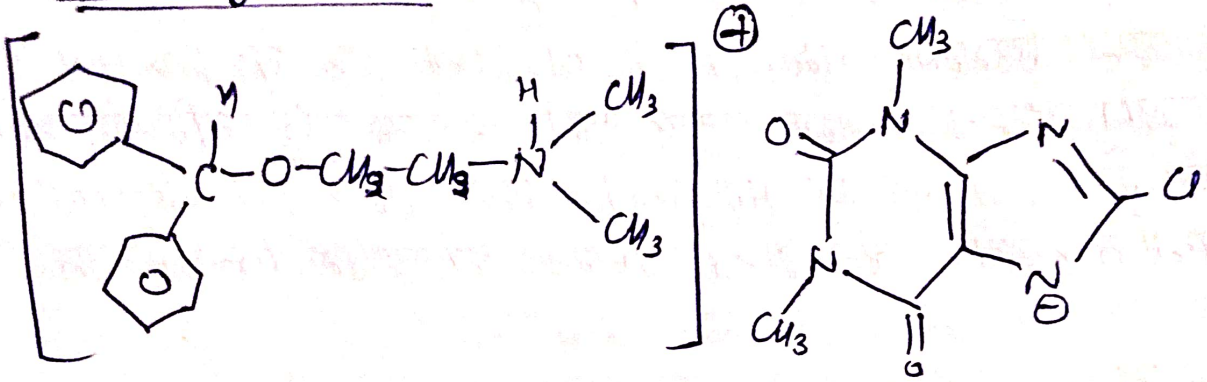


Ethanamine, 2-[(4-Bromophenyl) Phenylmethoxy]-N,N-dimethyl, hydrochloride

→ used for mild, local allergic reactions to insect bites, physical allergy and for minor drug reactions characterised by pruritis

Dose - 25 mg, usually 3 or 4 times daily

✡ Dimenhydrinate :-

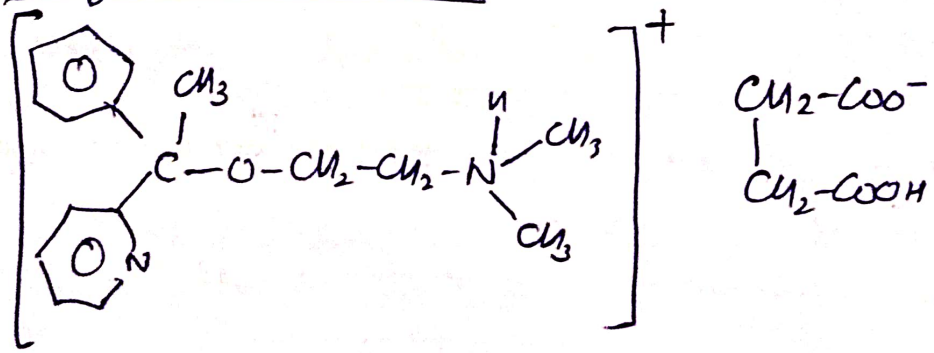


8-chlorotheophylline compound with 2-(diphenylmethoxy)-N,N-dimethyl-ethylamine

→ It is mostly used as antinauseant, in motion sickness, radiation sickness and also in nausea (vomiting feeling) of pregnancy.

Dose :- oral 50mg thrice per day.

✡ Doxylamine Succinate :

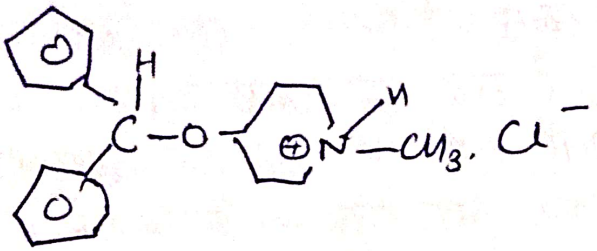


Ethanamine, N,N-dimethyl-2-[1-phenyl-1-(2-pyridinyl) ethoxy]-butanedioate.

→ used for allergic conjuctivitis due to allergens, allergic skin manifestations of urticaria.

→ Dose - 12.5 to 25mg ; adult, oral 4 to 6 times a day.

☆ Diphenylpyraline HCl:

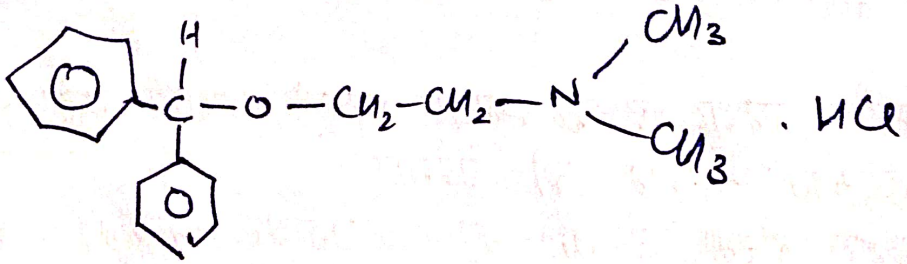


4-(Diphenylmethoxy)-1-methylpiperidine Hydrochloride.

→ used for Treatment of dermatographism, effective for conjuctivitis due to inhalant allergens and foods

Dose - usual, adult, oral 5mg, 2 times a day.

☆ Diphenhydramine HCl :-



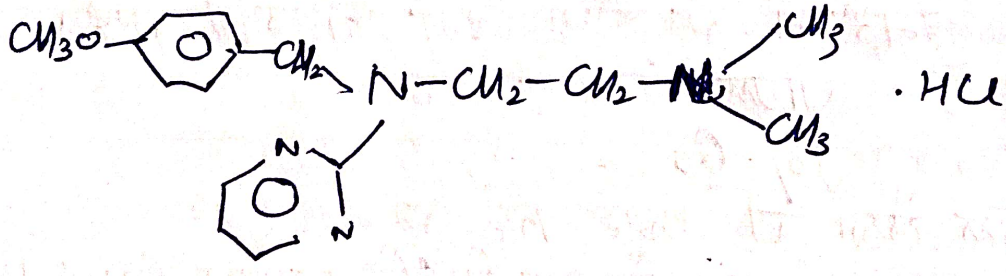
→ It has ability to minimize nasal discharge included in 'hay fever' and several 'cold' medicaments

2- [Benzyl [2- (dimethyl amino) ethyl] amino] Pyridine monohydrochloride

→ used in Treatment of seasonal allergic rhinitis, allergic conjuctivitis due to inhalant allergens and foods., dermititis, dermographism.

Dose - 25 to 50 mg ; in adult, orally · 4 to 6 times per day

★ Thonzylamine HCl



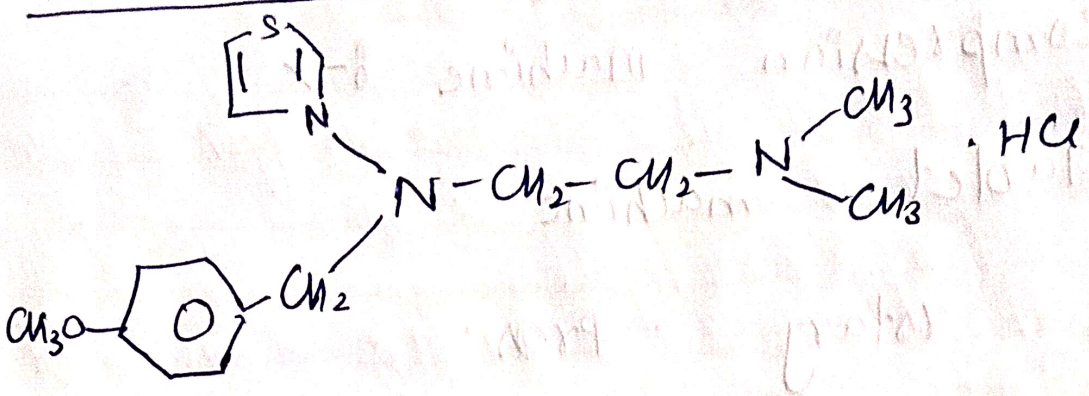
2- {[2- (Dimethylamino) ethyl] - (p-methoxybenzyl) amino} Pyrimidine HCl.

→ It recommended for use with Streptomycin in Human TB.

→ used in treatment of hay fever, drug reactions and other mild allergic conditions

Dose : 50 mg in adult 4 time a day (orally)

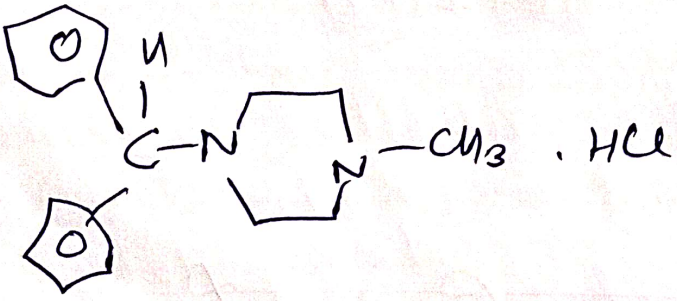
☆ Zolamine HCl :-



1,2- Ethanediamine, N- [(4- methoxyphenyl) methyl]- N', N- dimethyl- N - thiazolyl- monohydrochloride

(3) Cyclic Basic chain Analogues :-

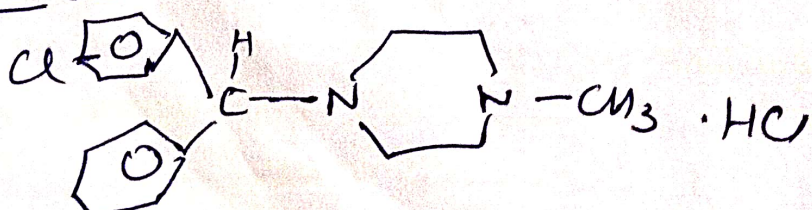
☆ Cyclizine HCl



Piperazine, 1- (diphenylmethyl) - 4- methyl, monohydrochloride.

→ used in treatment of Prophylascis and motion Sickness-

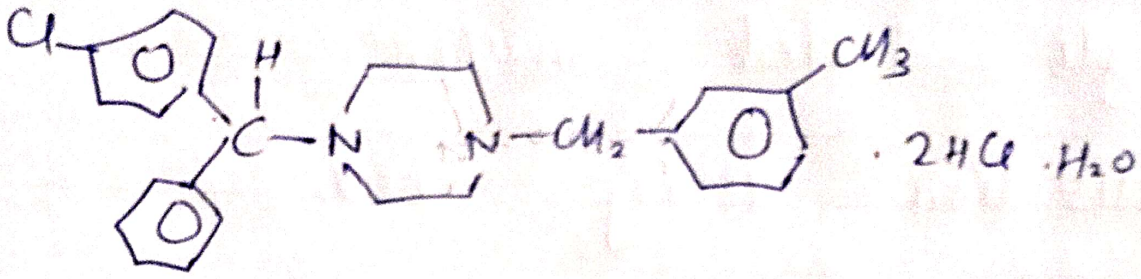
☆ Chlorcyclizine HCl :-



Piperazine, 1- [(4-Chlorophenyl) Phenylmethyl]- 4 methyl - monohydrochloride

→ It has local anaesthetic, antiemetic and anticholinergic properties.

☆ Meclizine HCl :-

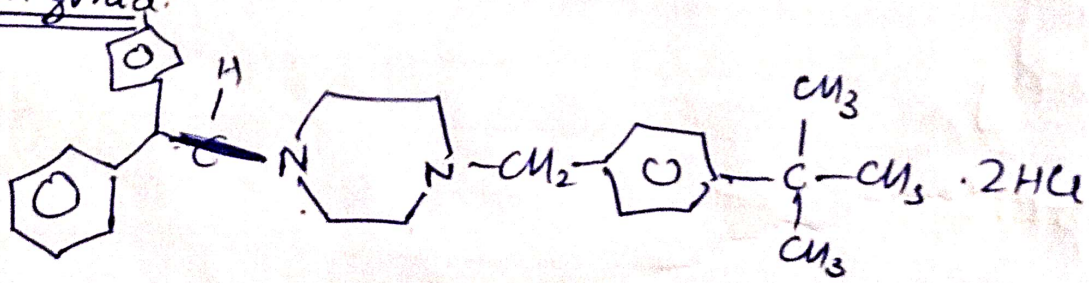


Piperazine, 1-[(4-Chlorophenyl)Phenylmethyl]-4-[(3 methyl Phenyl)-methyl]- dihydrochloride monohydrate

→ used for antiemetic action, prevent and treat motion sickness.

Dose - 25 to 50 mg.

☆ Buclizine :-



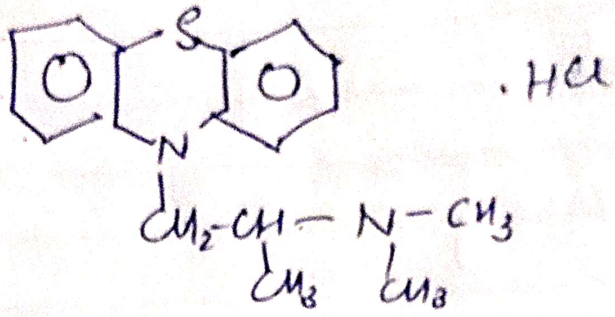
Piperazine, 1-[(4-Chlorophenyl) Phenylmethyl]-4-[(1,1-dimethylethyl) Phenyl] methyl]- dihydrochloride

→ Used as antiemetic for, and treat allergic conditions.

Dose - 25 to 50 mg, 2 to 3 times a days

(4) Phenothiazine Derivatives :

☆ Bromethazine HCl :

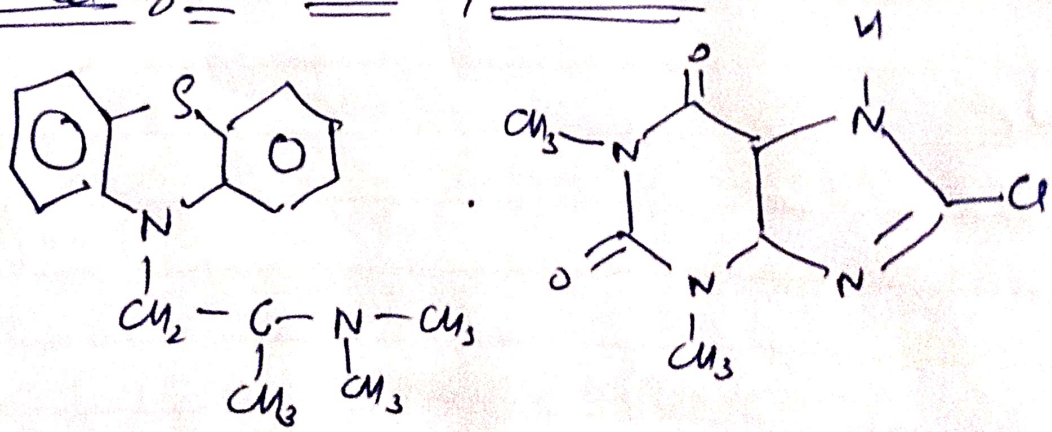


10-[2-Dimethylamino) Propyl] Phenothiazine monohydrochloride

→ Used effectively in Seasonal allergic rhinitis, conjuctivitis, skin manifestations of urticaria.

Dose - 20 to 50 mg per day. (B.P)

☆ Promethazine Teoclate/Theoclate :



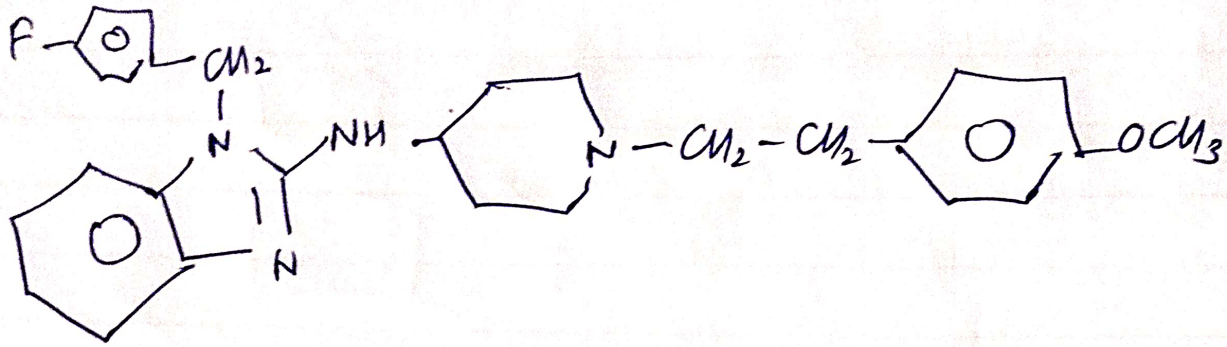
10-(2-Dimethylaminopropyl) Phenothiazine compound of 8-Chlorotheophylline.

→ Used as an antiemetic, treats motion sickness also treat post operative Vomiting

→ Dose - 25 to 50 mg per day.

☆ Second Generation Non Sedating Antihistamines

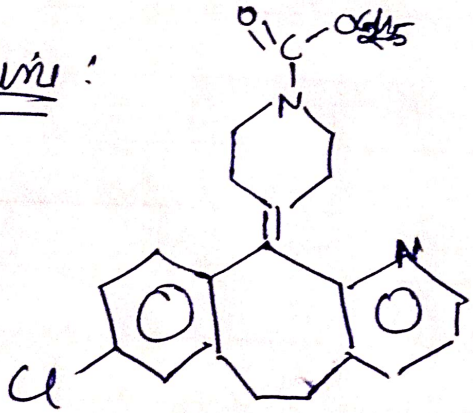
☆ Astemizol :



1H-Benzimidazol-2-amine, 1-[4-fluorophenyl]methyl]-N-[1-(2,4-methoxyphenyl)ethyl]-4-piperidinyl.

→ Used for allergic rhinitis, chronic urticaria.

☆ Loratidin :

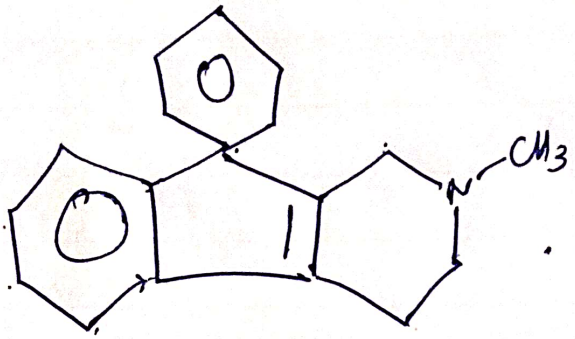


1-Piperidinecarboxylic acid, 4-(8-Chloro-5,6-dihydro-11H-benzo[5,6]-cycloheptal[1,2-b]pyridin-11-ylidene]-

→ It having anticholinergic activity.

☆ Miscellaneous

☆ Phenindamine Tartrate

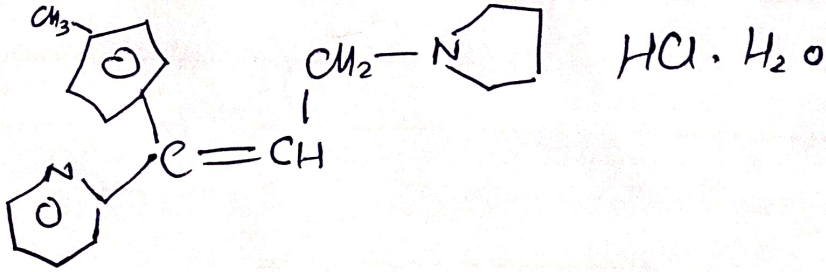


1,2,3,4- Tetrahydro -2- methyl - 9- Phenyl - 1H- indenol [2,1-c] pyridine hydrogen tartrate

→ less effective than Promethazine, causes mild drowsiness.

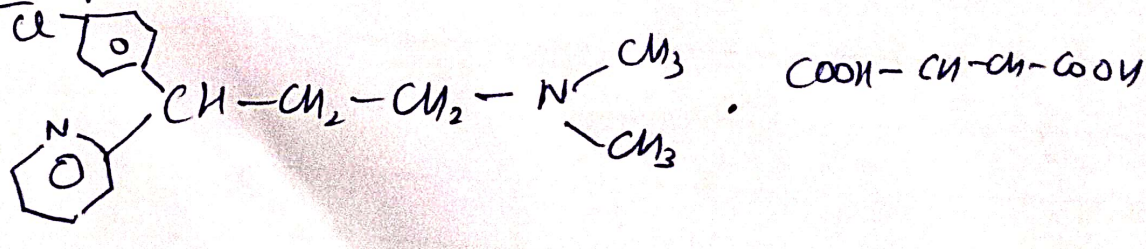
Dose - 75 to 150 mg per day

☆ Triprolidine HCl :



(E)- 2[3-(1-Pyrrolidinyl)-1- p- tolylpropenyl] Pyridine monohydrochloride monohydrate

☆ Chlorpheniramine maleate :

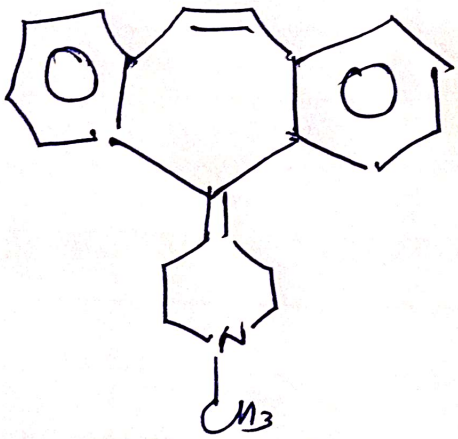


2-[p-Chloro-α-[2-(dimethylamino)ethyl] benzyl] Pyridine maleate.

→ one of the most potent antihistaminics, generally causes sedation than Bromethazine.

Dose - Usual, oral, 4mg 3 or 4 times per day.

☆ Cyproheptadine HCl :



, HCl · 3/2 H_2O

4-(5H-Dibenzo[a,d] cycloheptan-5-ylidene)-1-methylpiperidine Hydrochloride Sequihydrate.

→ help to stimulate Appetite (hunger).

Dose - 4mg 3 to 4 times a day, in adults.