SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

Coimbatore -641035

COURSE NAME : MEDICINAL CHEMISTRY II (BP 501 T)

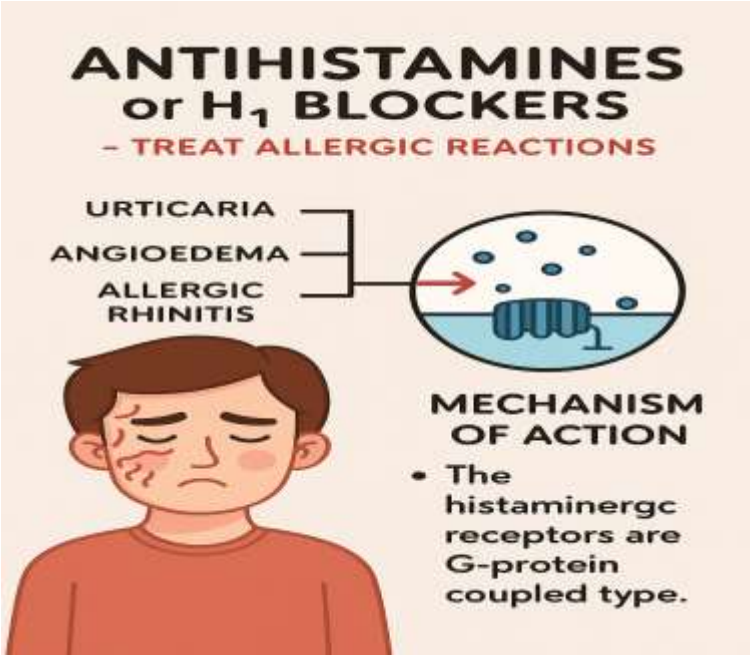
III YEAR / V SEM

TOPIC 1 : ANTIHISTAMINIC AGENTS

SUB TOPIC : H1 ANTAGONIST

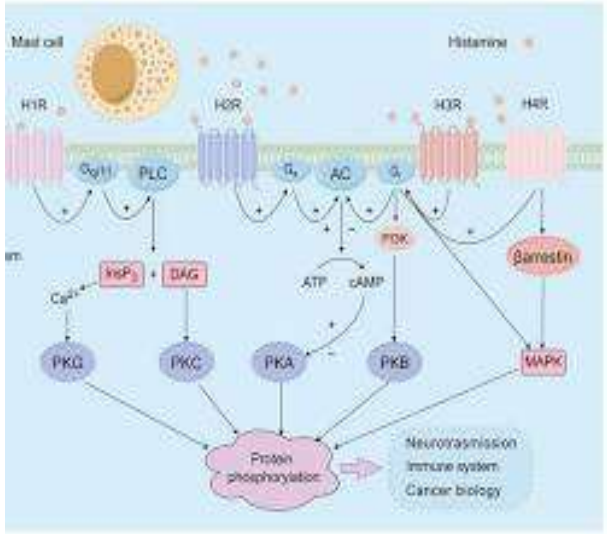
INTRODUCTION

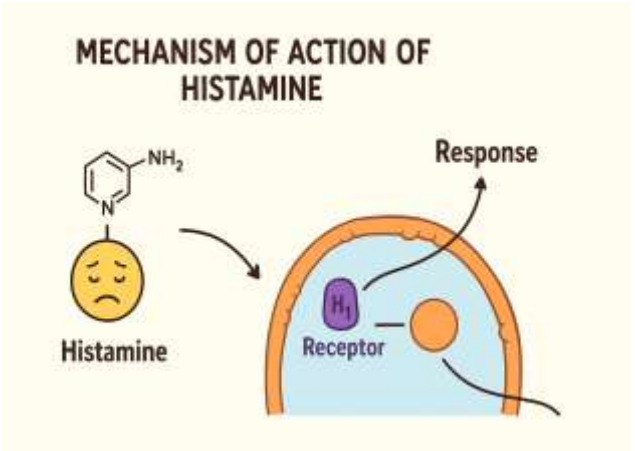
- These drugs cause blockade of H-receptors which results in decreased vascular permeability, relaxation of smooth muscle in respiratory or GI tracts and reduction of pruritis.
- H-receptors antagonists first generation) cause sedation due to lack of selectivity for the peripheral H-receptors.
- They are reversible competitive inhibitors of histamine at H-receptor and clinically used in the treatment of allergic conditions.
- The antihistamines do not prevent the formation of histamine or release of histamine.



Mechanism of Action

- The H-blockers H-receptors histaminergic receptors are G -protein coupled type.
- The H-receptors coupled to are phospho lipase-C and on activation they form inositol phosphate (IP3) and diacylglycerol(DAG) from the cell membrane
- Ca ions are rapidly released from endoplasmic reticulum under the influence of IP3. Protein kinase C is activated by DAG. Thus, the turnover of Ca ions and protein kinase C stimulates the Ca/calmodulin dependent protein kinase and phospholipase .

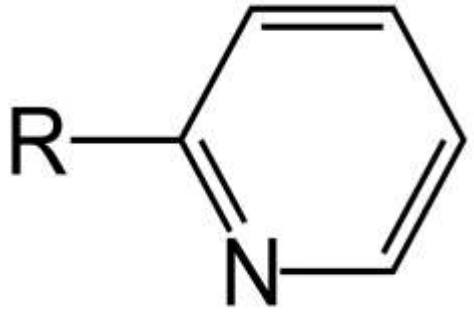




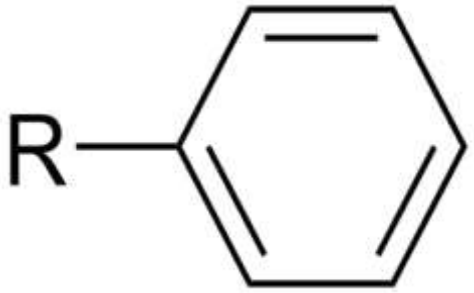
Structure Activity Relationship

Aryl groups

- Diaryl substitution is essential for significant H, affinity.
- The optimal antihistaminic activity depends on the co-planarity of two aryl substitutions.
- Active aryl substitutions are as follows:
- Ar -Phenyl and hetero aryl group like 2-pyridyl
- Ar -Aryl or aryl methyl group.



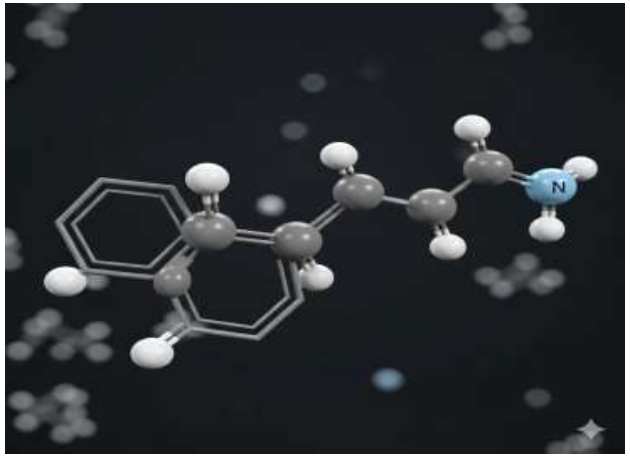
2-pyridyl



Aryl

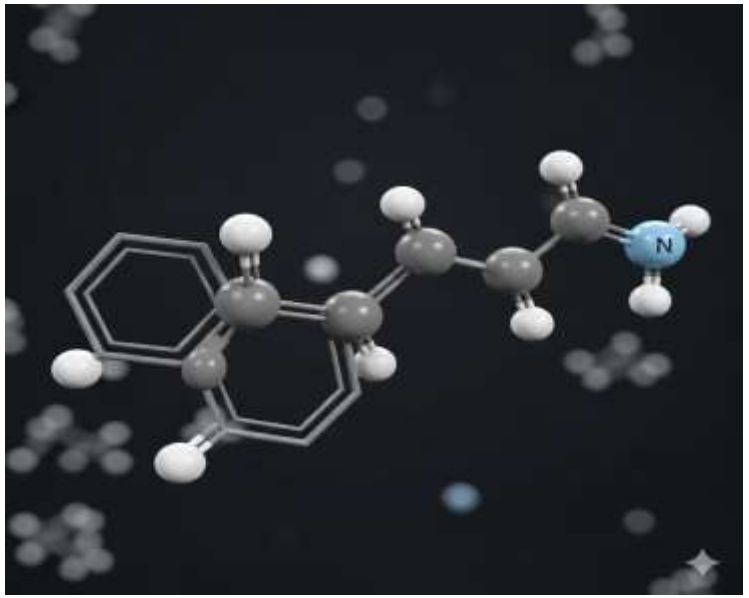
Connecting atom

- Antihistamines with X = carbon (pheniramine series) represents the stereo selective receptor binding to the receptors due to its chirality
- The actíve substitutions ofX are as follows:
- Where, X= Oxygen (amino alkyl ether analogue)
- X= Nitrogen (ethylene-diamine derivative)
- X= Carbon (mono amino propyl analogue)



The Alkyl Chain

Most of the antihistamines have ethylene chain, and R! branching (more than 2 or 3 atoms) of this chain -CH, CH,-N results in a less active compound.

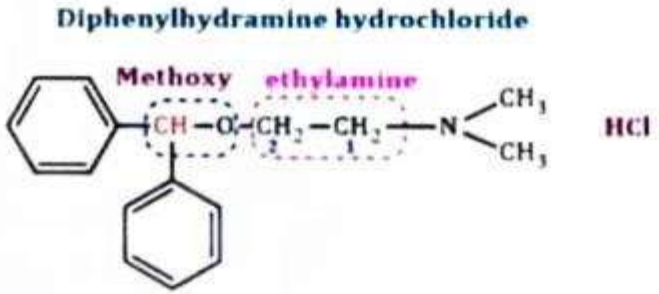


Terminal nitrogen atom

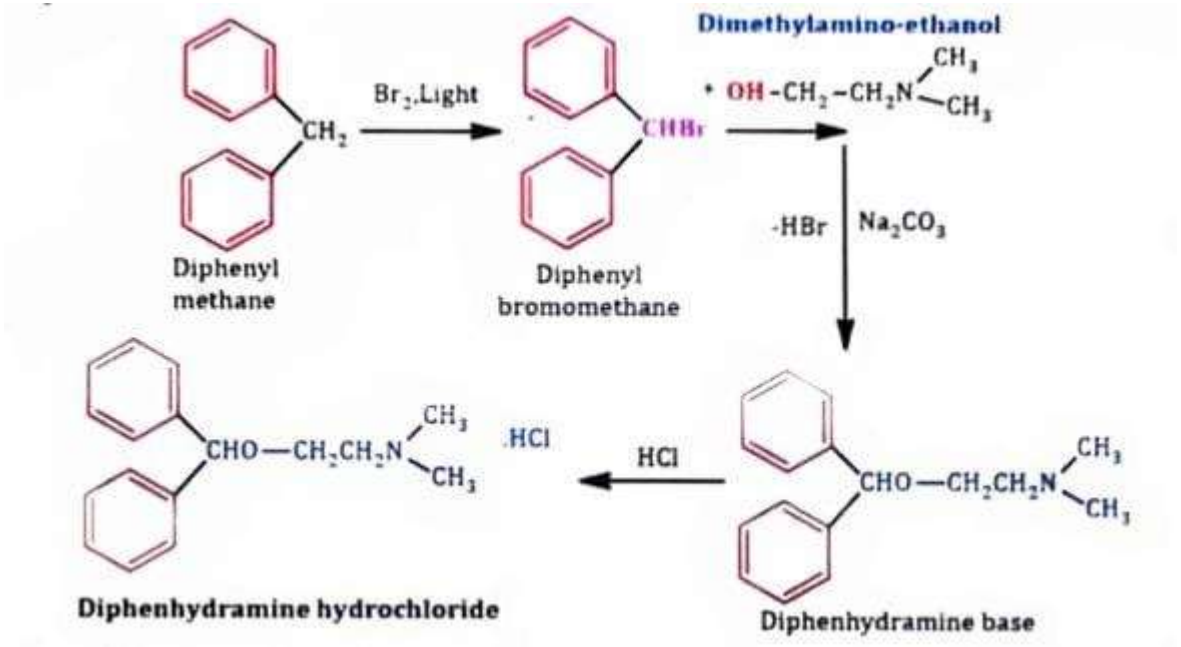
- The terminal N-atom should be a tertiary amine for maximum activity.
- The terminal nitrogen may be a part of heterocyclic ring Dimethyl substitution have optimum configuration.

Drugs of First generation

Diphenhydramine Hydrochloride



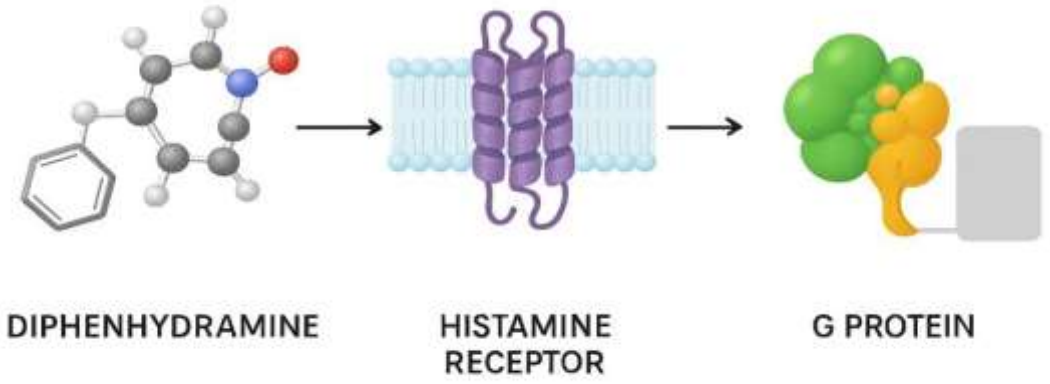
structure



Synthesis of Diphenhydramine Hydrochloride

Mechanism of action

Diphenhydramine functions as an inverse agonist at H,-receptors, and then it reversing the effect of the histamine on capillaries , reducing allergic reaction symptoms.



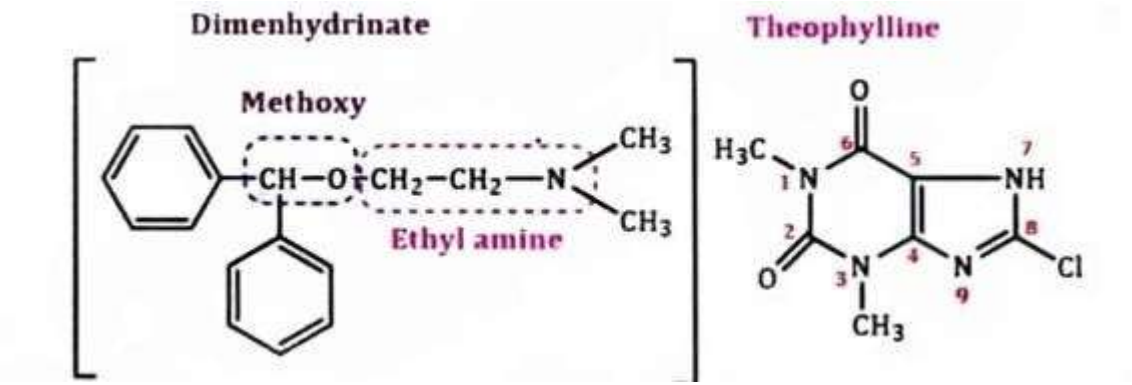
Properties

- " It is well absorbed from G.IT. It is metabolized and secreted in urine as metabolite conjugate

Uses

- It possesses sedative, antiemetic and anti-tussive properties It can be used in seasonal allergic rhinitis, allergic manifestations due to urticaria and allergic conjunctivitis of inhalant allergens.

2.Dimenhydrinate

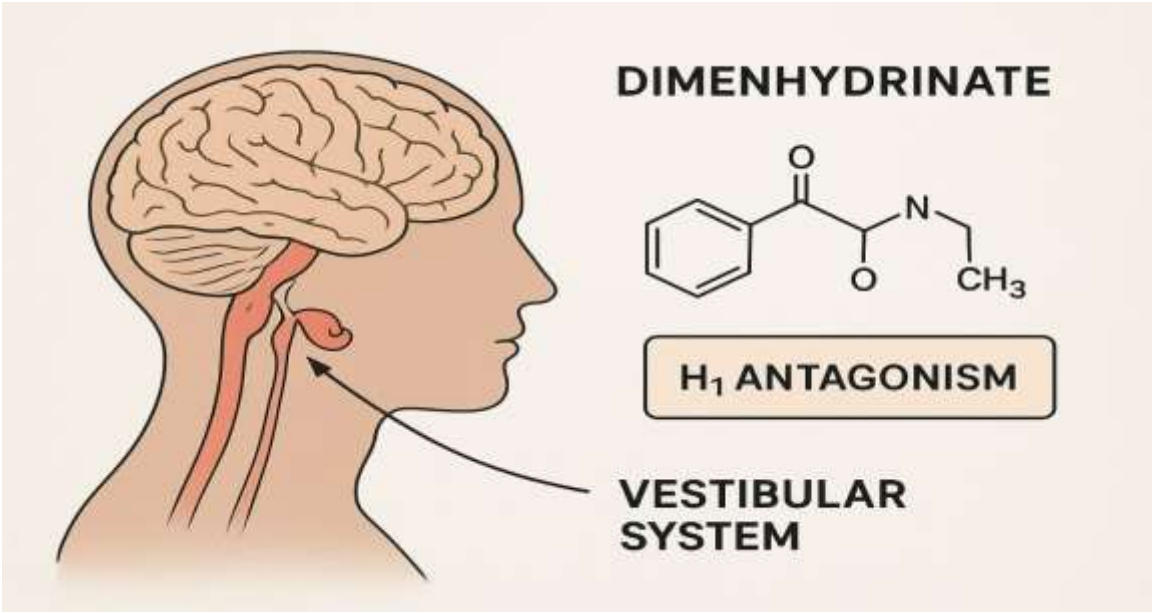


Structure of Dimenhydrinate

Dimenhydrinate is a combination drug as it comprises of diphenhydramine (53- 55.5%) and 8-chloro theophylline (not less than 44-47%) in a salt form, calculated on the dried basis.

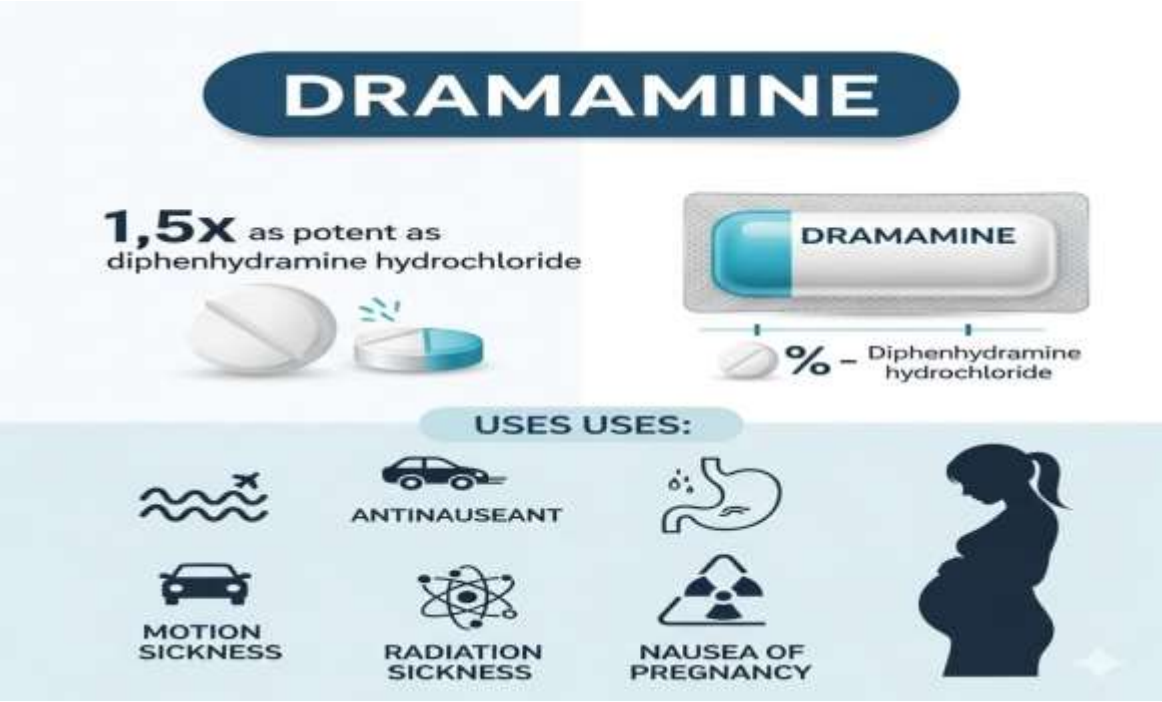
Mechanism of action

" The exact mechanism of dimenhydrinate is not known. Its effect is probably due to HËAntagonism in the vestibular system in brain.



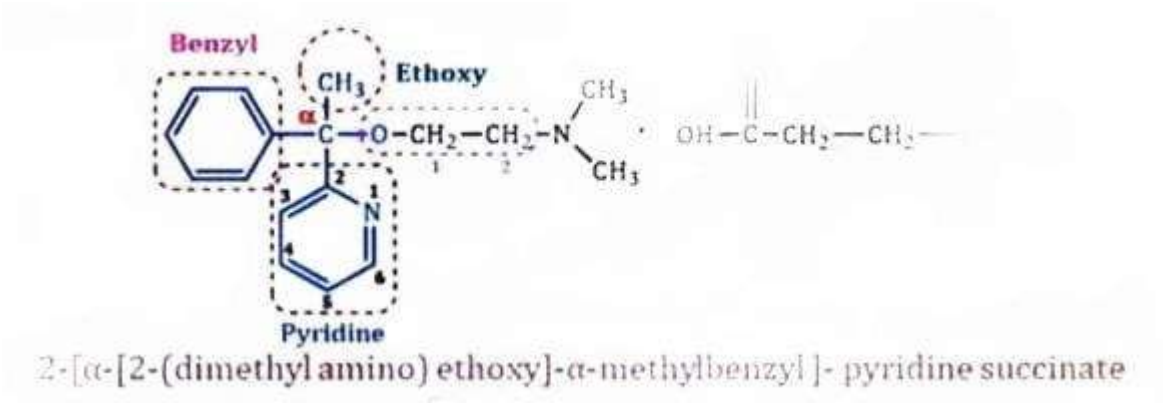
Uses

It is one and half time as potent as diphenhydramine hydrochloride



3.Doxylamine succinate

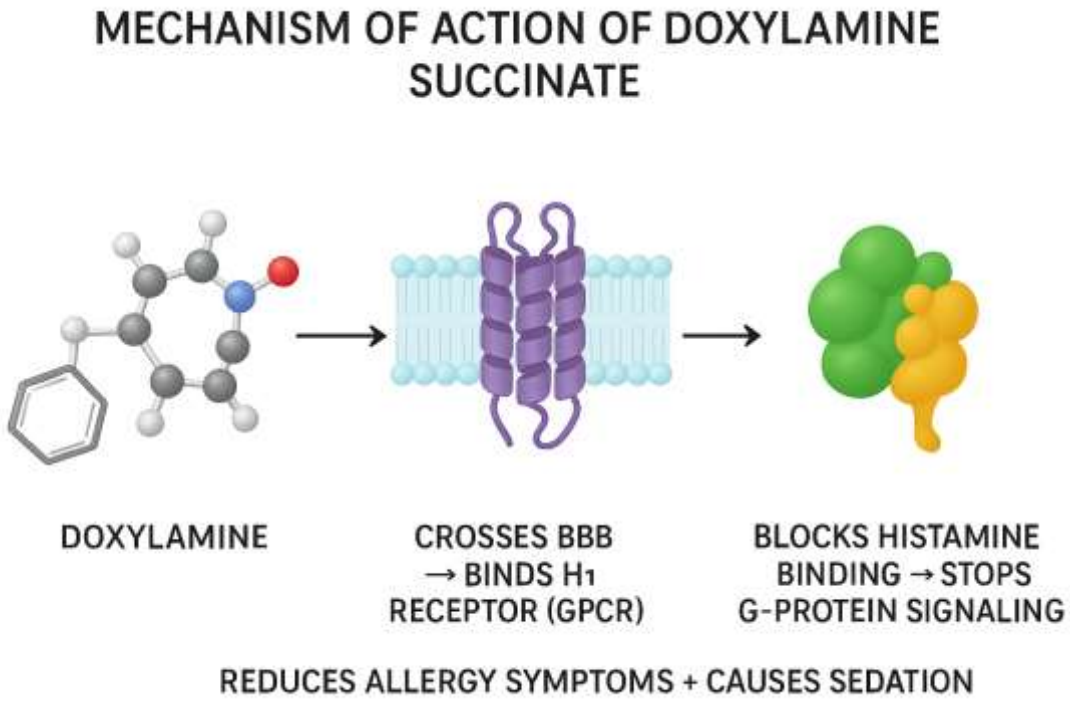
Doxylamine succinate is a pyridine derivative H-antagonist having sedative properties..



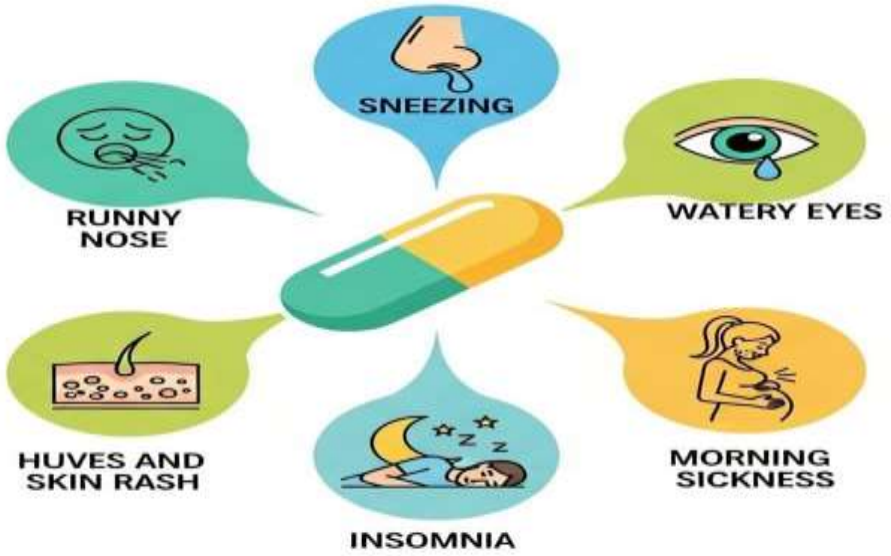
Structure of Doxylamine Succinate

Mechanism of action

Doxylamine shows antihistaminic and sedative effects because it acts as an antagonist of the H,-receptors. It also slightly antagonizes the muscarinic acetylcholine receptors.

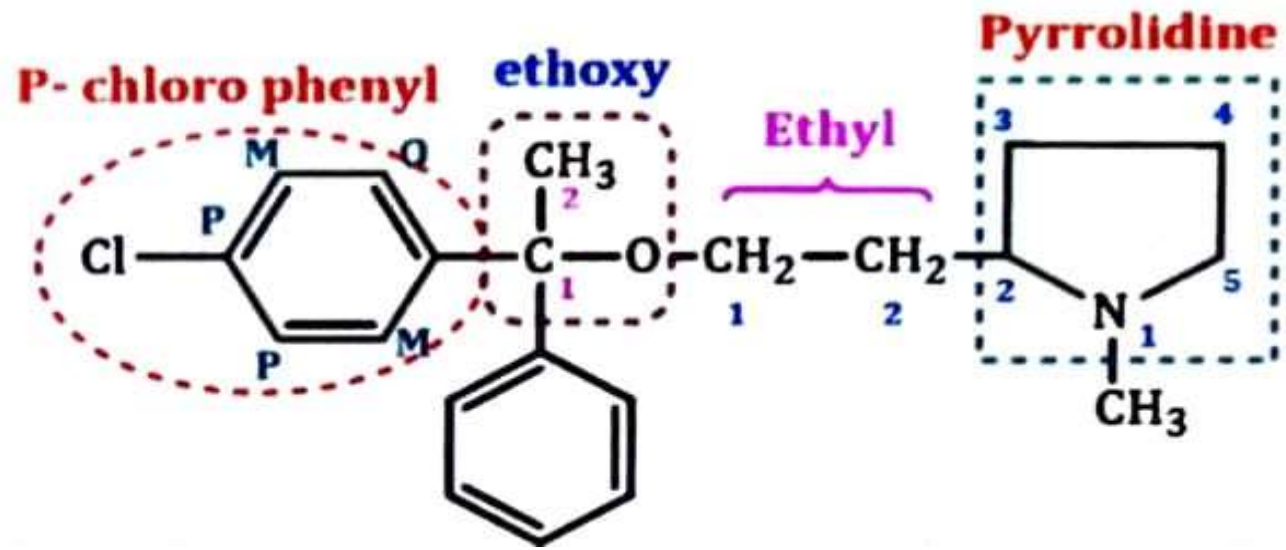


Uses


SNEEZING
RUNNY NOSE
WATERY EYES
HUVES AND SKIN RASH
INSOMNIA
MORNING SICKNESS

4.Clemastine Fumarate

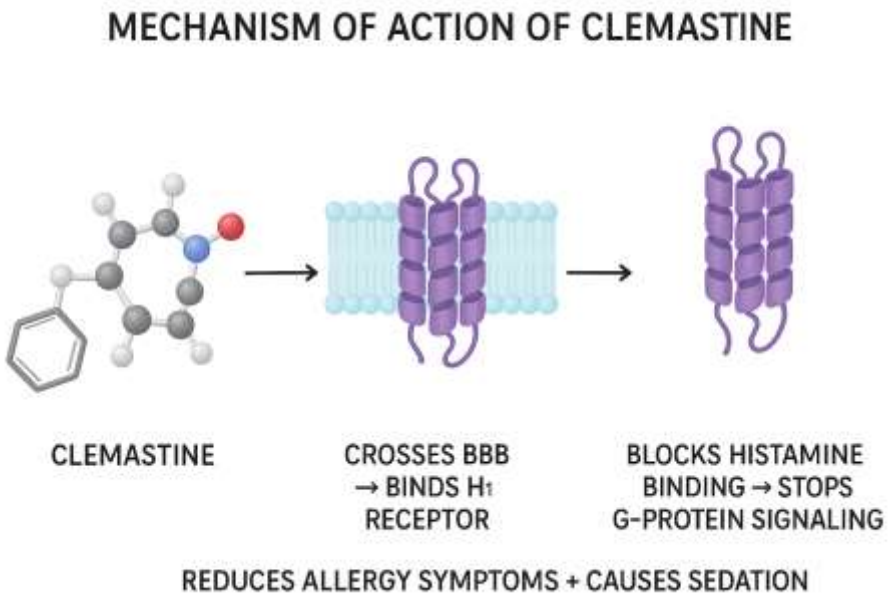
Clemastine fumarate is the fumaric acid salt of clemastine.



Structure of Clemastine fumarate

Mechanism of action

Clemastine selectively binds H,-receptor and blocks the action of histamine



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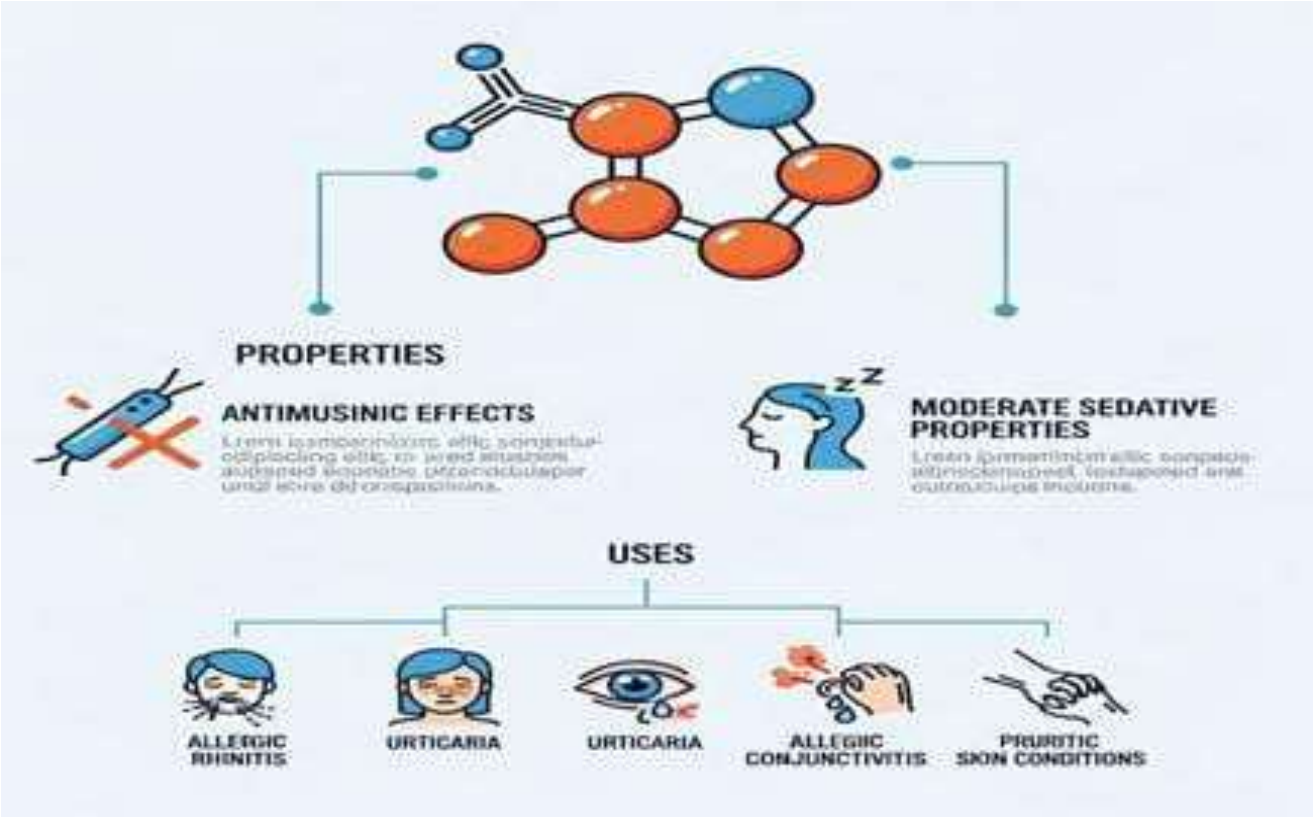
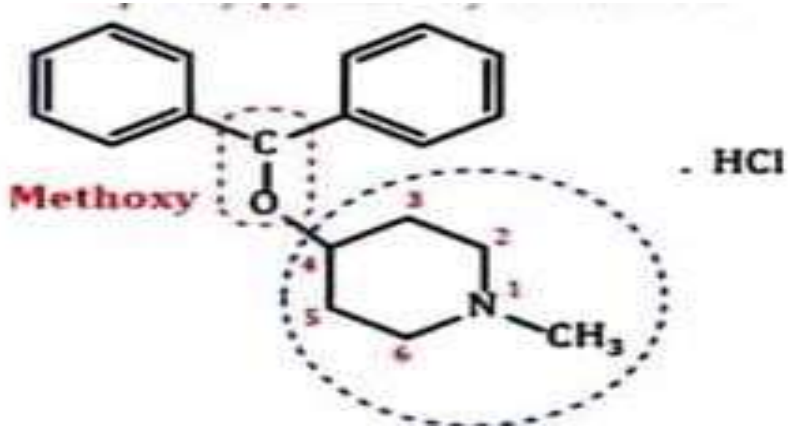

PROPERTIES
ANTIMUSINIC EFFECTS
MODERATE SEDATIVE PROPERTIES
USES
ALLERGIC RHINITIS
URTICARIA
URTICARIA
ALLERGIC CONJUNCTIVITIS
PRURITIC SKIN CONDITIONS

5. Diphenylpyraline hydrochloride

It is structurally related to diphenhydramine with the Amino alkyl side chain incorporated in a piperidine ring.

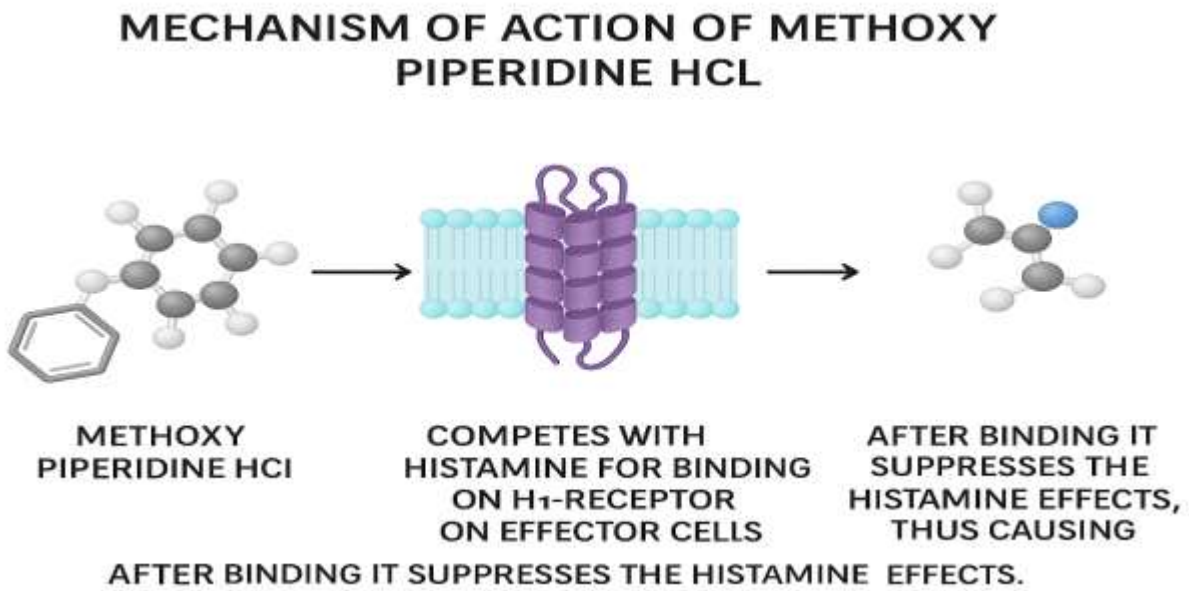
It is a potent antihistaminic agent



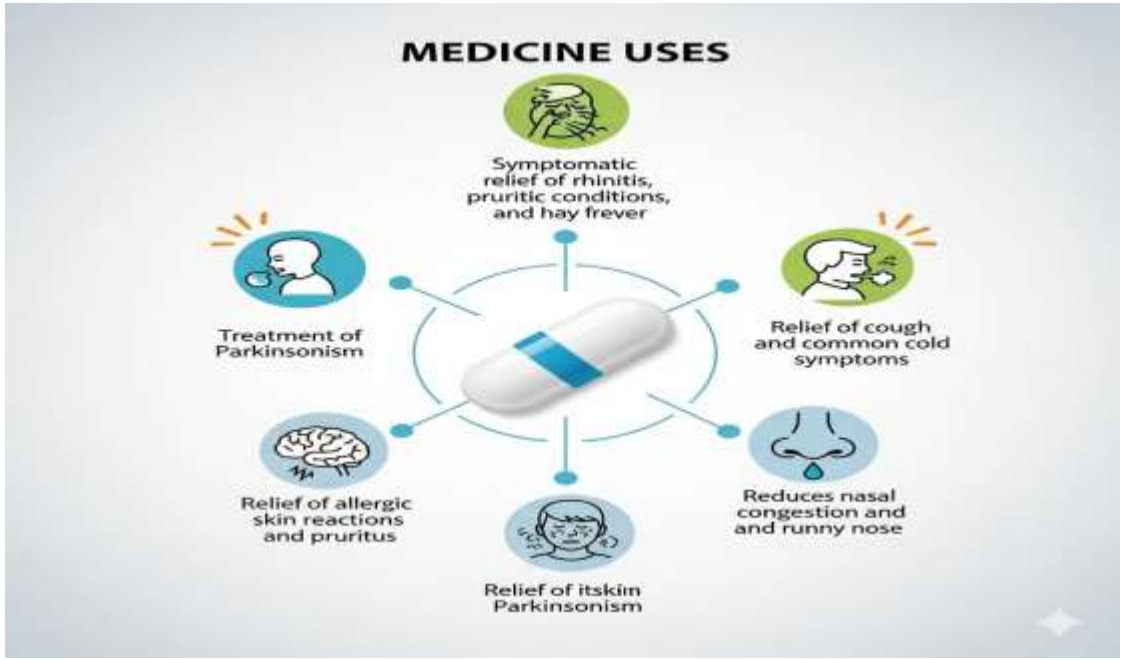
Structure of Diphenylpyraline hydrochloride

Mechanism of action

Methoxy Piperidine HCl , It competes with histamine for binding on the H,-receptor on effector cells. After binding it suppresses the histamine effects, thus causing temporary relief of the allergic symptoms.

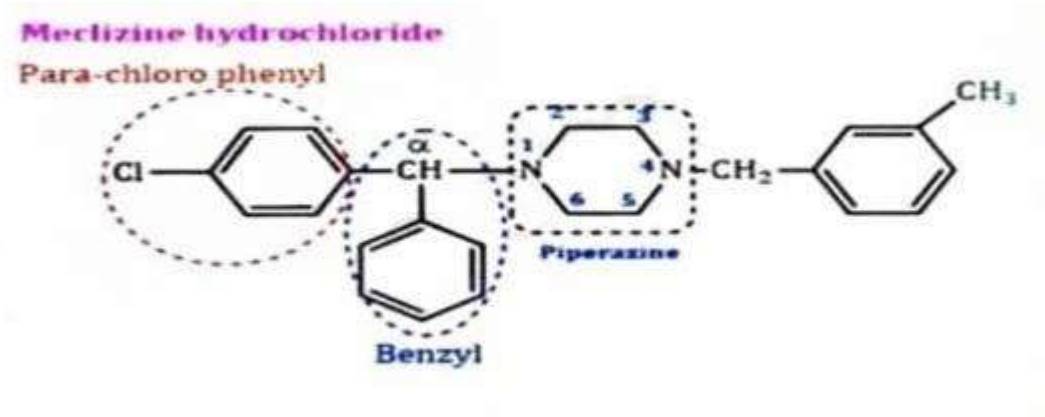


Uses


MEDICINE USES
Symptomatic relief of rhinitis, pruritic conditions, and hay frever
Treatment of Parkinsonism
Relief of cough and common cold symptoms
Relief of allergic skin reactions and pruritus
Reduces nasal congestion and and runny nose
Relief of itskin Parkinsonism

6.Meclizine hydrochloride

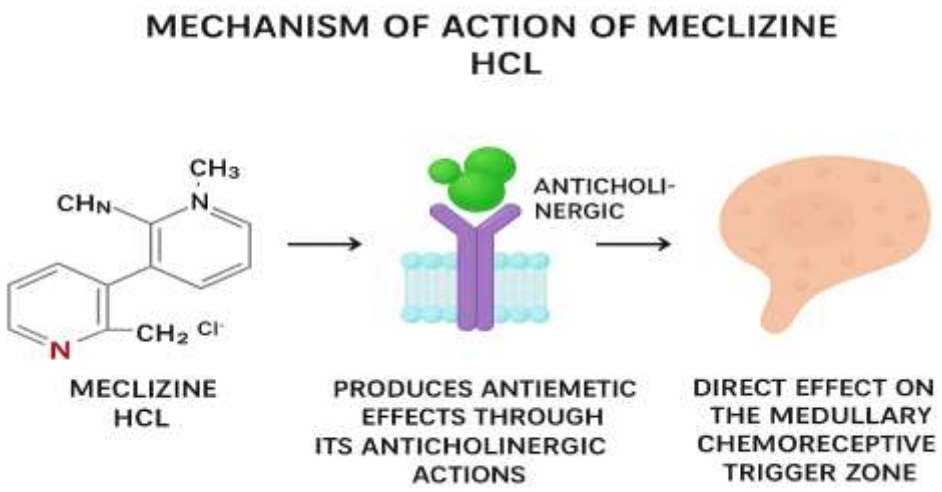
It is a synthetic piperazine having anti-emetic, sedative and H antagonistic properties.



Structure of Meclizine hydrochloride

Mechanism of action

Meclizine hydrochloride Para-chloro phenyl -CHN Benzyl CH, N-CH, Piperazine " It produces antiemetic effects through its anticholinergic actions or by direct effect on the medullary chemoreceptive trigger zone



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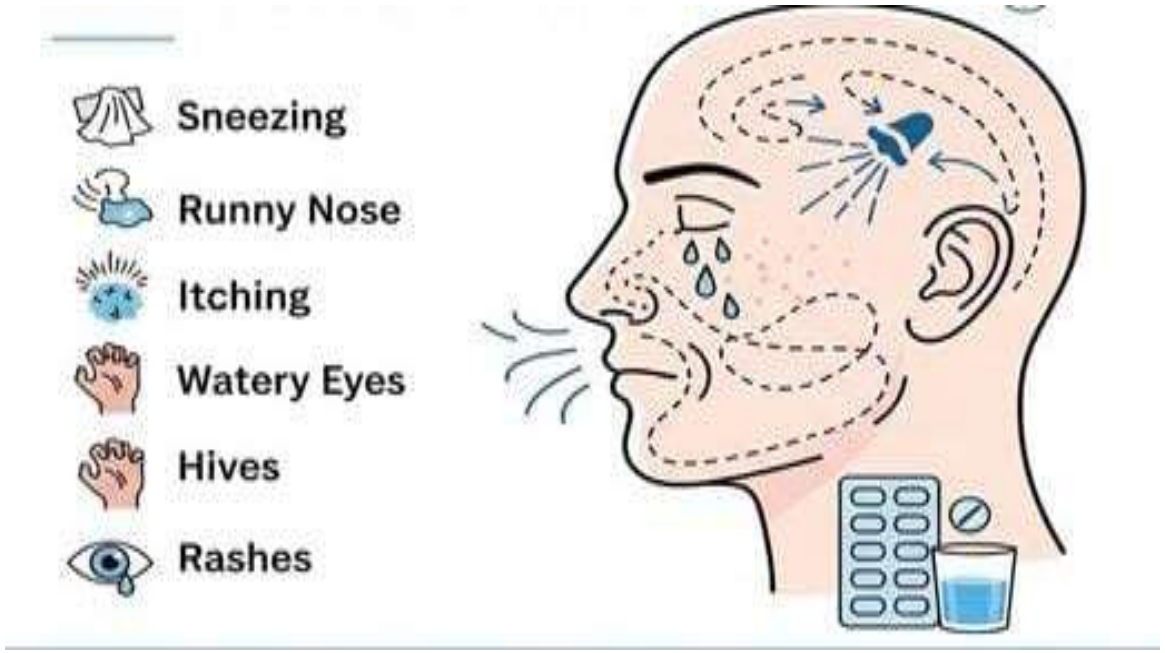


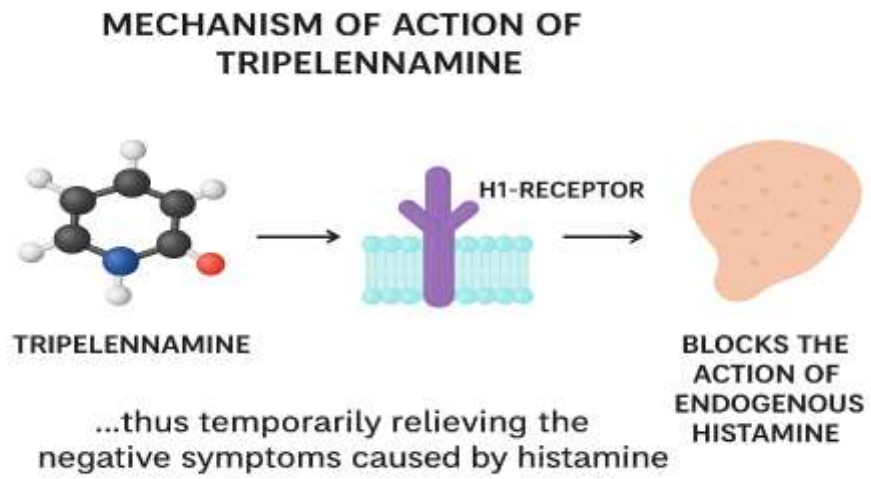
Chlorcyclizine hydrochloride

Chlorcyclizine is a first generation antihistamine belonging to phenylpiperazine class.

Structure Chlorcyclizine hydrochloride

Mechanism of action

Tripelennamine binds to the H,-receptor and blocks the action of endogenous histamine, thus temporarily relieving the negative symptoms caused by histamine.



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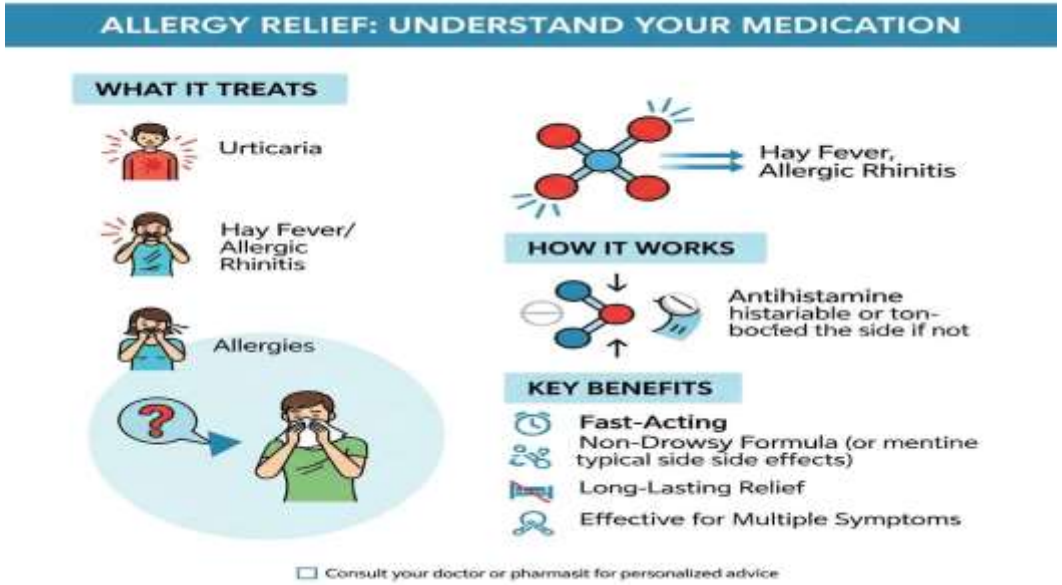
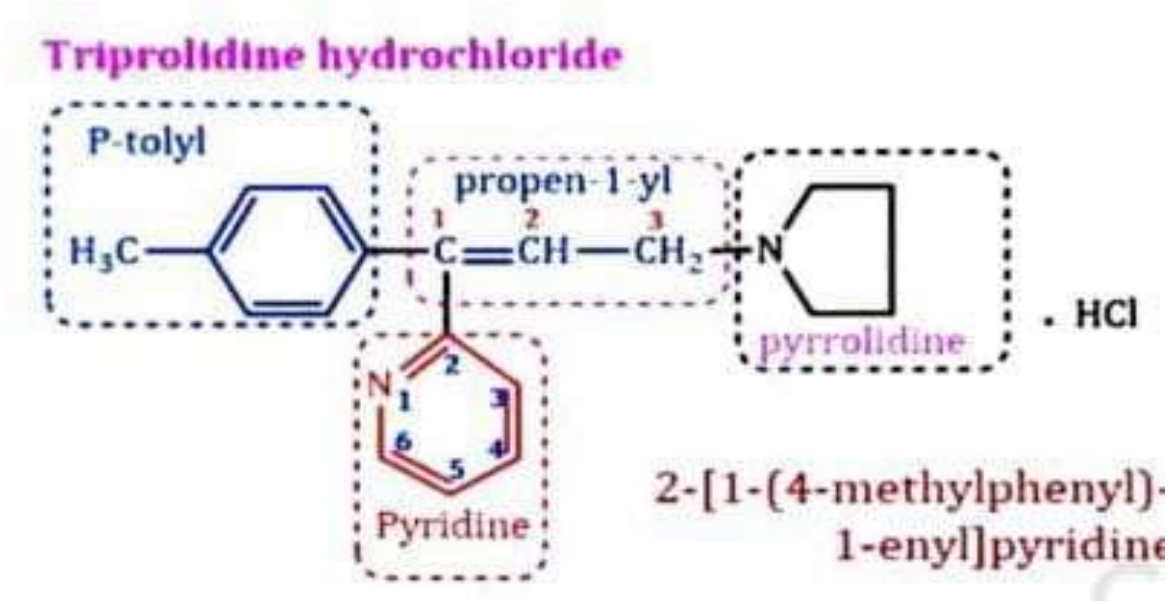

ALLERGY RELIEF: UNDERSTAND YOUR MEDICATION
WHAT IT TREATS
Urticaria
Hay Fever/ Allergic Rhinitis
Allergies
Hay Fever, Allergic Rhinitis
HOW IT WORKS
Antihistamine histariable or ton- bocfed the side if not
KEY BENEFITS
Fast-Acting
Non-Drowsy Formula (or mentine typical side side effects)
Long-Lasting Relief
Effective for Multiple Symptoms
Consult your doctor or pharmasit for personalized advice

Triprolidine hydrochloride

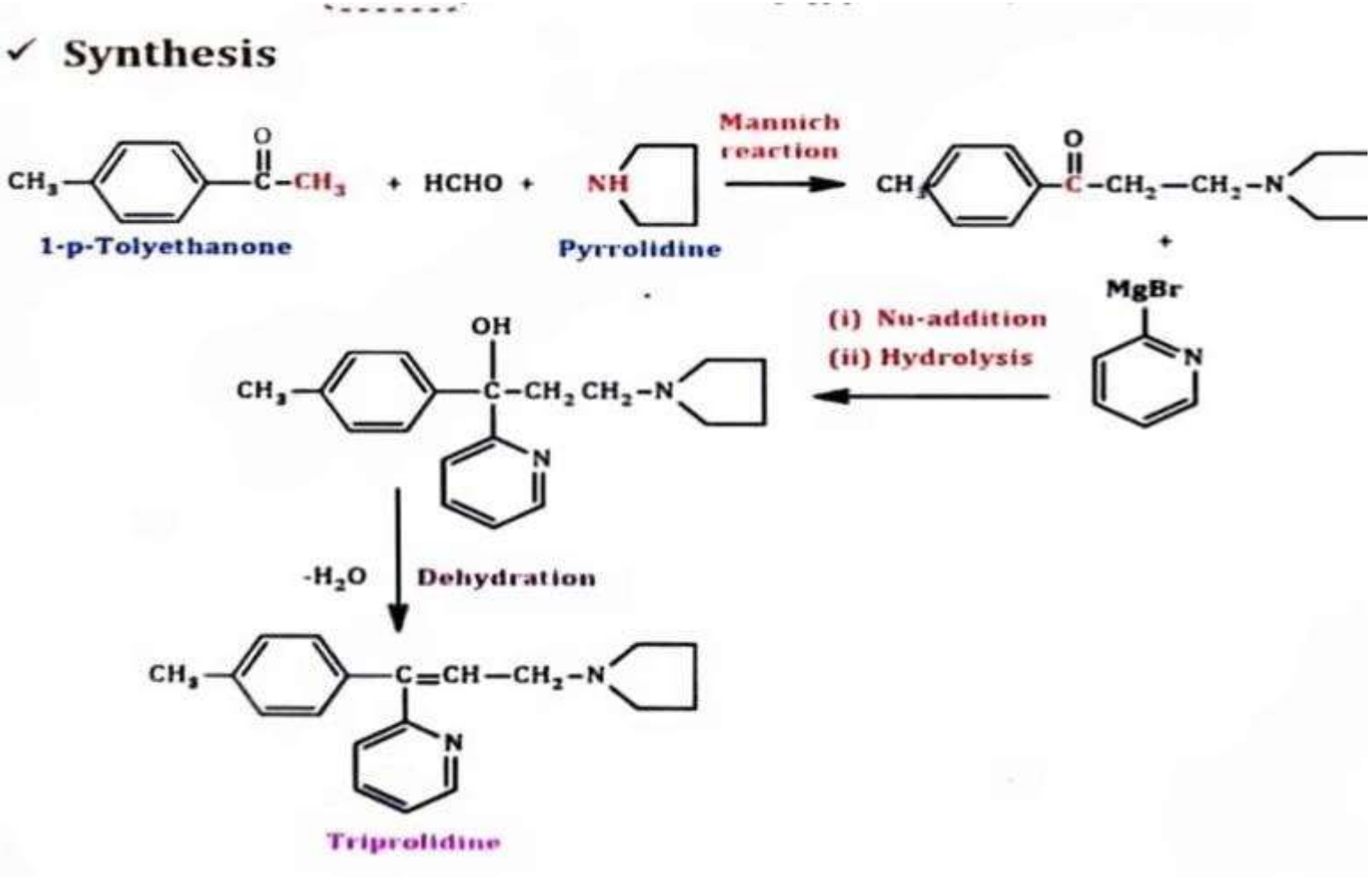
It is a sedating antihistamine combined with pseudoephedrine and guaifenesin in various types of cold and allergy medications to relieve allergy symptoms, and to aid in sleep



Structure of Triprolidine hydrochloride

Synthesis of Triprolidine hydrochloride

✓ **Synthesis**



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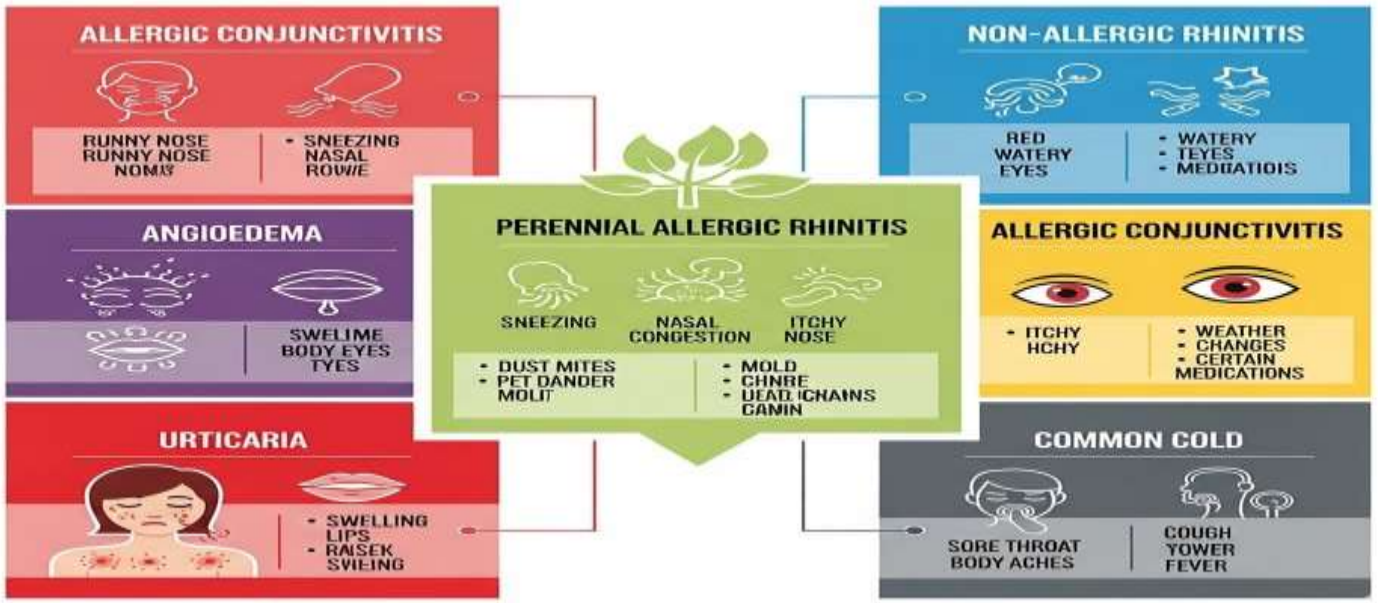
ALLERGIC CONJUNCTIVITIS
RUNNY NOSE
RUNNY NOSE
NOMS
- SNEEZING
NASAL
ROWIE
NON-ALLERGIC RHINITIS
RED
WATERY
EYES
- WATERY
- TEYES
- MEDIATIOIS
ANGIOEDEMA
SWELIME
BODY EYES
TYES
PERENNIAL ALLERGIC RHINITIS
SNEEZING
NASAL
CONGESTION
ITCHY
NOSE
- DUST MITES
- PET DANDER
MOLIT
- MOLD
- CHNRE
- UEAD ICHAINS
CAMIN
ALLERGIC CONJUNCTIVITIS
- ITCHY
HCHY
- WEATHER
- CHANGES
- CERTAIN
MEDICATIONS
URTICARIA
- SWELLING
LIPS
- RAISEK
SVIEING
COMMON COLD
SORE THROAT
BODY ACHES
COUGH
YOWER
FEVER


Thank You!