MEDICINAL CHEMISTRY - II

UNIT 1 NOTES

- ANTIHISTAMINIC AGENTS
- PROTON PUMP INHIBITORS
- ANTINEOPLASTIC AGENTS

IMPERFECT PHARMACY

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ANTIHISTAMINIC AGENTS

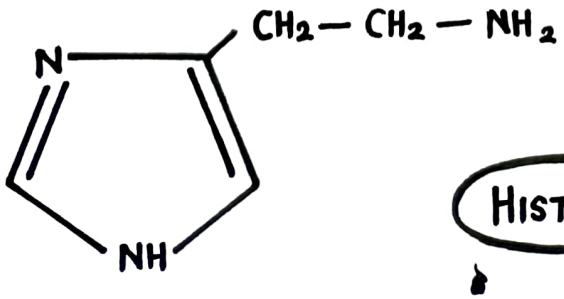
- Antihistaminic Agents, more commonly known as Antihistamines, are class of drugs used primarily to treat allergic reactions.
- They work by blocking the action of Histamine, a chemical in the body that is involved in allergic reactions.
- Histamine is released by immune system in response to allergens and is responsible for many of the symptoms associated with allergies such as itching, swelling and mucus production.

HISTAMINE

- Histamine is a type Amine Autacoid that plays several crucial roles in our body.
- It acts as a local hormone, act near the site of synthesis.
- It is stored in inactive form in granules of Mast Cells & Basophills and released upon activation.

CHEMICAL NATURE

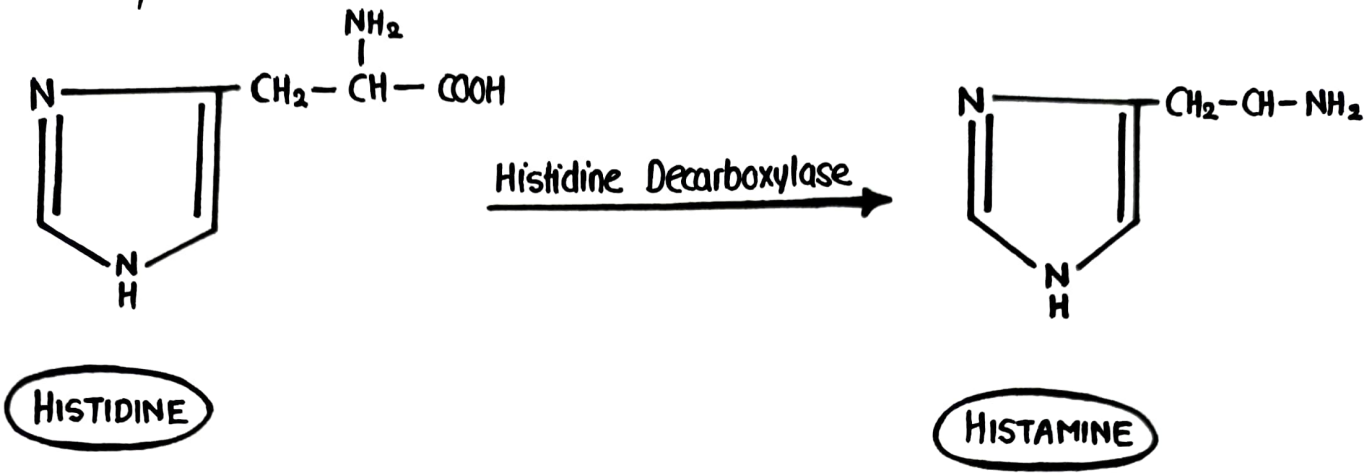
- Histamine is an organic nitrogenous compound with formula $C_5H_7N_3$
- It composed of an Imidazole Ring & Ethylamine side chain.



HISTAMINE

SYNTHESIS

Histamine is derived from amino acid Histidine through a process a process called Decarboxylation, catalyzed by enzyme Histidine Decarboxylase.



HISTIDINE

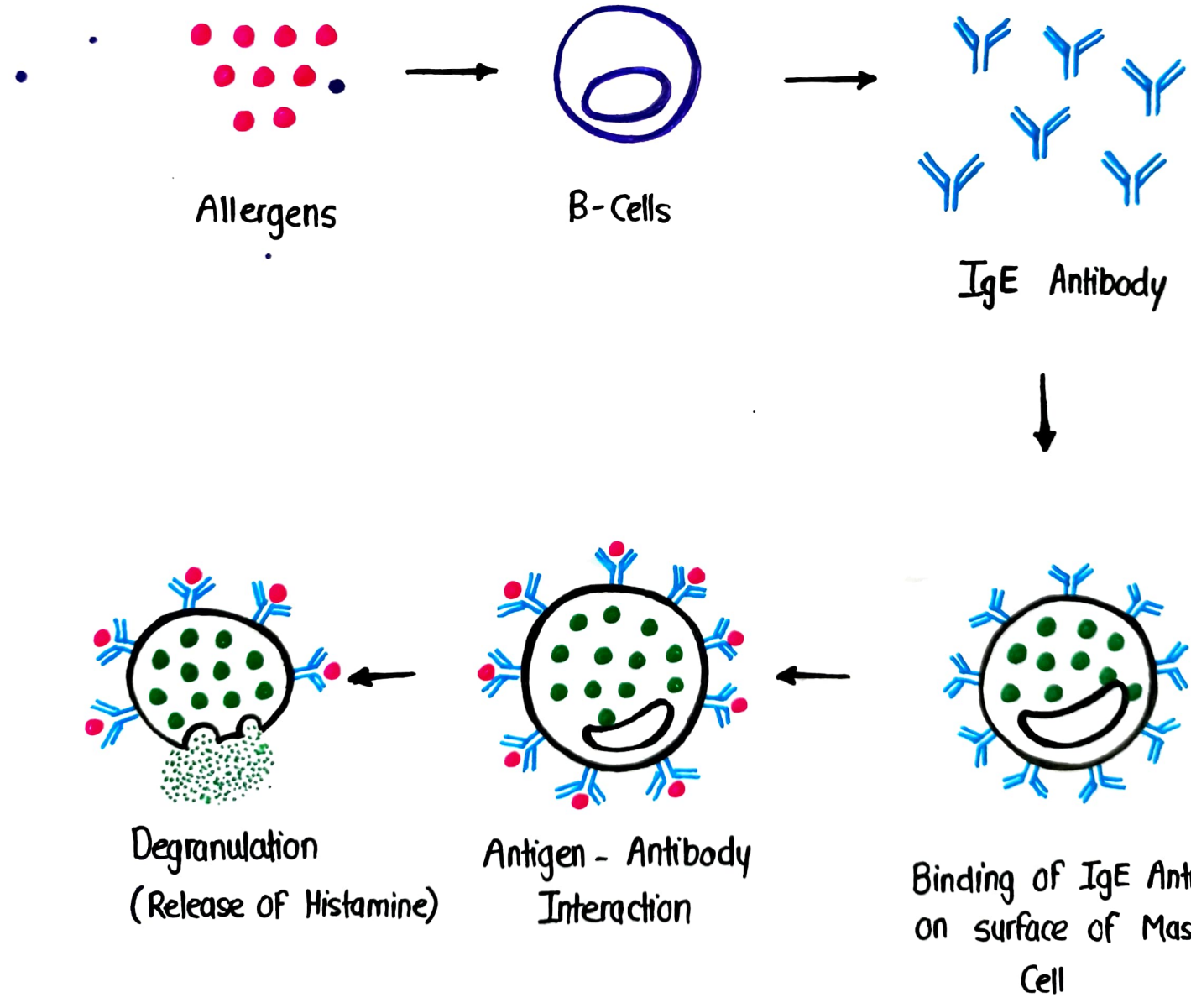
HISTAMINE

STORAGE

- Histamine is stored in the body primarily within Mast Cells and Basophills.
- It is stored in the granules of Mast Cells & Basophills.
- These granules are membrane bound vessicles that also contain other chemical mediators involved in inflammatory responses.
- It is stored in Mast Cells in complex with 'Heparin' while in basophills stored in complex with 'Chondrotin'.
- Tissues that are rich in Histamines are skin, gastric and intestinal mucosa, lungs, liver, placenta & neurons of CNS.
- In stomach, Histamine is stored in Enterochromaffin - like cells (ECL Cells) that are found in gastric mucosa.
- In CNS, it is synthesized and released by specific neurons in brain as neurotransmitters.

Release Mechanism

- Histamine is released from Mast Cells & Basophills through a process called Degranulation.
- The process typically occurs in responses to an allergen or other immune triggers.
- In allergic reactions, Histamine is often released by triggers such as binding of allergen to IgE antibodies that are attached to the surface of Mast Cells & Basophills.



Histamine Receptors

	Location	Receptor	Effect
H_1	Throughout the body, specially in smooth muscles, vascular endothelial cells, Heart, CNS	Gi-Protein linked to intracellular Gq that activates Phospholipase C	Increased Vascular Permeability Bronchoconstriction, Increased Gut Motility
H_2	In more specific locations in the body mainly in gastric parietal cells, a low level can be found in vascular smooth muscles, Neutrophills, CNS, Heart, Uterus	Gi-Protein linked to intercellular Gs that stimulates Adenylcyclase and increases cAMP	Increase in Gastric Acid Secretion, Vasodilation
H_3	Found mostly in the CNS, with a high level in the thalamus, caudate nucleus & cortex, also a low level detected in small intestine, testis and prostate.	Gi-Protein possibly to intercellular Gi	Inhibit the synthesis and release of Histamine
H_4	Thymus Gland, Small intestine, Spleen Colon, Bone Marrow, Basophills	Unknown, Most likely also GPCR	Immune System Regulation

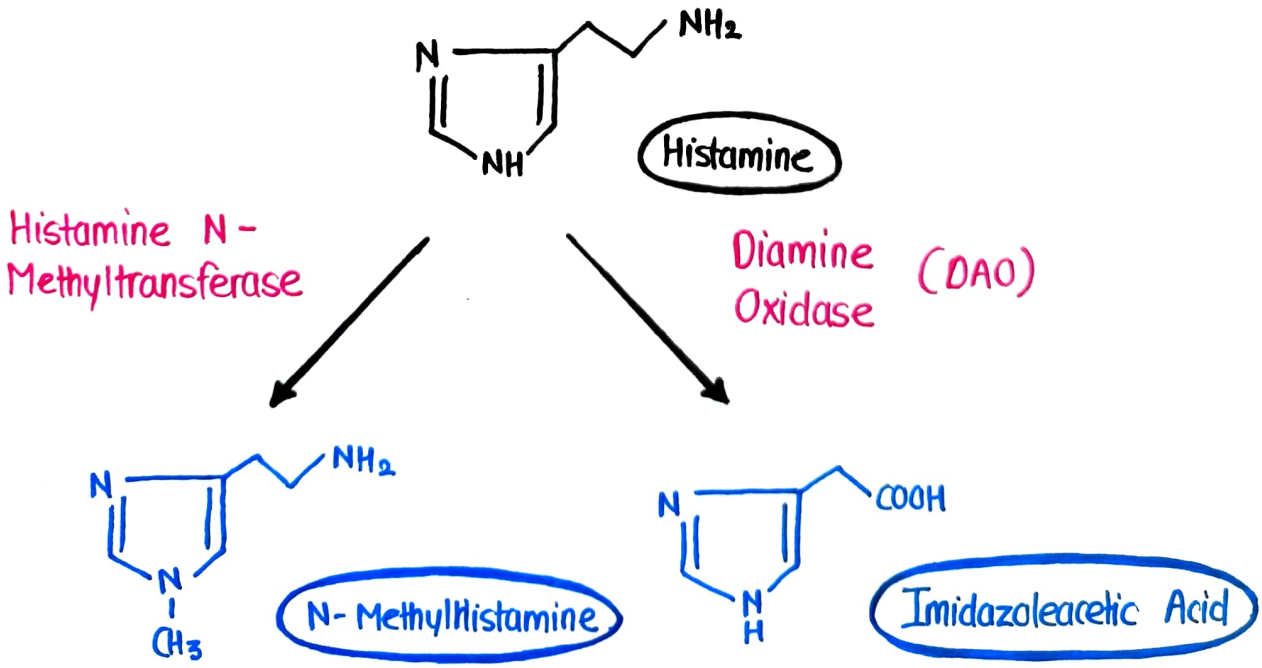
Action Of Histamines

- As immune response it cause several symptoms such as itching, swelling & increased mucus production.
- Histamine cause blood vessels to dilate & become more permeable This results in increased blood flow to the affected area, which helps immune cells reach the site of infection or injury more efficiently
- It also leads to bronchoconstriction.
- In stomach it stimulates parietal cells to secrete gastric acid.
- In brain it acts as neurotransmitter and involved in regulating sleep-wake cycles, apetite & cognitive functions.

Histamine Metabolism

Histamine Metabolism occurs in the body through two major pathways:

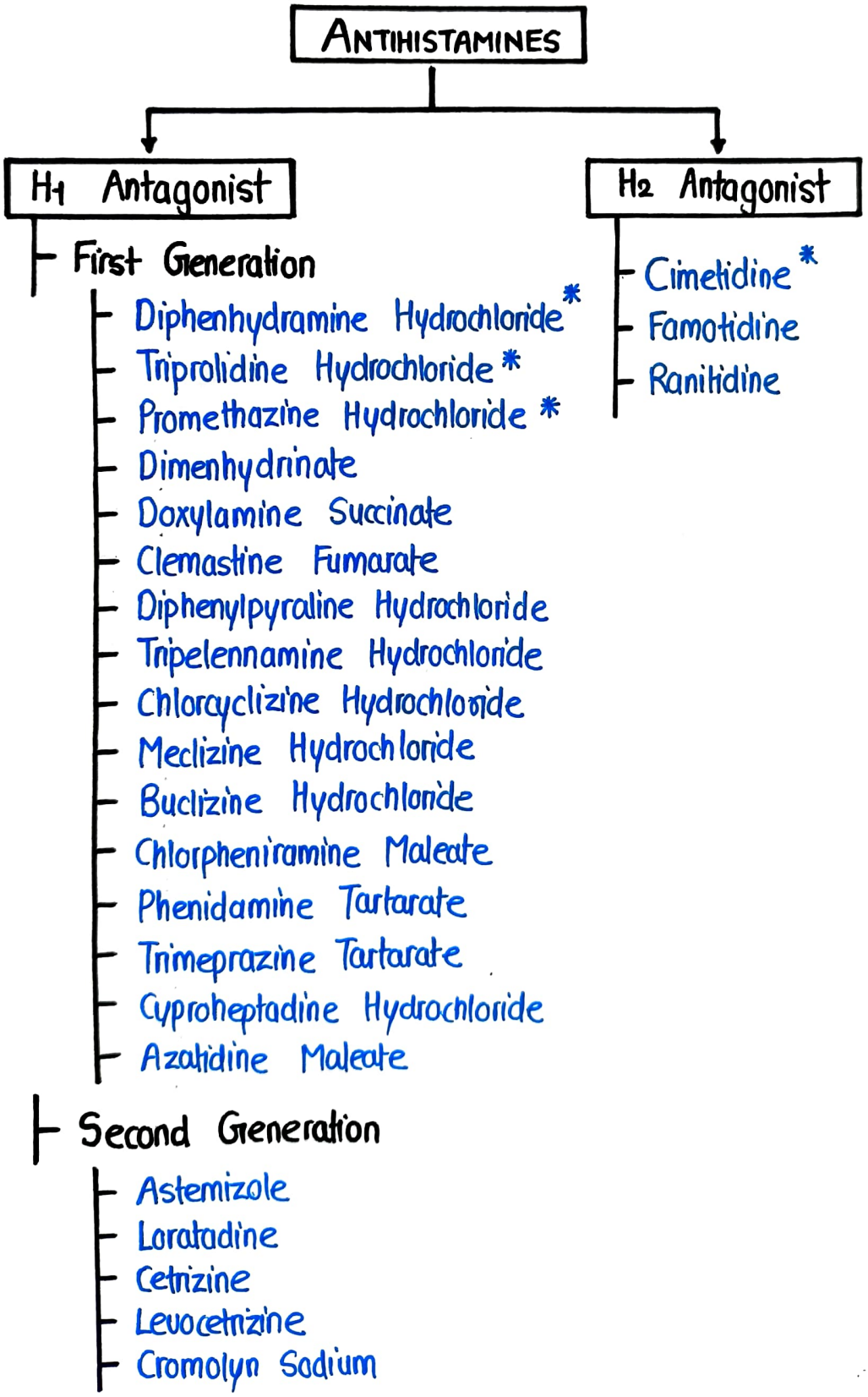
- Oxidation : By diamino Oxidase (DAO) to produce Imidazole Acetic Acid
- Methylation : By Histamine N-Methyltransferase to produce N-MethylHistamine.



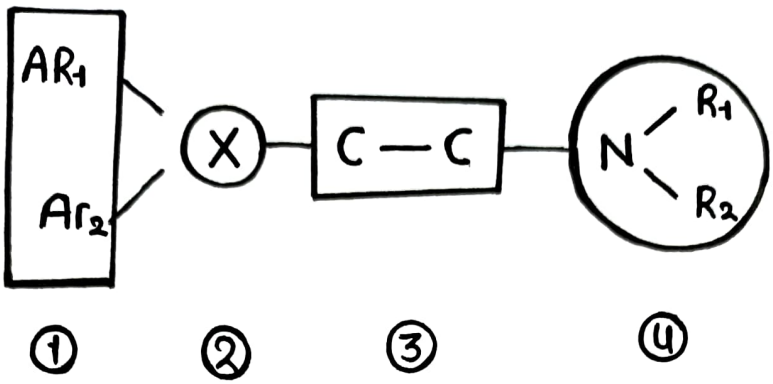
Classification Of Antihistamines

Antihistaminic Drugs can be mainly classified into two types :

① H_1 Antagonist
② H_2 Antagonist



SAR Of Antihistamines



The general structure of Antihistamines consist of :

① An Aryl Group (Ar_1, Ar_2)
② Connecting Atom (X)
③ Alkyl Group (C-C)
④ Terminal Nitrogen Atom ($N<^{R_1}_{R_2}$).

Aryl Groups

- Diaryl substitution is essential for significant H_1 affinity.
- The maximum antihistaminic activity depends upon co-planarity of two aryl substitution.

① Ar_1 : Generally Phenyl or Heteroaryl group like 2-Pyridyl
② Ar_2 : Generally Aryl or Aryl Methyl Group

Connecting Atom

In the structure of Antihistamines the X can be :

- X = O (Amino Alkyl Ether Derivative)
- X = N (Ethylene - Diamene Derivative)
- X = C (Mono - Amino Propyl Analogue)

Alkyl Group

- The carbon chain in Antihistaminic Drugs consist of two or maximum 3 carbon atoms
- Most of the ~~carbon atoms~~ in Antihistamines have Ethylene Chain
- Branching of this carbon chain leads decrease in Antihistaminic Activity (exception : Promethazine)

Terminal Nitrogen Atom

- The terminal N- atom should be a Tertiary amine for maximum activity.
- It can be a part of Heterocyclic Ring.
- Dimethyl Substitution has maximum Antihistaminic Activity.

H_1 ANTAGONIST

- These are the classical Antihistaminic Agents that blocks physiological effects of Histamine & used in Allergic Conditions.
- They block Histamine H_1 receptor in the body.
- H_1 Antagonist help reduce symptoms associated with Allergic reactions such as Itching, Sneezing & Runny Nose.
- H_1 Antagonist are often classified into two generations:

① First Generation H_1 Antagonists
② Second Generation H_1 Antagonists

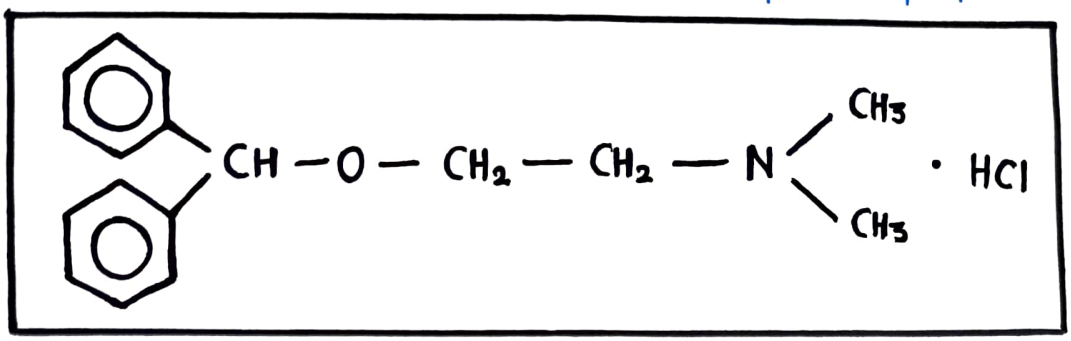
First Generation H_1 Antagonists

- These drugs include medications like Diphenhydramine and Chlorpheniramine.
- They can easily cross the Blood - Brain Barrier & may cause Drowsiness or Sedation as a side effect.
- These drugs includes:

① Diphenhydramine Hydrochloride *
② Triprolidine Hydrochloride *
③ Promethazine Hydrochloride *
④ Dimenhydrinate
⑤ Doxylamine Succinate
⑥ Clemastin Fumarate
⑦ Diphenylpyraline Hydrochloride
⑧ Tripelennamine Hydrochloride
⑨ Chlorcyclizine Hydrochloride
⑩ Meclizine Hydrochloride
⑪ Buclizine Hydrochloride
⑫ Chlorpheniramine Maleate
⑬ Phenidamine Tartarate
⑭ Trimeprazine Tartarate
⑮ Cyproheptadine Tartarate
⑯ Azatadine Maleate

① DIPHENHYDRAMINE HYDROCHLORIDE

Diphenhydramine is a first generation Antihistamine which is mainly used for treating seasonal allergies, but it also exhibits Antiemetic, Anti-Parkinson, Antitussive & Hypnotic properties.



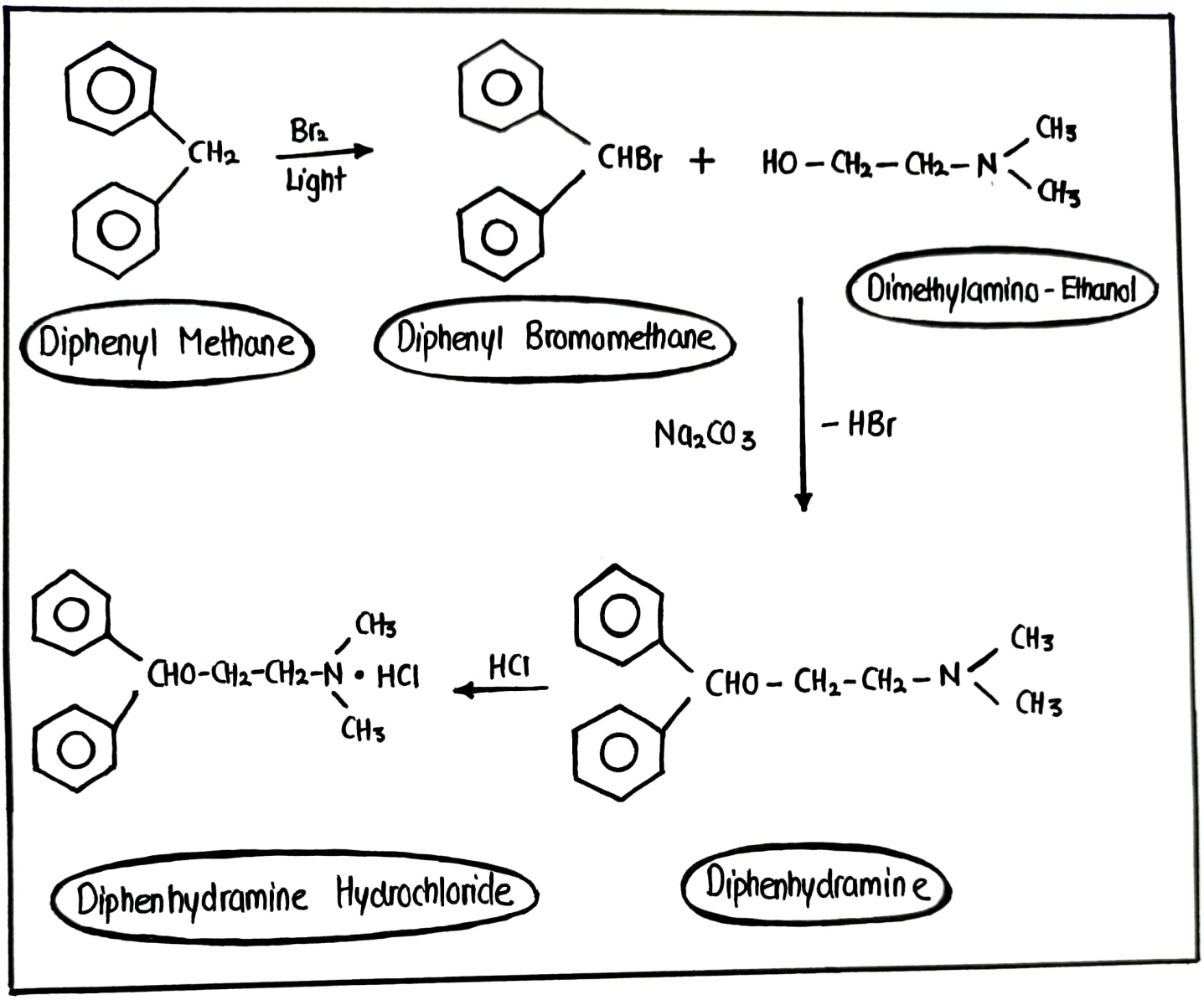
Mechanism of Action

- Diphenhydramine acts as a competitive Antagonist at H_1 Receptor.
- It reverse the effect of the Histamine on capillaries, reducing allergic reaction symptoms.
- It works on H_1- Receptors found on the respiratory smooth muscles, vascular endothelial Cells, GIT, Cardiac Tissue, Immune Cells, Uterus and CNS Neurons.

Properties

- It occurs as a white crystalline powder.
- It is soluble in water & alcohol.
- It is stored in well closed dark coloured light resistant container.
- It is well absorbed from GIT
- It is metabolized and secreted in Urine as Metabolite Conjugate.

Synthesis

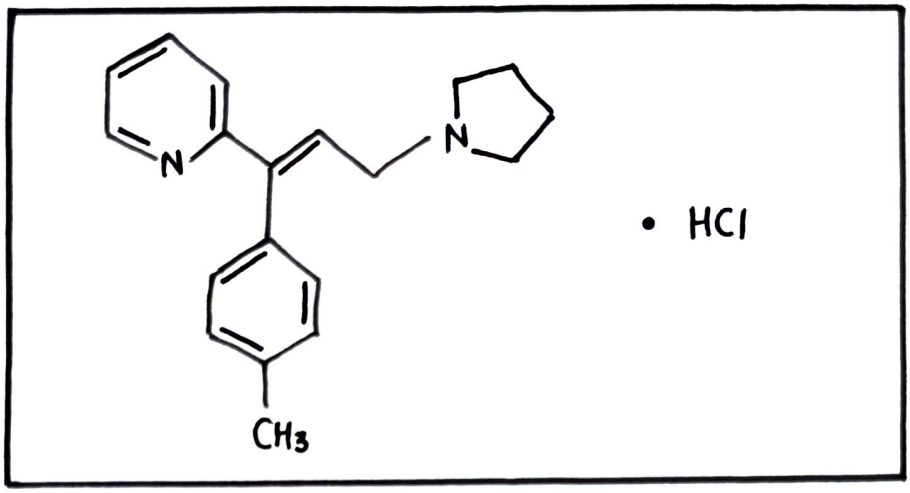


Uses

- It used for preventing and curing nausea, vomiting & dizziness caused by motion sickness.
- It can also be used as Antitussive, Antiparkinson & Sedative drug.
- It is used for treatment of allergies.
- It can also be used for treatment of Insomnia

② TRIPROLIDINE HYDROCHLORIDE

It is a sedating Antihistaminic drug used in various type of cold & allergy medications to relieve allergy symptoms and to aid in sleep



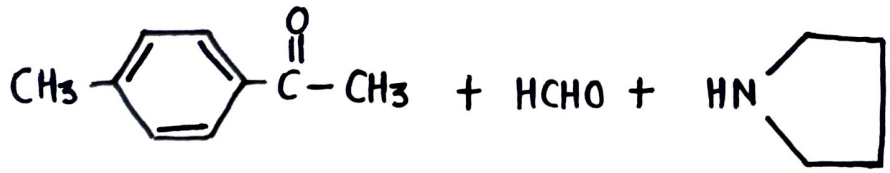
Mechanism Of Action

- Triprolidine hydrochloride binds to H_1 receptors and inhibits the action of Histamine, thus temporarily releasing the symptoms of Histamine
- It is absorbed by GIT, metabolised by carboxylation & excreted through urine

Properties

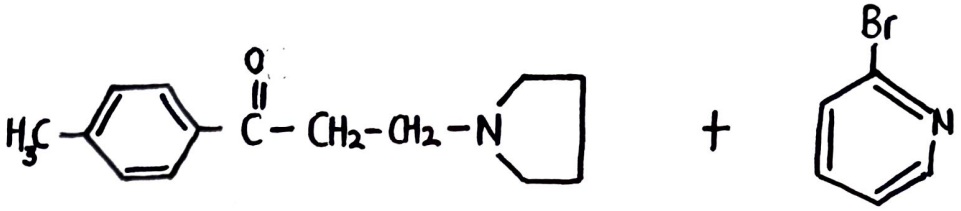
- It is white crystalline powder, insoluble in ether, soluble in water.
- It have unpleasant odour.
- Trans foom is more active.

Synthesis



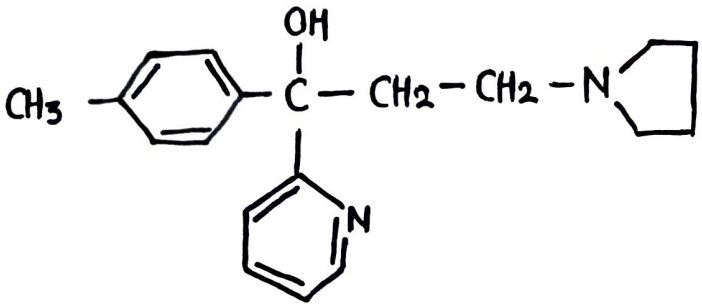
1- P- Tolyethanone + HCHO + Pyrrolidine

↓ Mannich Reaction

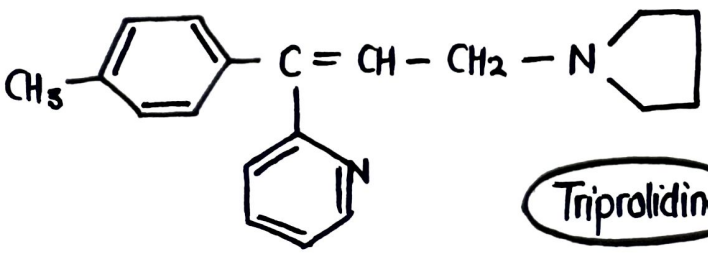


4'-methyl 3- Pyrrolidinopropiophenone + 2-Bromopyridine

↓ Li/H_2 Nu- Addition



↓ Dehydration



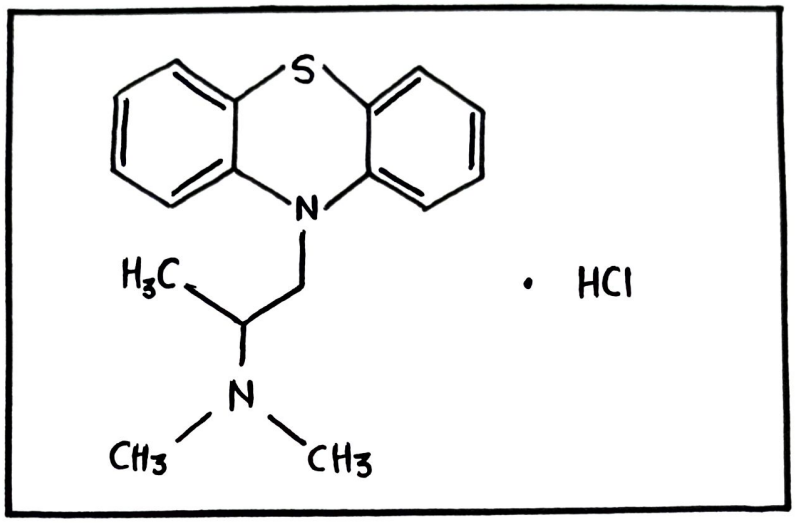
Triprolidine

Uses

- It is used for treatment of various allergic conditions.
- It also used in combination with cold drugs to get relief from Fever.
- It helps releive symptoms such as sneezing, runny nose, itchy or watery eyes & nasal congestion.
- It often used in combination with other drugs such as pseudoephedrine in treating symptoms related to cold and allergies.

③ PROMETHAZINE HYDROCHLORIDE

Promethazine Hydrochloride is the Hydrochloride salt form of promethazine, which is phenothiazine derivative having Antihistaminic sedative and antiemetic properties.



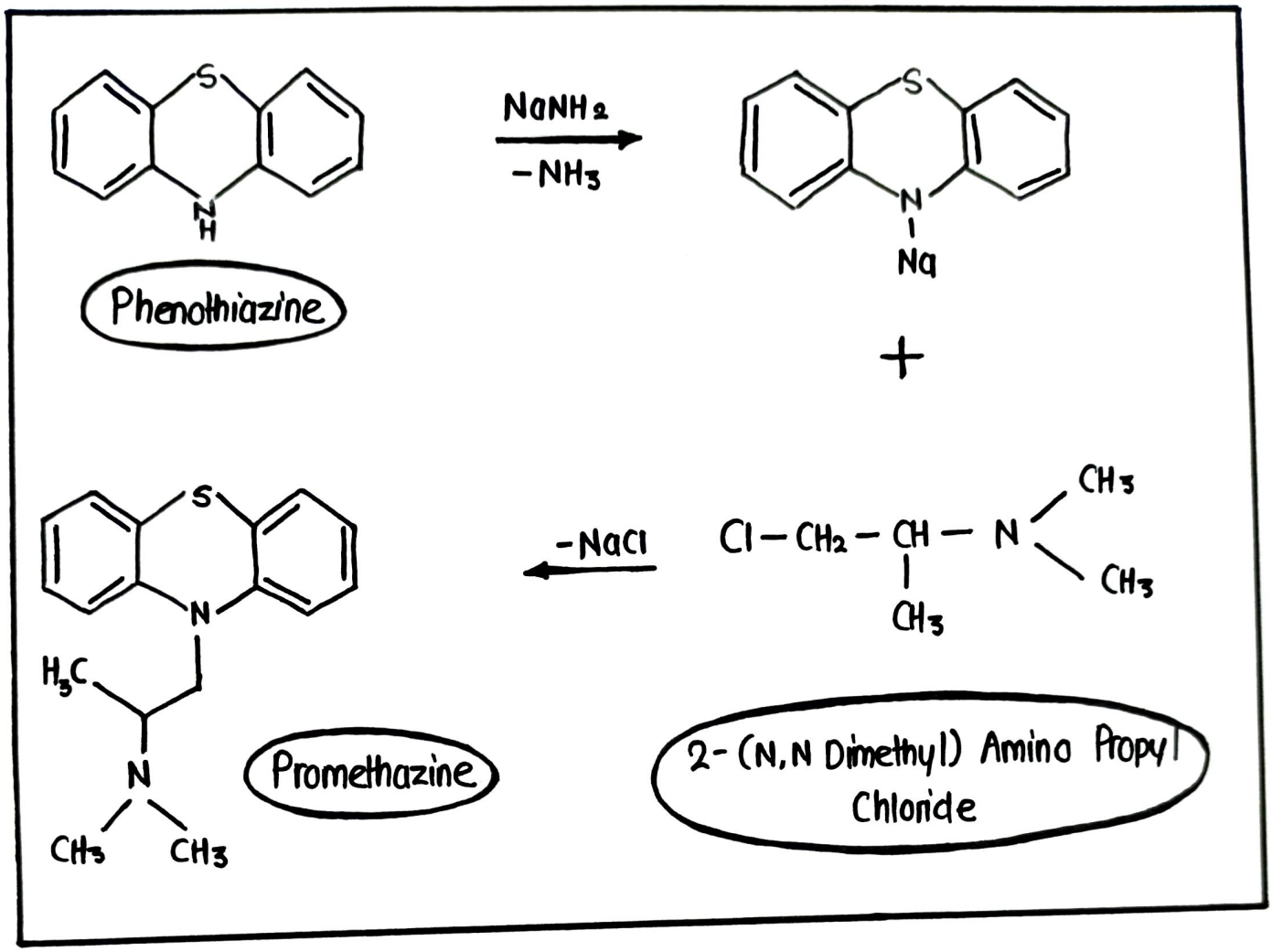
Mechanism Of Action

- It acts primarily as H_1 receptor antagonist and also have moderate Anticholinergic Activity.
- It also have weak to moderate affinity for Dopamine, Serotonin or adrenergic receptor as antagonist

Properties

- It is a white or pale yellow, crystalline powder
- It is soluble in water
- It is stored in well closed, Air tight, light resistant container.

Synthesis

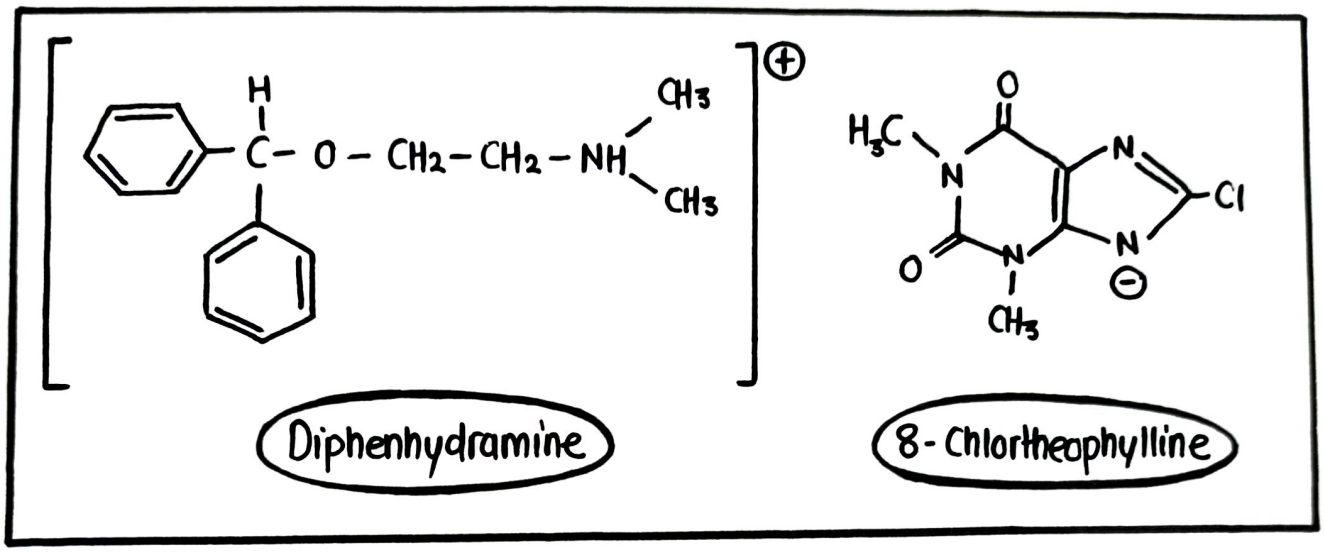


Uses

- It is used as sedative for treatment of insomnia.
- It can also be used as Antiemetic Agent.
- It is also used for Anaesthetic premedication through I.M. with ~~through~~ Atropine & meperidine.

④ DIMENHYDRINATE

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



Mechanism Of Action

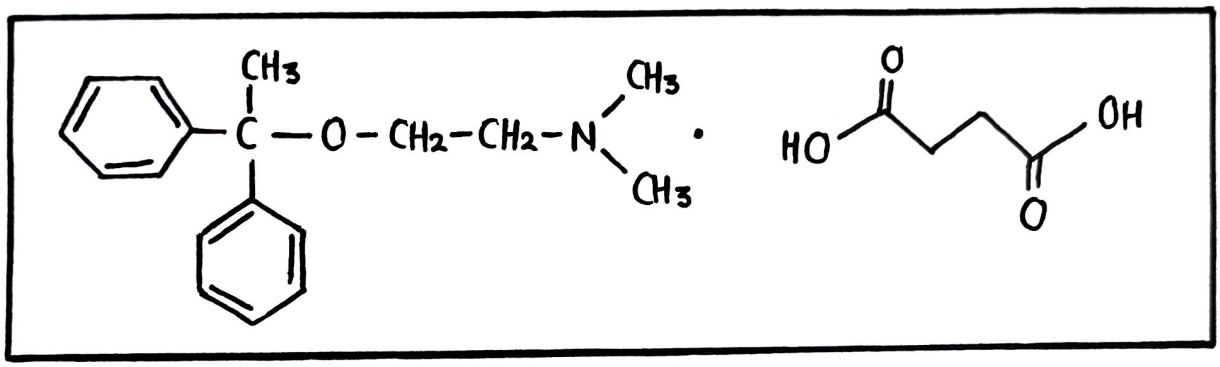
- The exact mechanism of Dimenhydrinate is not known.
- Its effect is probably due to H_1 Antagonism in vestibular system in brain
- It acts as a competitive antagonist of H_1 receptors found in Human Brain.

Uses

- It is used for preventing Motion Sickness, Nausea & Vomiting
- It helps in treatment of Ear Congestion
- It is used for vestibular disorders

⑤ Doxylamine Succinate

- Doxylamine Succinate is a pyridine derivative H_1 Antagonist having sedative properties.
- It completely blocks H_1 receptors & controls Allergic reactions.
- It also prevents pain and itching of skin & mucous membrane induced by Histamine



Mechanism Of Action

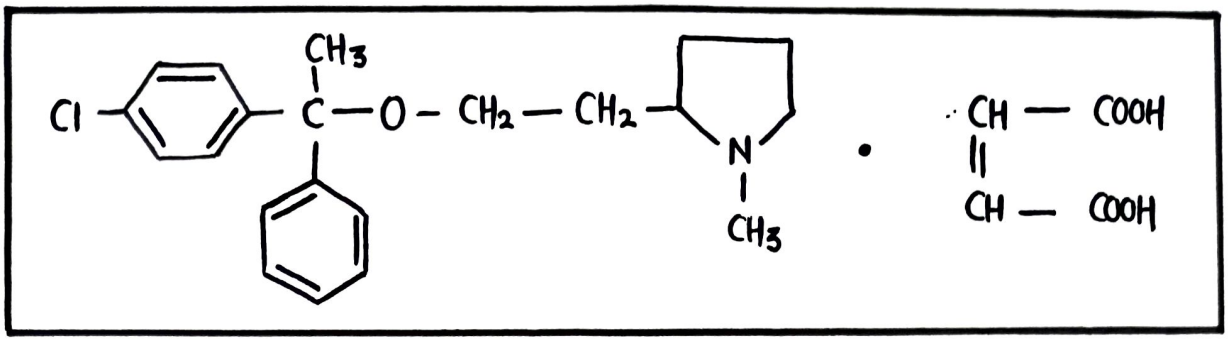
- It is a competitive antagonist of H_1 Receptor.
- It shows Antihistaminic and sedative effect
- It also slightly antagonises the Mascuranic Acetylcholine receptors

Uses

- It relieves the symptoms of Allergy, Fever & Common Cold.
- It relieves sneezing, runny nose, watery eyes & skin rash.
- It is used for treating insomnia.

⑥ CLEMASTINE FUMARATE

- Clemastine Fumarate is the Fumaric acid salt of Clemastine.
- It is an Antihistamine having Antimuscuranic & moderate sedative properties.



Mechanism Of Action

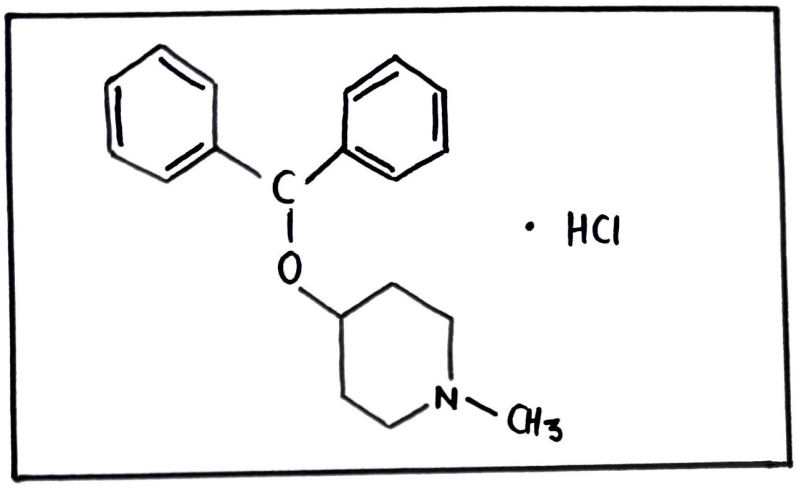
Clemastine is a selective H_1 Antagonist. It binds to H_1 Receptors and blocks the action of Histamine, thus temporarily releiving the negative symptoms caused by Histamine.

Uses

- It is an Antihistamine having Antimuscuranic & moderate sedative properties
- It is used for treatment of allergic conditions such as Conjuctivitis, urticaria etc.

⑦ Diphenylpyraline Hydrochloride

- It is an Antihistamine used for treating Allergy by competing with Histamine to bind to the H_1 receptor.
- It is a potent Antihistaminic Agent



Mechanism Of Action

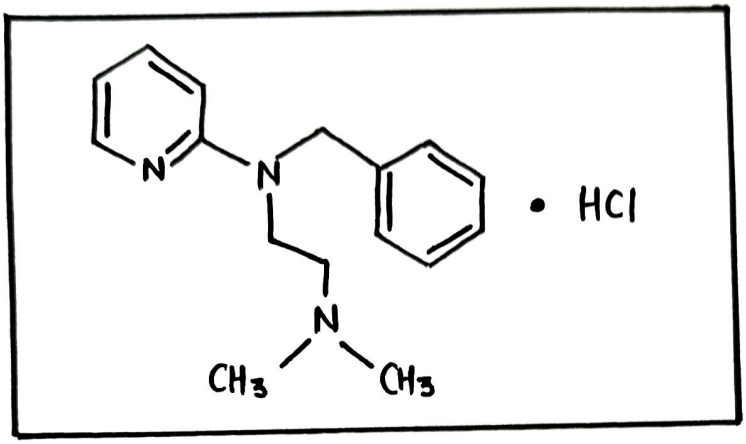
- It is used for treating Allergies as it competes with Histamine for binding on H_1 receptors on effector cells.
- After binding it suppresses the Histaminic effects, thus causing temporary relief from Allergic Symptoms.

Uses

- It is used for treating Allergic Rhinitis.
- It is also used for treatment of hay fever.
- It is used for treatment of allergic skin disorders.

⑧ TRIPELENNAMINE HYDROCHLORIDE

- Tripelennamine is an ethylenediamene derivative having Anti-Histaminergic property.
- Tripelennamine Hydrochloride is Hydrochloride salt of Tripelennamine.



Mechanism of Action

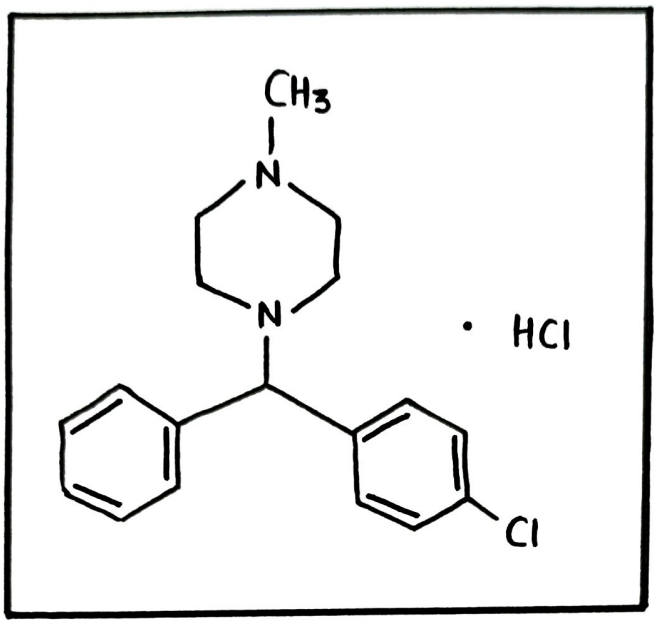
Tripelennamine binds to H_1 receptor & blocks the action of Histamine thus temporarily releiving the negative symptoms caused by Histamine.

Uses

- It treats the condition of Upper respiratory tract.
- It relelves sneezing, runny nose, itching, watery eyes, rashes and other symptoms of allergy & common cold.

⑨ CHLORCYCLIZINE HYDROCHLORIDE

Chlorcyclizine is a first generation Antihistamine belonging to Phenylpiperazine Class



Mechanism Of Action

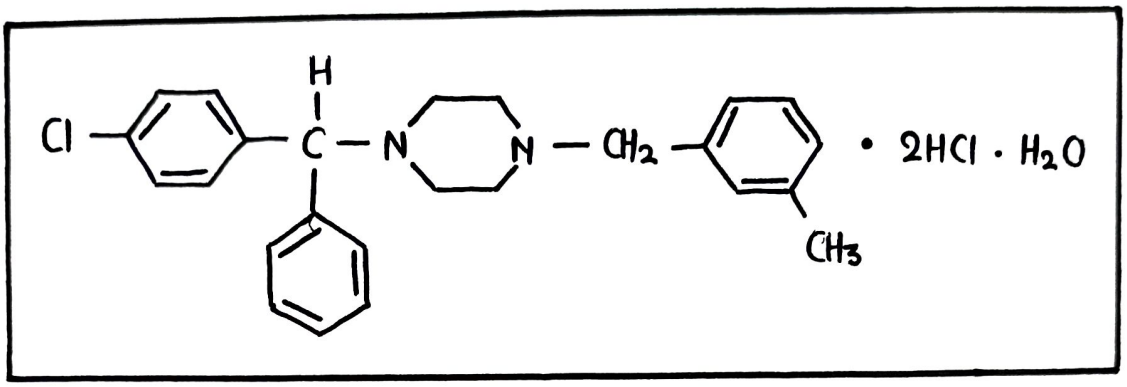
- Chlorcyclizine hydrochloride binds to H_1 receptor and blocks the action of Histamine.
- It also have some Antimascuranic activity.

Uses

- It is used for treatment of Allergic symptoms.
- It can also be used as Anticholinergic & Antiemetic Agent.

⑩ MECLIZINE HYDROCHLORIDE

Meclizine Hydrochloride is the Hydrochloride salt of Meclizine, which is a synthetic piperazine having Anti-emetic, sedative and H_1 antagonistic properties.



Mechanism Of Action

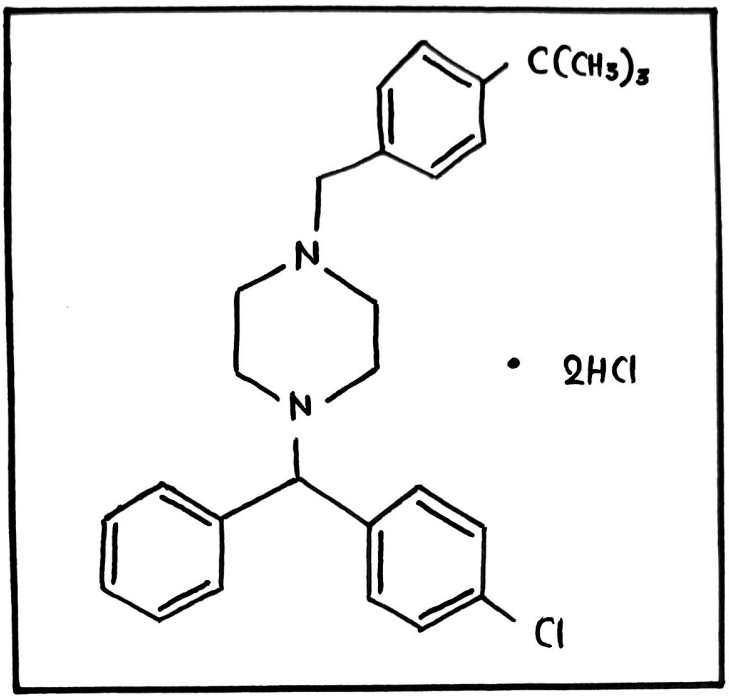
- Meclizine Hydrochloride inhibits the H_1 Receptors.
- It prevents Histamine actions on capillaries, Bronchial & Gastrointestinal smooth muscles.

Uses

- It is used for treating motion sickness.
- It is safely used in treatment of nausea in pregnancy.
- It is also used as Antiemetic, Local Anaesthetics.

(11) BUCLIZINE HYDROCHLORIDE

Buclizine Hydrochloride is the Hydrochloride salt form of Buclizine. It is a piperazine H_1 receptor antagonist.



Mechanism Of Action

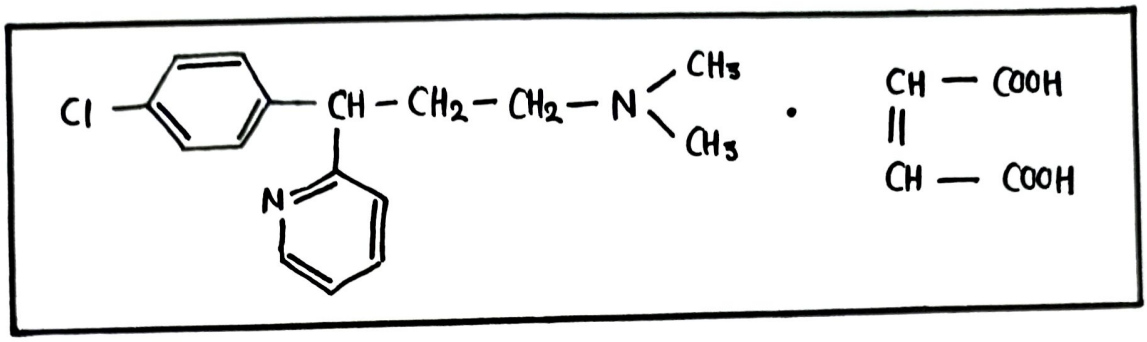
- Buclizine blocks the histamine receptors in the vomiting centers and decreases the activity along these pathways.
- Buclizine also has Anticholinergic properties and blocks the Muscuranic Receptors.

Uses

- It is highly lipid soluble and can cross blood brain barrier, so it is used as CNS Depressant.
- It is used as Antihistamine, Anti-Cholinergic & Local Anaesthetics

(12) CHLORPHENIRAMINE MALEATE

- Chlorpheniramine Maleate is a H_1 receptors Antagonist
- It is used in treatment of various Allergic Reactions.



Mechanism Of Action

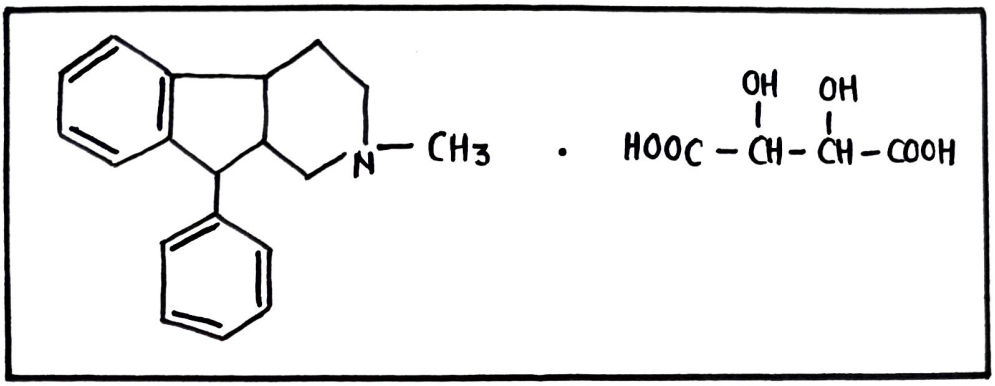
Chlorpheniramine is a typical H_1 - receptor antagonist and lead to temporary relief from the symptoms caused by Histamine.

Uses

- It is used for relieving the symptoms of Allergy, common cold rashes, watery eyes, itchy nose etc.
- It often used in combination with other drugs such as Hydrocodone, Phenylpropanolamine etc.

⑬ PHENIDAMINE TARTARATE

- Phenidamine Tartarate is a first generation Antihistamine drug.
- It exhibits apetite depressant property and having effects on naturally occuring histamine in the body.



Mechanism Of Action

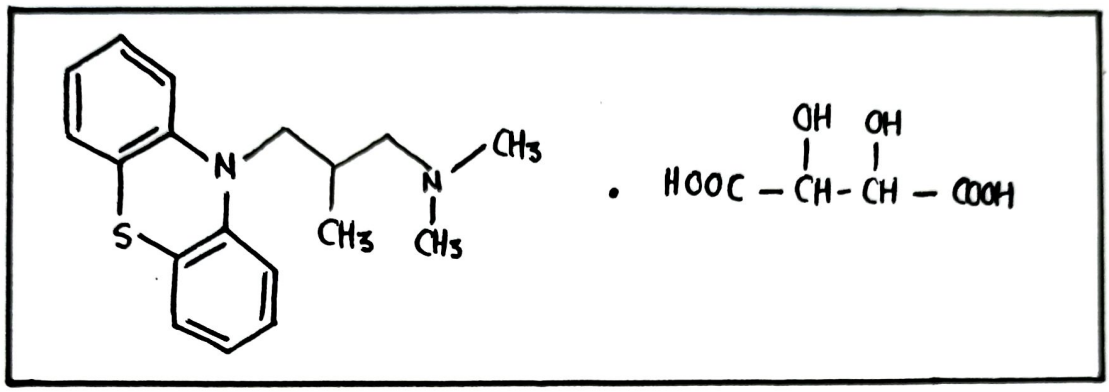
Phenidamine Tartarate antagonizes the pharmacological action of Antihistamines by binding on H_1 receptor & reduces the allergic reactions caused by Antihistamine

Uses

It is used for releiving symptoms of sneezing, runny nose. itching, watery eyes rashes & common cold.

(14) Trimeprazine Tartarate

- It is a phenothiazine derivative & a tartarate salt.
- It is an antihistaminic agent also acts as sedative, Hypnotic or antiemetic.



Mechanism Of Action

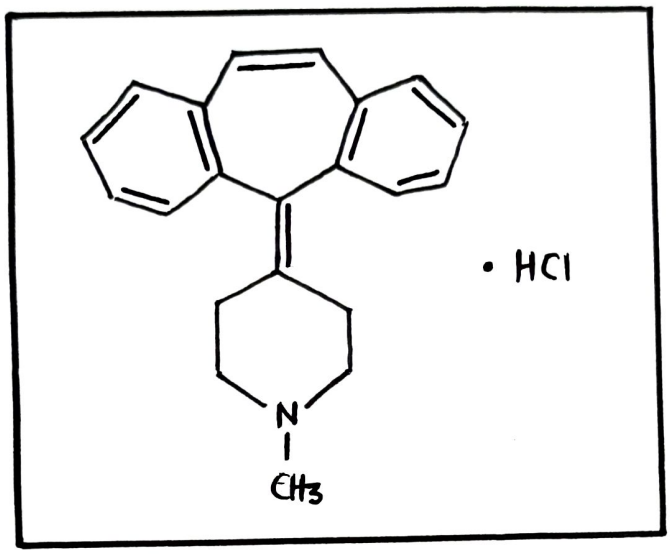
- Trimeprazine Tartarate is a competitive antagonist of H_1 receptor.
- It binds on H_1 receptor & blocks the effect of Histamine.

Uses

- It is used alone or along with corticosteroids in controlling Allergic or inflammatory problems.

(15) Cyproheptadine Hydrochloride

It is a first generation Antihistamine having Serotonin- Antagonist and calcium channel blocking activities.



Mechanism Of Action

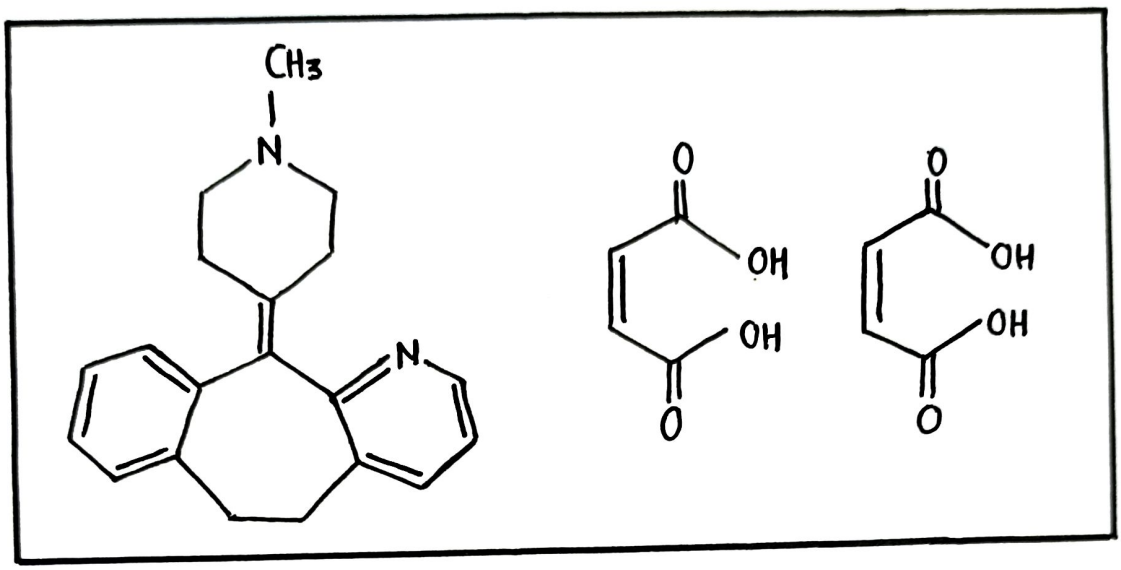
- It is a potent antagonist of H_1 receptor
- In high concentration it also has anticholinergic and antidopaminergic activity.

Uses

- It is used for treating various allergic conditions.
- It is also used as Apetite stimulant.
- It also have some antiserotonin activity.

⑯ AZATADINE MALEATE

- Azatadine Maleate is a first generation Antihistamine
- It is dimaleate salt of Azatadine.



Mechanism Of Action

- It acts as a potent H_1 receptor antagonist.
- It blocks H_1 receptor & reduces effect of Histamine.

Uses

- It is used for treatment of upper respiratory mucosal congestion.
- It is used for treatment of allergic rhinitis.

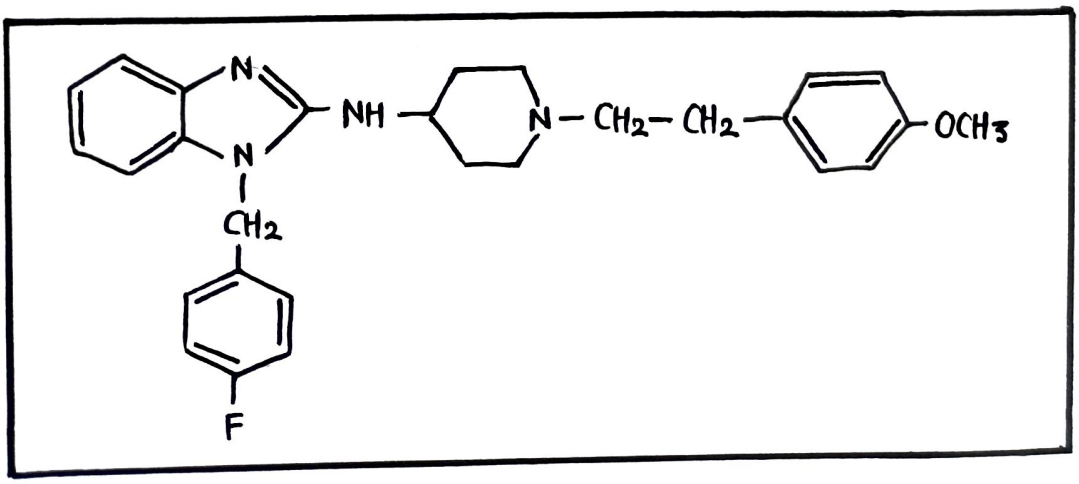
SECOND GEN H_1 ANTAGONIST

- These are the new generation antihistamine (H_1 Antagonist) that are less likely to cross the Blood Brain Barrier, resulting a minimal sedation.
- They are designed to provide effective relief from allergy symptoms with fever sedative effects compared to First Gen Antihistamines.
- These drugs generally include :

① Astemizole
② Loratidine
③ Cetrizine
④ Levocetrizine
⑤ Cromolyn Sodium

① ASTEMIZOLE

- Astemizole is a potent antihistaminic agent having longer duration of action.
- At higher doses, it causes arrythmias due to which it was withdrawn from the market by manufacturer in 1999.



Mechanism Of Action

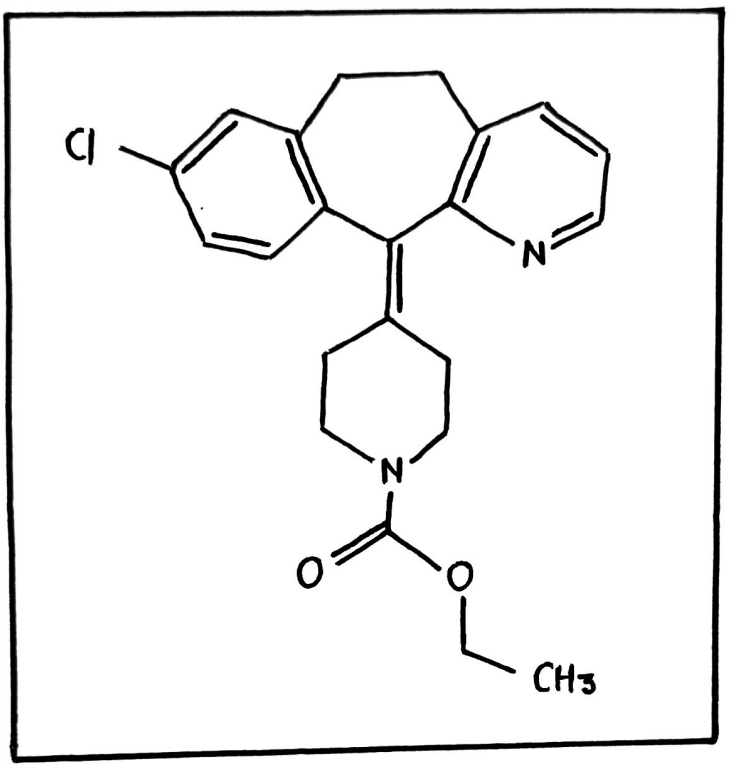
- It acts by competing with Histamine for binding on H_1 receptor sites in the GUT, Uterus, Large Blood Vessels, Bronchial Muscles.
- Since Astemizole does not cross the blood brain barrier easily it binds to the peripheral H_1 receptors.

Uses

It is used for treating allergic symptoms such as Rhinitis & Conjuctivitis.

② LORATIDINE

- Loratidine is an azo isomer of Cyproheptidine.
- It is a second generation H_1 Antagonist & often used for releiving the symptoms of Allergic Rhinitis & Urticaria.



Mechanism Of Action

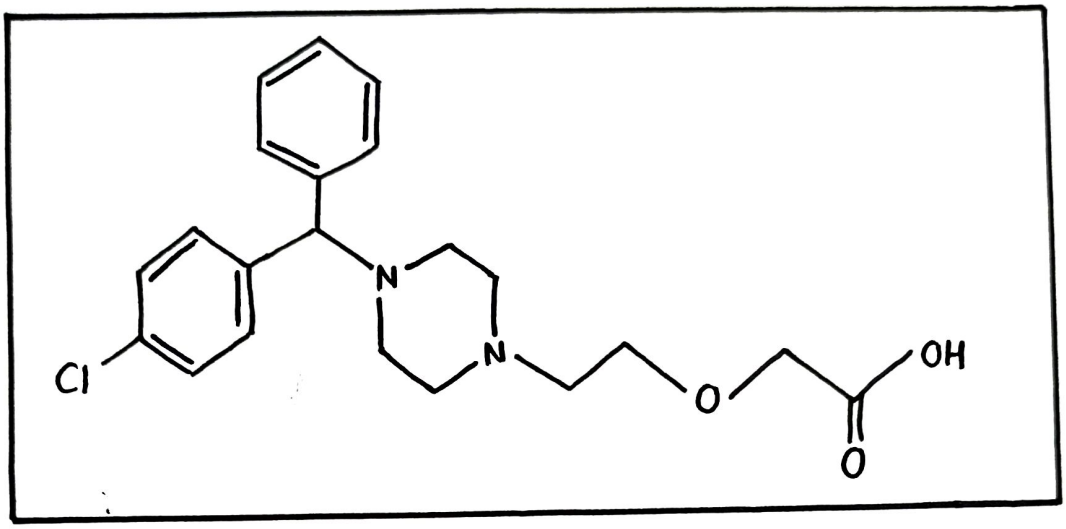
- It is a competitive antagonist of Histamine at peripheral H_1 receptors.
- It inhibits the action of Histamine & temporarily releives nasal congestion & watery eyes caused by Histamine.

Uses

- It is often used in combination with pseudoephedrine for treatment of seasonal allergic rhinitis.

③ CETIRIZINE

- Cetirizine is an orally active second generation H_1 Antagonist.
- It penetrates brain poorly but can cause Mild Sedation.



Mechanism Of Action

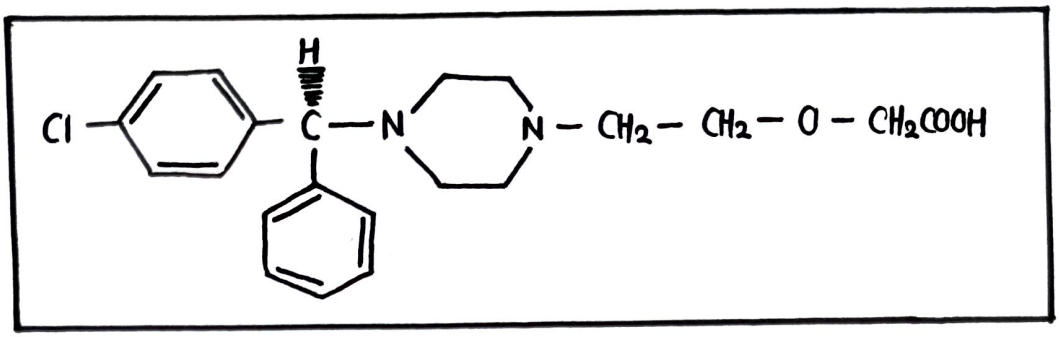
- It mainly acts by selective inhibition of Peripheral H_1 receptors.
- It has long duration of action & rapid onset of activity.

Uses

- It is used for treatment of seasonal allergic rhinitis.
- It often used for treatment of various allergic symptoms like runny nose, itching, skin rashes etc.

④ LEVOCETIRIZINE

- It is levorotatory enantiomer of Cetirizine.
- It is thirty times more active than dextro form
- It is rapidly absorbed after oral administration & poorly metabolized thus shows longer duration of action.



Mechanism Of Action

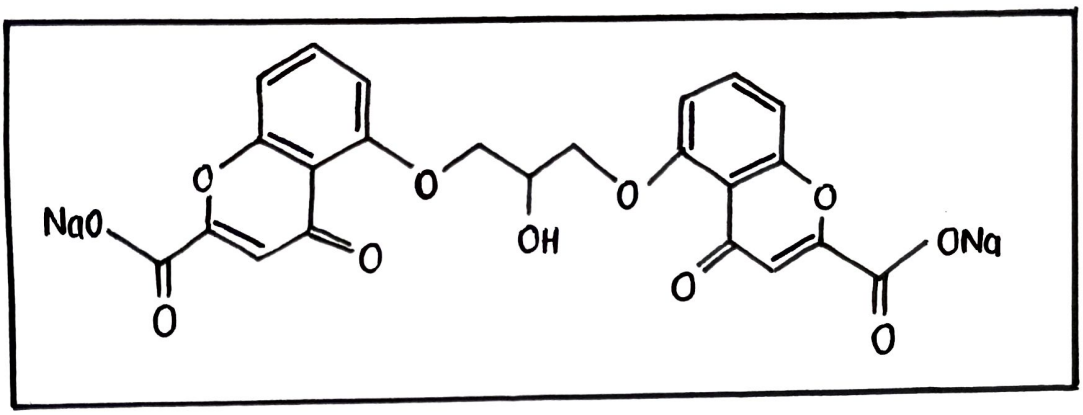
- Levocetirizine is active enantiomer of Cetirizine.
- Its affinity for H_1 receptor is twice than that of cetirizine.
- It selectively binds to H_1 receptor and antagonize the effect of Histamine.

Uses

- It is used for treating symptoms related to seasonal allergies in adults and childrens of 6 years of age and above.
- It is used for treating symptoms like watery eyes, runny nose etc.

⑤ CROMOLYN SODIUM

- Cromolyn Sodium is the sodium salt form of Cromolyn.
- Although we are studying this drug under Antihistamines but actually it is a Mast Cell Stabilizer.
- It has Anti-inflammatory activity.
- It stabilizes the mast cell, hence inhibits the release of Histamine, Leukotrienes and other inflammatory mediators that causes hypersensitivity reactions.



Mechanism Of Action

- Cromolyn Sodium prevents the degranulation of Mast Cells, and thus prevents release of Histamine & other inflammatory substances.
- It acts by inhibiting calcium influx.

Uses

- It is used for treatment of bronchial asthama.
- Its nasal solution is used for allergic rhinitis.

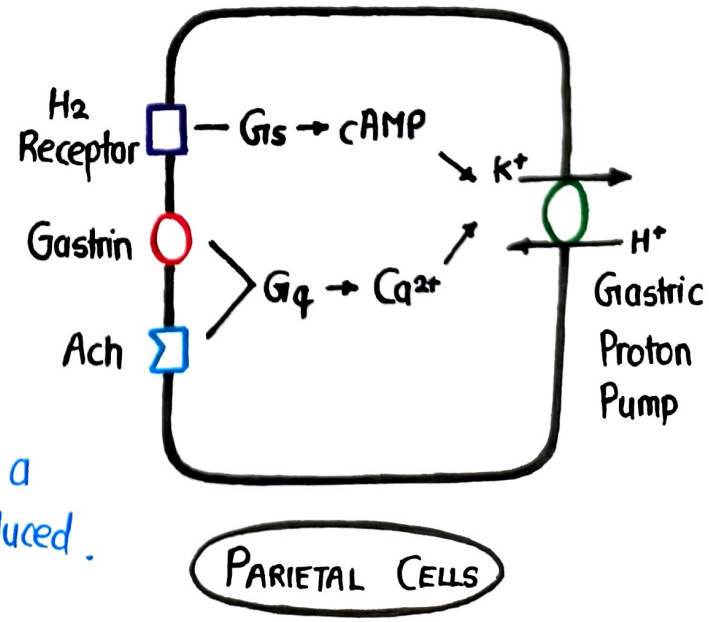
H_2 Antagonist

- H_2 Antagonist, also known as H_2 blockers, are a class of medications that reduce stomach acid production by blocking Histamine H_2 receptors on cells in stomach lining.
- The H_2 Receptors present on parietal cells of stomach.
- H_2 Antagonists help decreases acid production.
- These drugs are commonly used to treat conditions related to excess stomach acid such as GERD disease, Peptic Ulcers, Zollinger - Ellison Syndrome etc.
- In H_2 Antagonists we have to study about

① Cimetidine *
② Famotidine
③ Ranitidine

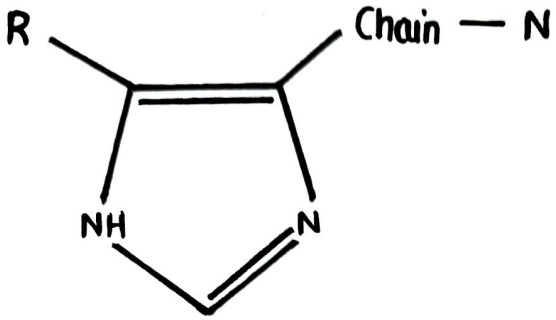
Mechanism Of Action

- The H_2 Antagonist are competitive antagonist of Histamine at H_2 receptor in parietal cells.
- H_2 Antagonist binds with H_2 receptor & block the Histamine from binding on H_2 receptor
- When Histamine is unable to bind to H_2 receptor, parietal cells do not receive the signal to produce & secrete gastric acid, As a result overall acid production is reduced.



SAR OF H_2 ANTAGONIST

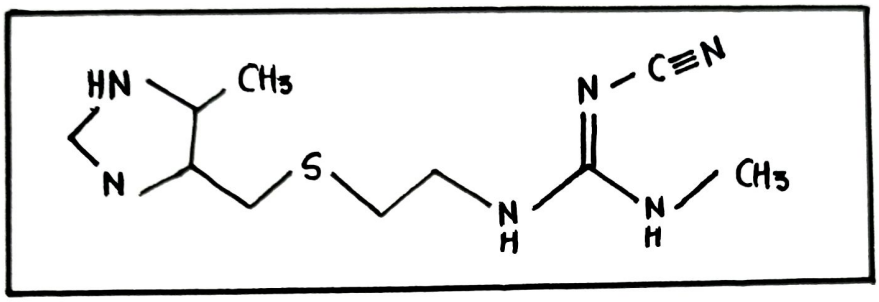
- The H_2 receptor antagonist were the result of international modification of Histamine structure & deliberate search for a chemically related substance that would act as a competitive inhibitor of H_2 Receptor.



- Imidazole ring is not the only required ring for competitive antagonism of Histamine H_2 receptor.
- Other heterocyclic ring (Furan, Thiophene, Thiazole) etc. that inhance the potency and selectivity of H_2 - receptor antagonism can be used
- The ring and terminal nitrogen should be separated by at least 4 carbon atom for optimum antagonist property
- The teominal nitrogen group should be Polar, Non basic for maximum antagonistic activity.

① CIMETIDINE

- Cimetidine was the first agent to be clinically used as an H_2 Antagonist .
- Cimetidine competitively inhibits the binding of Histamine to H_2 Receptors & prevents gastric acid secretion .



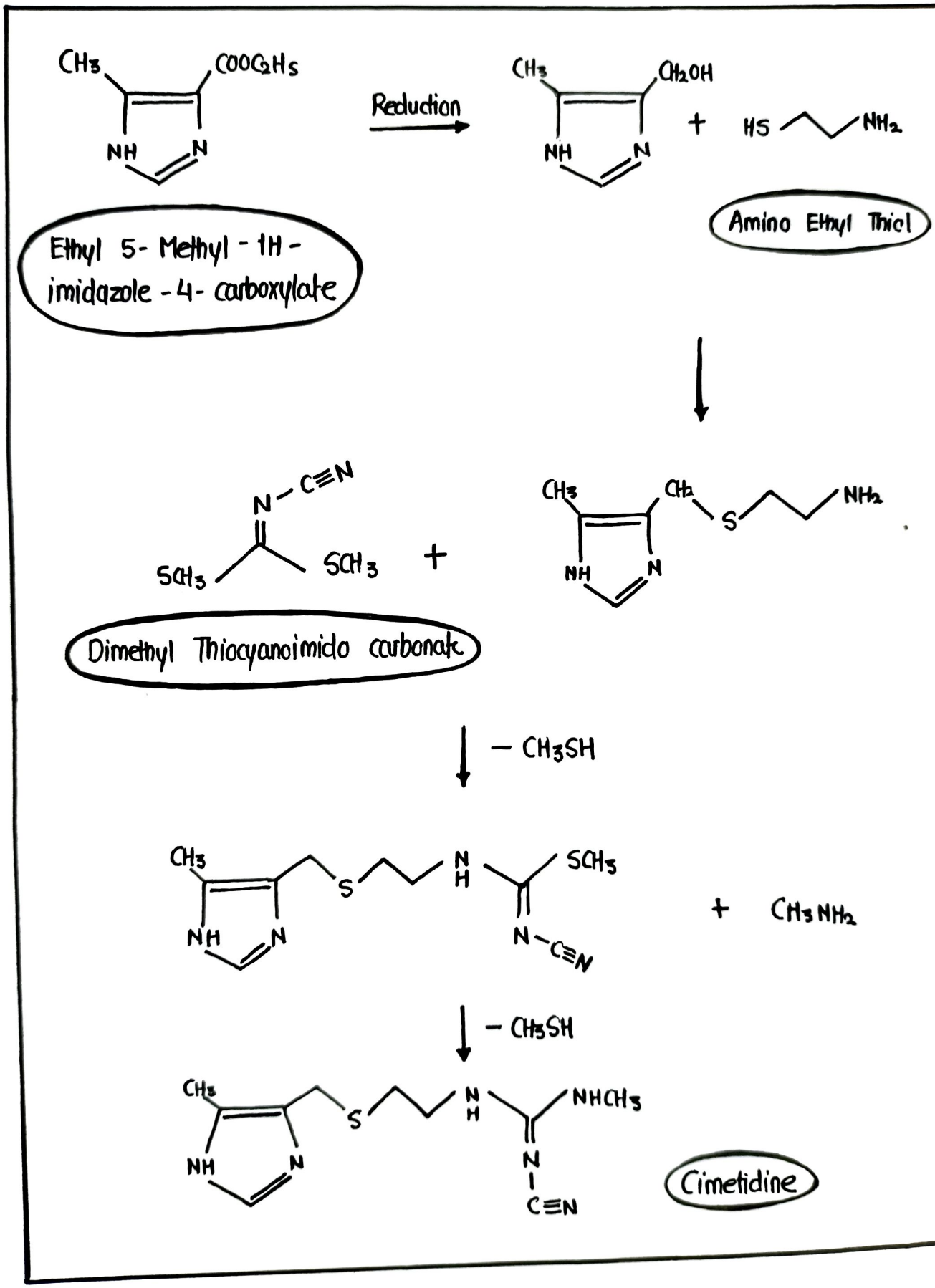
Mechanism Of Action

- Cimetidine blocks the histamine effects by binding on H_2 receptor presents on parietal cells of stomach .
- Due to this competitive inhibition , amount of gastric acid secretion , gastric volume and acidity is reduced .

Properties

- It is a white crystalline powder.
- It is soluble in water & sparingly soluble in ethanol .
- It is stored at a dark place in well closed air tight conditioner.

SYNTHESIS

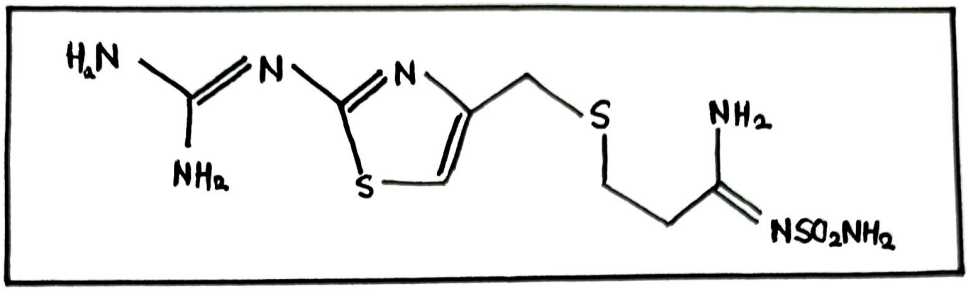

CH3
COOC2H5
NH
N
Reduction
CH3
CH2OH
NH
N
+
HS
NH2
Ethyl 5- Methyl - 1H - imidazole - 4- carboxylate
Amino Ethyl Thiol
N
C≡N
SCH3
SCH3
+
CH3
CH2
S
NH2
NH
N
Dimethyl Thiocyanoimido carbonate
– CH3SH
CH3
S
N
H
SCH3
NH
N
N
C≡N
+
CH3NH2
– CH3SH
CH3
S
N
H
NHCH3
NH
N
N
C≡N
Cimetidine

Uses

- It is used to treat various types of ulcers.
- It is used for treating the conditions in which too much acid is secreted by the stomach.
- It is also used for treating acid-reflux disorders like GERD, peptic ulcer disease, Heartburn etc.

② FAMOTIDINE

Famotidine is a competitive H_2 receptor antagonist and its main pharmacological effect is inhibition of gastric secretion.



Mechanism of Action

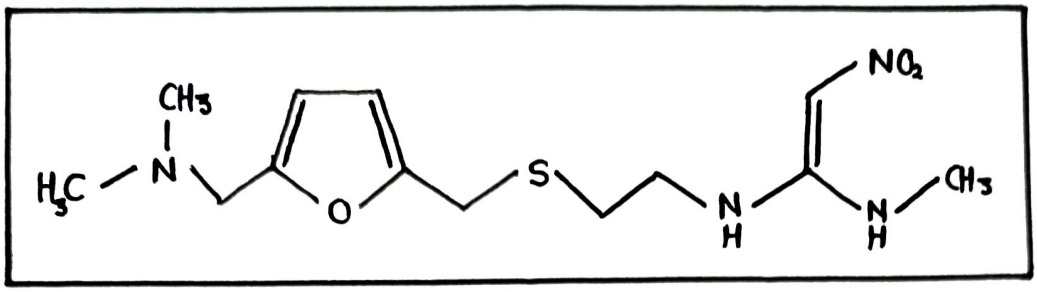
- Famotidine blocks the histamine effects by competitively binding to H_2 receptor found on parietal cells of stomach.
- This competitive inhibition reduces gastric acid secretion, gastric volume, acidity and amount of gastric acid produced in response to stimulus including Food, Caffiene, Insulin etc.

Uses

- It is used for treating stomach & intestinal ulcers.
- It is used in the treatment of Zollinger-Ellison Syndrome.
- It is used to treat GERD.

③ RANITIDINE

- Ranitidine is a non- imidazole H_2 receptor blocker.
- It is used for treating gastrointestinal ulcers.



Mechanism Of Action

Ranitidine reduces normal as well as meal- stimulated acid secretion of acid by parietal cells by two mechanism :

- Histamine is released by ECL cells in stomach is prevented from binding to H_2 receptor on parietal cells that stimulate acid secretion.
- When H_2 receptor are blocked, substances promoting acid secretion (e.g. Gastrin & Acetylcholin) have a decreased effect on parietal cells.

Uses

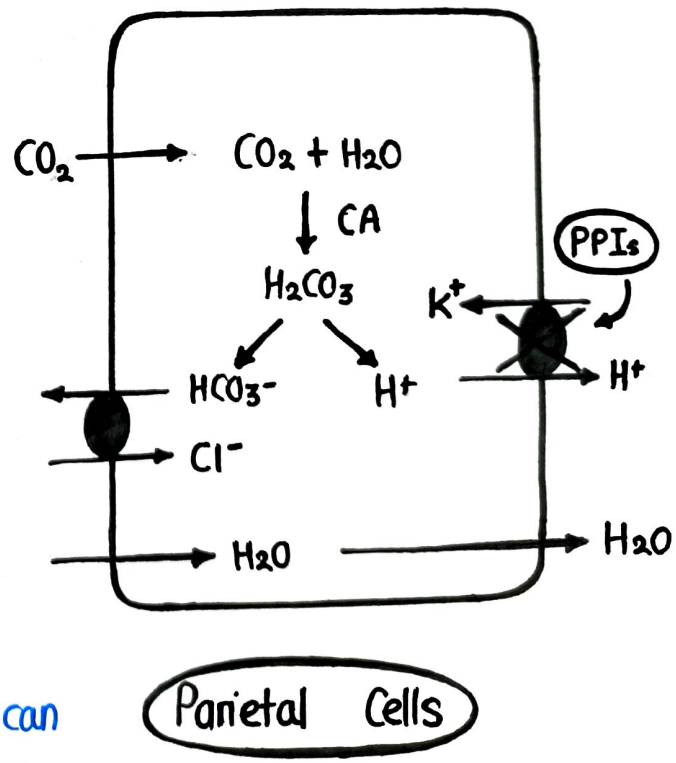
- It is used for treating Ulcers & GERD.
- It is used in various conditions in which stomach produces too much acid.

Gastric Proton Pump Inhibitors

- Gastric Proton Pump Inhibitors are the class of drugs that are used to control the gastric acid & ulcers.
- They work by inhibiting the proton pump in gastric parietal cells which is responsible for secreting Hydrochloric acid (HCl) in the stomach.
- The reduction in acid can help manage conditions such as
  - Gastroesophageal Reflux Disease
  - Peptic Ulcer Disease
  - Zollinger - Ellison Syndrome etc.

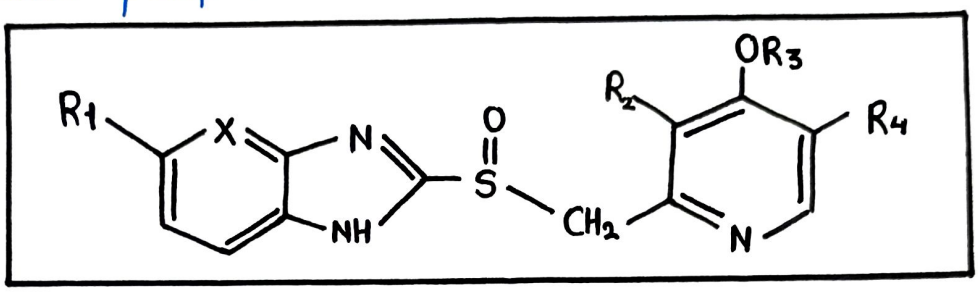
Mechanism Of Action

- Gastric proton pump inhibitors work by specifically targeting & inhibiting the proton pump that is H^+/K^+ ATPase enzyme located in gastric parietal cells of stomach lining.
- By binding to the proton pump, the PPIs effectively block its ability to exchange potassium for Hydrogen ions.
- The inhibition of proton pump is irreversible. New proton pumps needs to be synthesized by parietal cells to restore acid secretion, that can take several days, Hence PPIs have a prolonged duration of action.



CLASSIFICATION

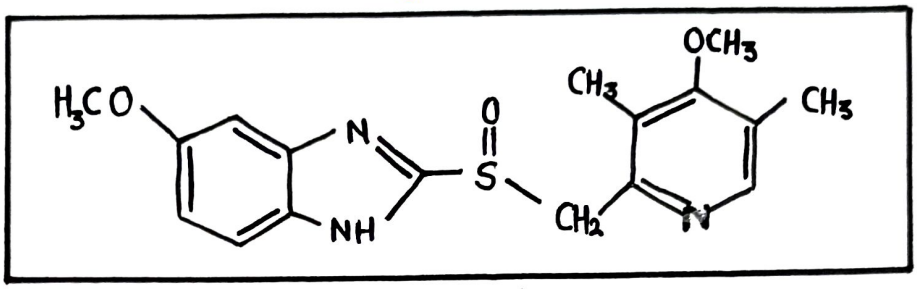
- Proton Pump Inhibitors are prodrugs, means they are initially inactive.
- They are absorbed into the bloodstream & then converted into their active form in the highly acidic environment of stomach.
- The proton pump inhibitors are classified as follows:



DRUGS	X	R_1	R_2	R_3	R_4
Omeprazole	CH	OCH_3	CH_3	CH_3	CH_3
Lansoprazole	CH	H	CH_3	CH_2CF_3	H
Rabeprazole	CH	H	CH_3	$[CH_2]_3OCH_3$	H
Pantoprazole	CH	$OCHF_2$	OCH_3	CH_3	H

① OMEPRAZOLE

- Omeprazole is a medication that belongs to a class of drugs known as Proton Pump Inhibitors (PPIs).
- It is a powerful inhibitor of gastric acid, that totally inhibits HCl secretion, both resting as well as food stimulated.



Mechanism Of Action

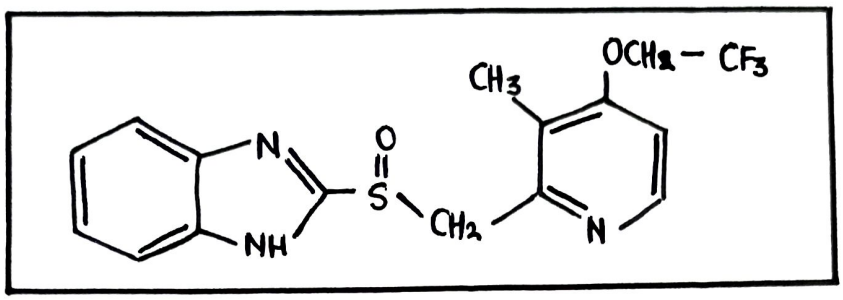
- Omeprazole is a selective and irreversible proton pump inhibitor.
- It suppresses gastric acid secretion by inhibiting H^+/k^+ ATPase in gastric parietal cells.
- By acting specifically on the proton pump it blocks final step in acid production & reduces gastric acidity.

Uses

- For treatment of GERD
- For treatment of Gastric & Duodenal Ulcers.
- To relieve Heartburn
- To promote the healing of Erosive oesophagitis.

② LANSOPRAZOLE

- Lansoprazole is a substituted benzimidazole prodrug having selective and irreversible proton pump inhibitor activity.
- It prevents production of acid in the stomach.



Mechanism Of Action

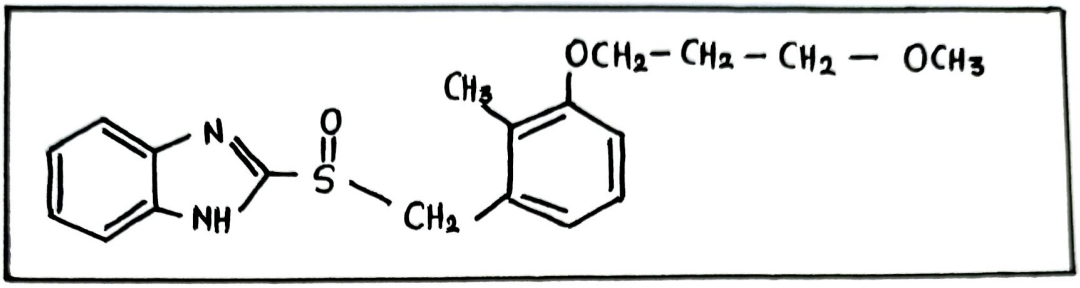
- It suppresses gastric acid secretion by inhibiting H^+/K^+ ATPase enzyme system at the surface of gastric parietal cell.
- It has higher oral bioavailibility, faster onset of action & slightly longer $t_{1/2}$ than omeprazole.

Uses

- It is used for treating acid-reflux disorders (like GERD).
- It is used for treatment of NSAIDs induced gastric ulcers.
- Treatment of Heartburn.

③ RABEPRAZOLE

- Rabeprazole is an antiulcer drug that blocks H^+/K^+ ATPase.
- It is absorbed & metabolized in liver by oxidation.



Mechanism Of Action

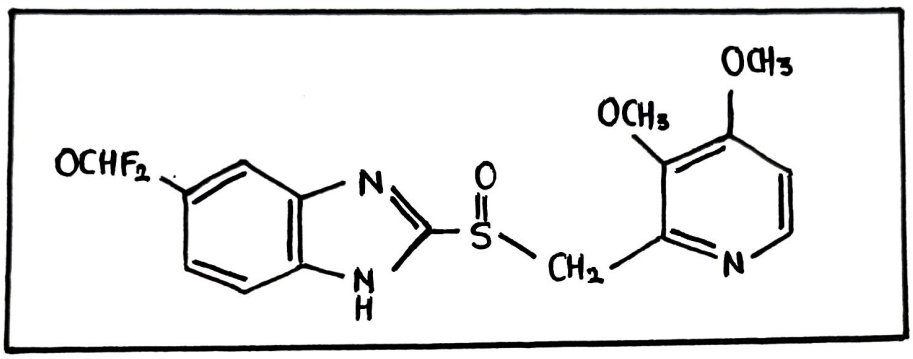
Rabeprazole suppresses gastric acid secretion by inhibiting H^+/K^+ ATPase enzyme system

Uses

- In GERD
- In severe erosive esophagitis
- In zollinger - Ellison syndrome
- In duodenal ulcers

④ PENTOPRAZOLE

- Pentoprazole is a proton pump inhibitor similar to Omeprazole.
- It works by decreasing the amount of acid produced in the stomach & used to treat conditions involving excess stomach acid.



Mechanism Of Action

- Pentoprazole's mechanism of action involves inhibiting the proton pum in the parietal cells.
- This leads to inhibition of gastric acid secretion.

Uses

- Treatment of GERD
- Treatment of Zollinger- Ellison Syndrome.
- Treatment of erosive oesophagitis

Antineoplastic Agents

- Antineoplastic Agents are the drugs that are used to treat cancer.
- Antineoplastic Agents are also known as Anticancer, Chemotherapy or cytotoxic drugs.
- They work by targeting and killing cancer cells by inhibiting their growth and proliferation.
- They work through different mechanisms depending on their class and type.

Cancer

- Cancer is a very serious disease characterized by uncontrolled growth & spread of abnormal cells in the body.
- These abnormal cells can form Tumour & spread throughout the body via blood & lymphatic system.
- Cancer can start almost anywhere in the human body & often named after organ or type of cell where it starts, such as **Breast Cancer**, **Lung Cancer**.
- Other terms like Neoplasm & Tumour are also used for Cancer, however they have slight different meaning.

Tumour

- A Tumour is an abnormal growth of cells that forms a Mass or Lump.
- It can be classified into two types :

① Benign Tumour
② Malignant Tumour

Benign Tumour	Malignant Tumour
• It is a Non-Cancerous Tumour • It generally doesn't spread to other parts of body • It can be easily removed through surgery	• It is a Cancerous Tumour • It spreads to other part of body through Bloodstream or Lymphatic System. • It can not be easily removed.

Classification Of Cancer

On the basis of tissue involved it can be classified into following types :

- Carcinomas
- Sarcomas
- Leukamias
- Lymphomas

① CARCINOMAS

- Cancer that originates in epithelial cells, which line the inner & outer surfaces of body.
- Example : Breast Cancer, Lung Cancer etc.

② SARCOMAS

- These are the cancer that arises from connective tissues.
- Example : Bone, Muscle, Joints etc.

③ LEUKAMIAS

- It is also known as Blood Cancer.
- It begins when healthy blood cell changes & grow uncontrollably.

④ LYMPHOMAS

- Cancer that originates in the Lymphatic System.
- Example : Hodgkin's Lymphoma

CAUSES

Cancer is often caused by changes (mutations) in the DNA within cells, which lead to uncontrolled cell division & growth.
These mutations can be triggered by various factors as follows:

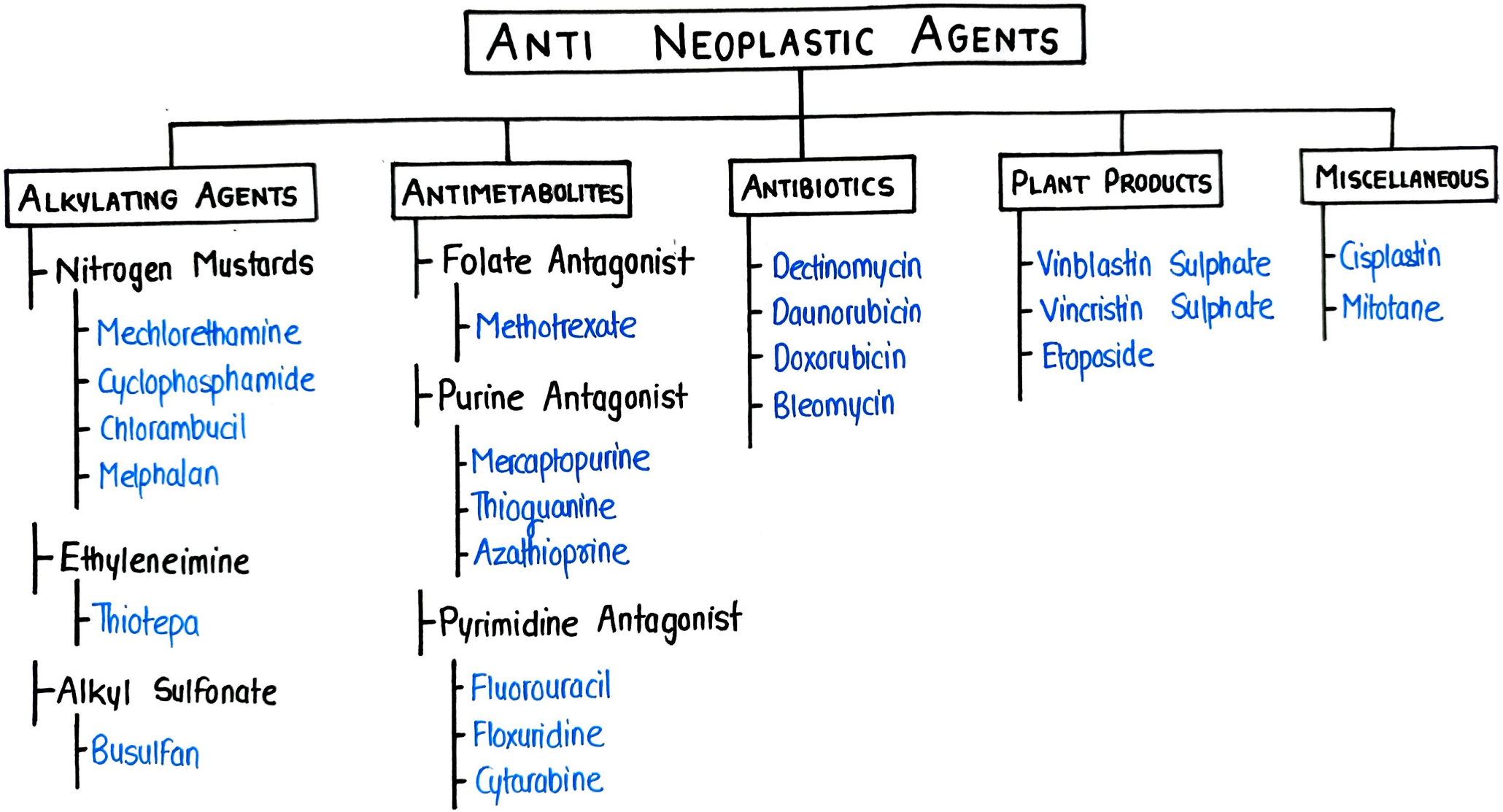
- Genetic Mutations
- Environmental Exposures
- Smoking
- Alcohol
- Virus, Bacteria, Parasites
- Hormonal Imbalances

SIGN & SYMPTOMS

- Fatigue
- Weight Changes
- Skin Changes
- Bowel Changes
- Persistent Cough
- Breathing Trouble
- Fever/ Night Sweats

TREATMENT

- Surgery
- Chemotherapy
- Radiation Therapy etc.


ANTI NEOPLASTIC AGENTS
ALKYLATING AGENTS
Nitrogen Mustards
Mechlorethamine
Cyclophosphamide
Chlorambucil
Melphalan
Ethyleneimine
Thiotepa
Alkyl Sulfonate
Busulfan
ANTIMETABOLITES
Folate Antagonist
Methotrexate
Purine Antagonist
Mercaptopurine
Thioguanine
Azathioprine
Pyrimidine Antagonist
Fluorouracil
Floxuridine
Cytarabine
ANTIBIOTICS
Dactinomycin
Daunorubicin
Doxorubicin
Bleomycin
PLANT PRODUCTS
Vinblastin Sulphate
Vincristin Sulphate
Etoposide
MISCELLANEOUS
Cisplastin
Mitotane

Alkylating Agents

- Alkylating Agents are a type of Antineoplastic drug used in cancer treatment.
- They are the oldest and most useful Antineoplastic drugs.
- They work by directly damaging the DNA within cancer cells.
- Effectiveness of Alkylating Agents as Anticancer Drugs was confirmed by clinical trials in middle 1940s.
- They are often used in treatment of various types of cancer because they can target rapidly dividing cancer cells.

Classification

Alkylating Agents are classified as follows:

① Nitrogen Mustards
- Mechlorethamine
- Cyclophosphamide
- Chlorambucil
- Melphalan
- Ifosfamide

② Ethyleneimine
- Thiotepa

③ Alkyl Sulfonate
- Busulfan

④ Nitroscureas
- Carmustine
- Lomustine

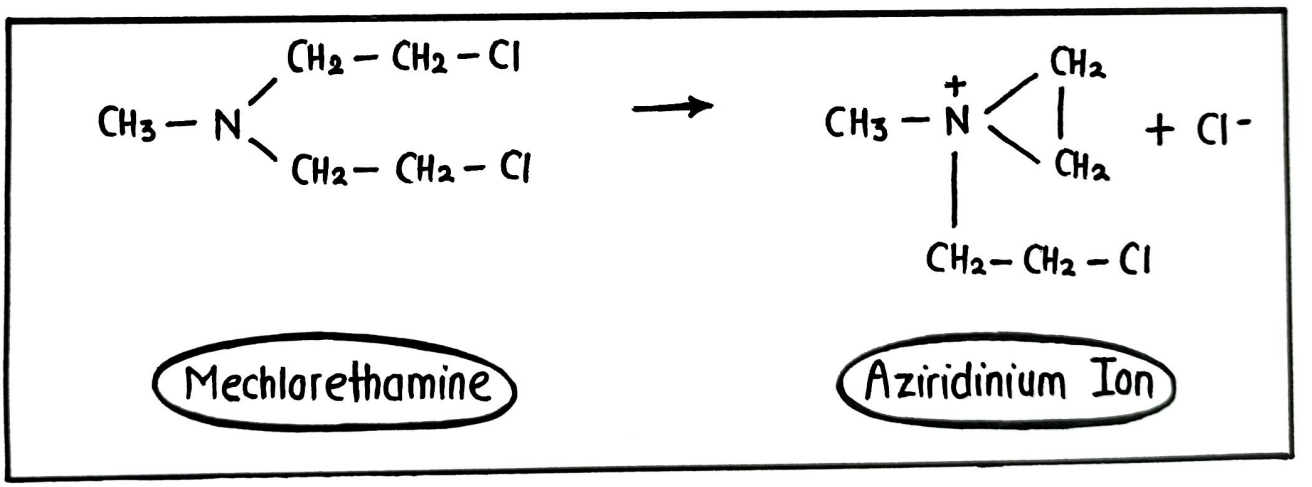
⑤ Triazine
- Dacarbazine

Mechanism Of Action

- Alkylating Agents are a class of chemotherapy drugs that work by adding alkyl groups to DNA, which interferes with DNA replication & transcription.
- Here's a detailed overview of their mechanism of action:

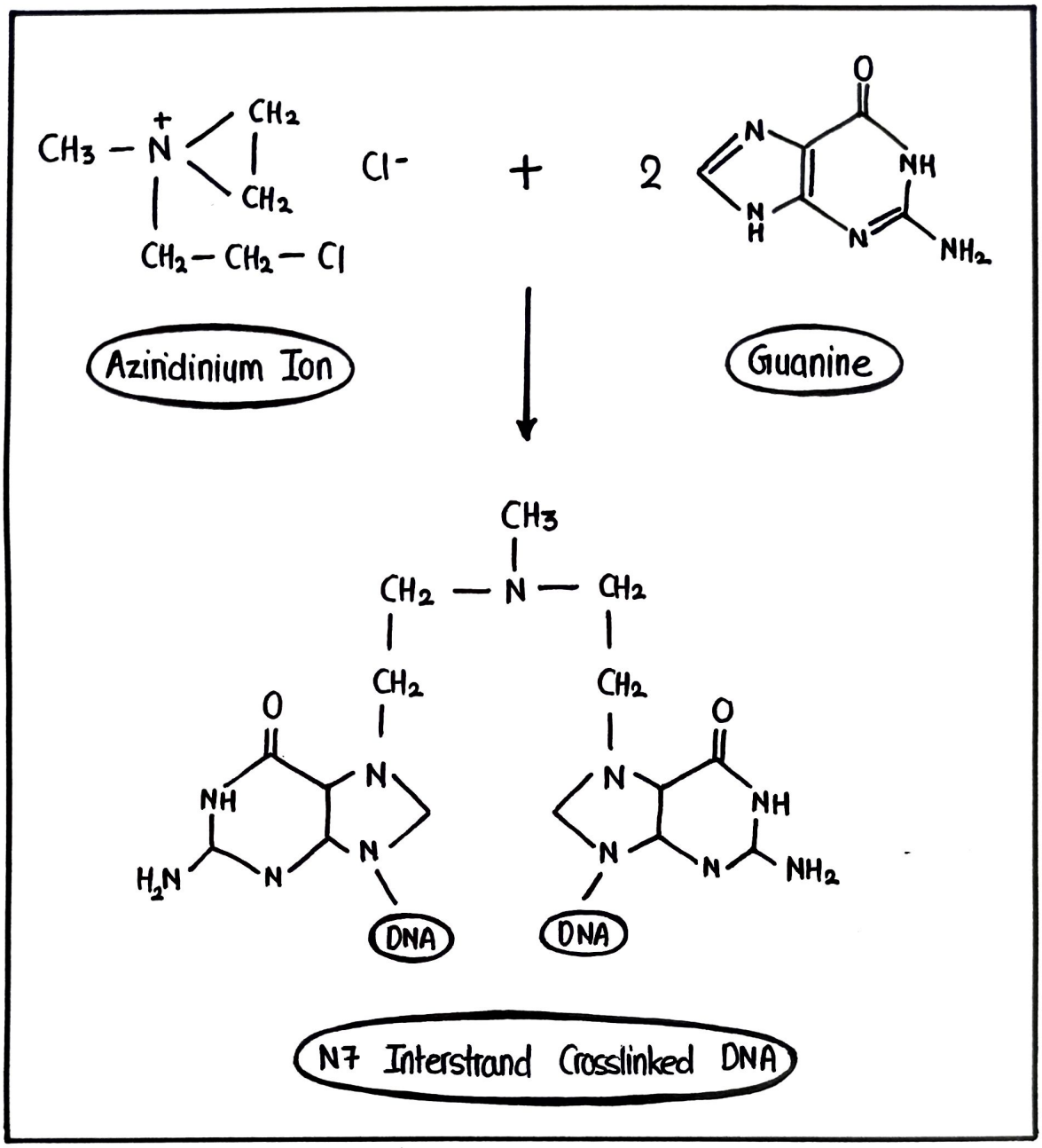
① Alkylation

- Alkylating Agents transfer an alkyl group (typically methyl or ethyl) to the DNA molecule.
- This usually occurs at the N7 position of Guanine bases, leading to the formation of N-7 alkylguanine.
- First these Alkylating Agents (specially Nitrogen Mustards derivatives) undergoes intermolecular cyclization to form Aziridinium Ion.



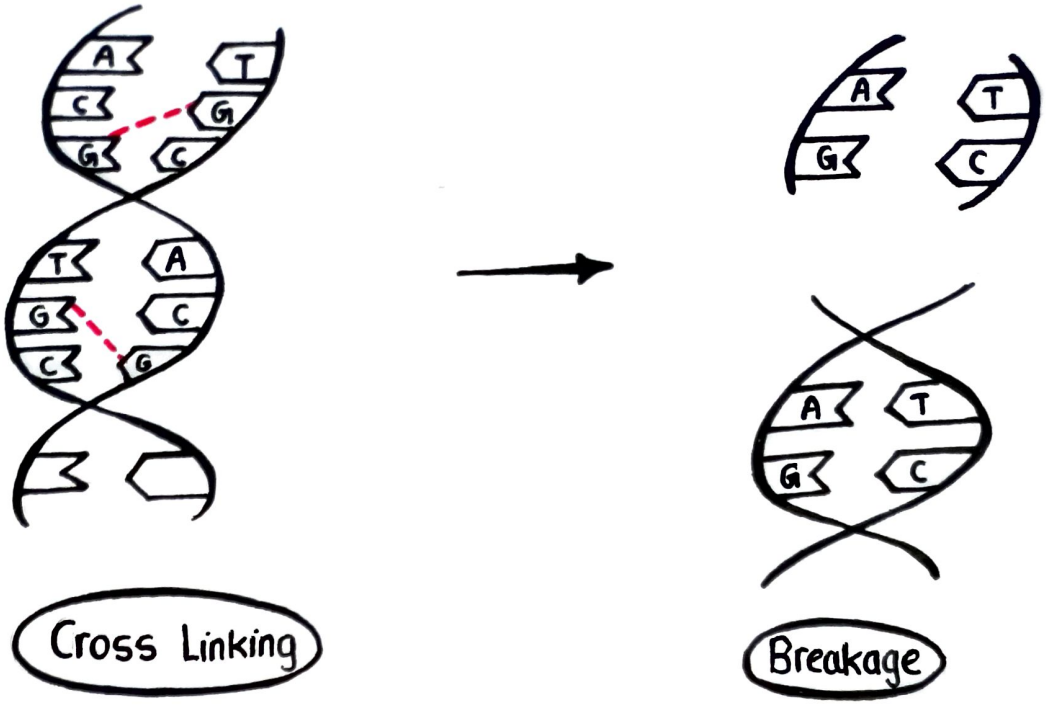
- By this reaction, tertiary amine is converted to an unstable quaternary ammonium compound, which react by forming carbonium ion.

- Now this unstable quatenary ammonium compound alkylates two guanine bases at 7th N atom



② Cross Linking

- The alkyl groups form covalent bond between different DNA strands (interstrand cross linking) or within same strand (intrastrand cross linking).
- This prevents separation of DNA strands necessary for replication & transcription.



③ DNA Damage

- The alkylation of DNA causes structural distortions and breaks in the DNA.
- This breaks leads to errors during DNA replication & eventually leads to cell death.

④ Cell Death

Ultimately, the accumulation of DNA damage & inability to repair it lead to cell death, particularly in rapidly dividing cancer cells

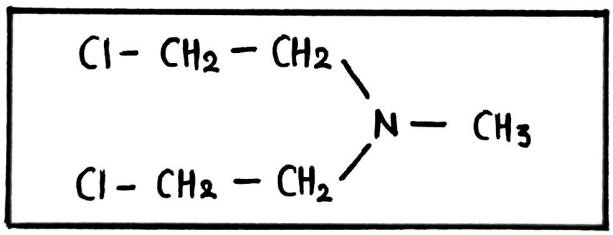
DRUGS IN OUR SYLLABUS

In our syllabus, we have to study about following drugs :

- Mechlorethamine *
- Cyclophosphamide
- Melphalan
- Chlorambucil
- Busulfan
- Thiotepa

① MECHLORETHAMINE

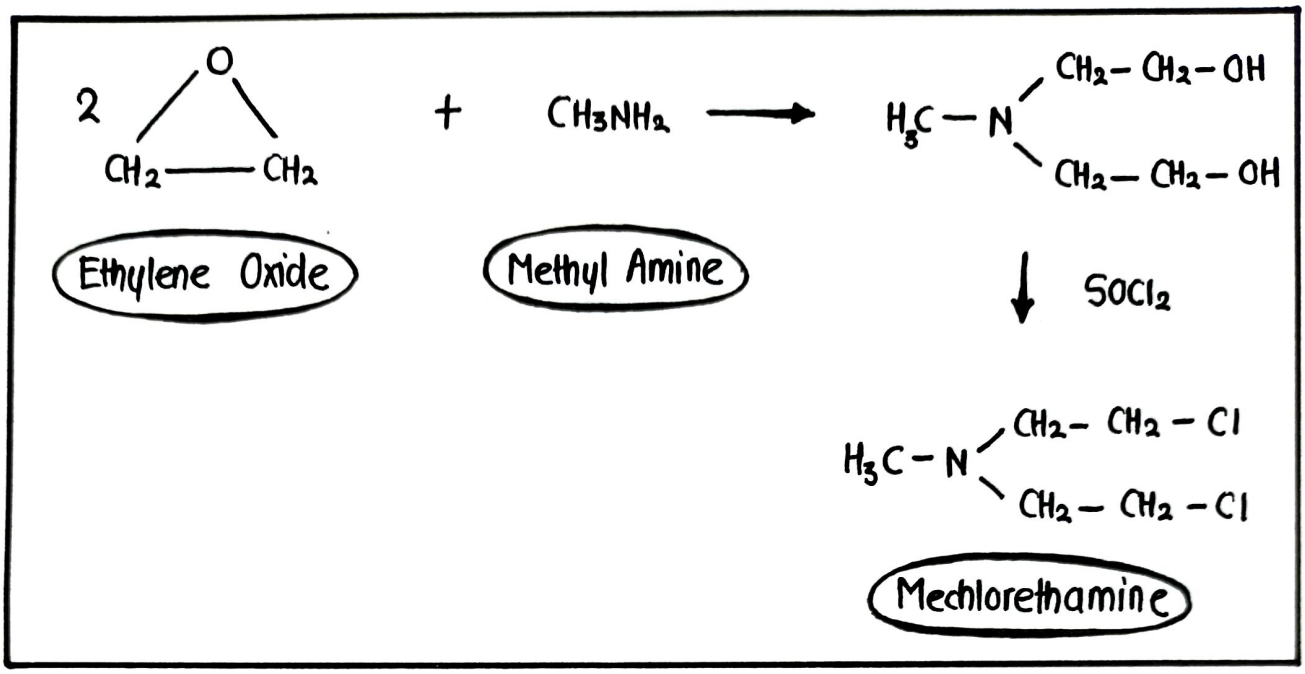
- It is also known as Mustine HCl
- It is first nitrogen mustard and highly reactive in nature
- It is administered by IV route (Intravenously).



Mechanism Of Action

- The drug undergoes rapid chemical transformation & converted to reactive aziridinium ion.
- It damages DNA via cross links formation.
- It prevents DNA synthesis & RNA transcription by attachment of alkyl groups to DNA bases (mostly Guanine at N-7 position).
- The cross links formation leads to cell death.

Synthesis



Properties

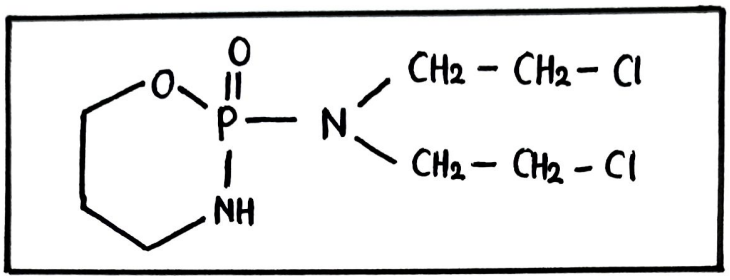
- It is white crystalline hygroscopic powder.
- Soluble in water and alcohol.

Uses

- It is used to treat Hodgkin's Lymphoma.
- Treatment of T-Cell lymphoma.
- Often used to treat certain types of Non-Hodgkin's Lymphoma.
- Also used to treat Lung cancer.

② CYCLOPHOSPHAMIDE

- Cyclophosphamide is a widely used alkylating agent
- It has immunosuppressant property.
- It is well absorbed orally & activated in liver.



Mechanism Of Action

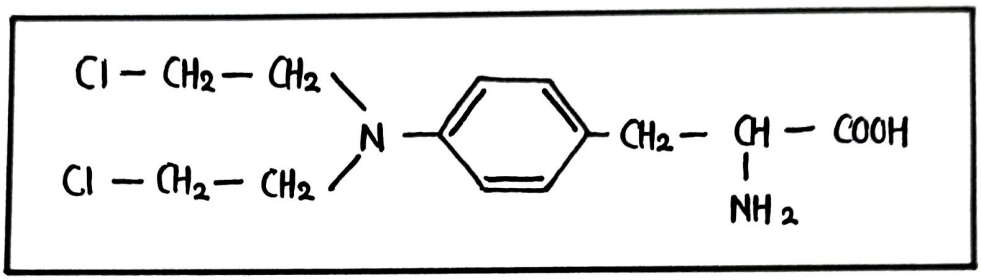
- Cyclophosphamide acts against the cells that are actively dividing and resting before entering the cell cycle.
- The hepatic cytochrome P-450 enzyme system activates cyclophosphamide to make it cytotoxic
- The active metabolite of cyclophosphamide forms DNA cross links. between & within DNA strands at Guanine N-7 positions.
- This is irreversible & leads to cell death.

Uses

- It is used in acute leukemia of children.
- In Hodgkin's disease, Breast Cancer, Ovarian cancer & Lung cancer.

③ MELPHALAN

- Melphalan is an Alkylating nitrogen mustard whose levo isomer, dextro isomer and racemic mixture are used as Antineoplastic Agents.
- It causes bone marrow toxicity but a potential anticancer agent.



Mechanism Of Action

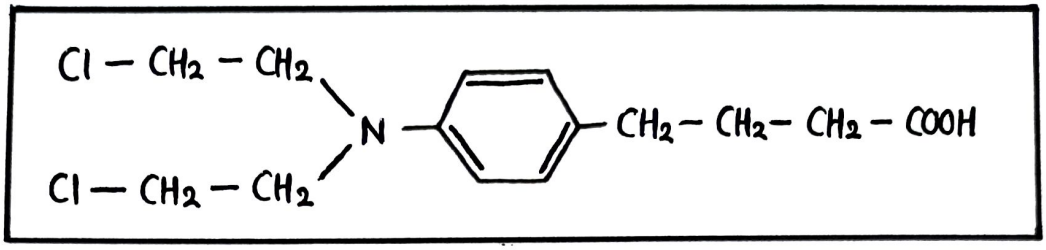
- Melphalan acts by Alkylation causes breaks & cross-linkage in DNA strands leading to cell death.

Uses

- It is used for treatment of Multiple Myeloma
- Used in the treatment of Breast cancer & ovarian cancer

④ CHLORAMBUCIL

- It is a slow acting Alkylating Agent
- It also have some immunosupressant activity.



Mechanism Of Action

- Chlorambucil acts by alkylating & cross-linking the DNA of cancer cells.
- The cross linking leads to breakage of DNA & ultimately leads to cell death.

Uses

- It is used in the treatment of chronic lymphocytic leukemia. Used in treatment of Hodgkin's & Non-hodgkin's lymphoma.
- It can be used in treatment of ovarian cancer.

⑤ BUSULFAN

- It belongs to the class of Alkyl Sulfonate
- It exerts a selective immunosuppresive effect on bone marrow.

$$CH_3SO_2O - CH_2 - CH_2 - CH_2 - CH_2 - OSO_2CH_3$$

Mechanism Of Action

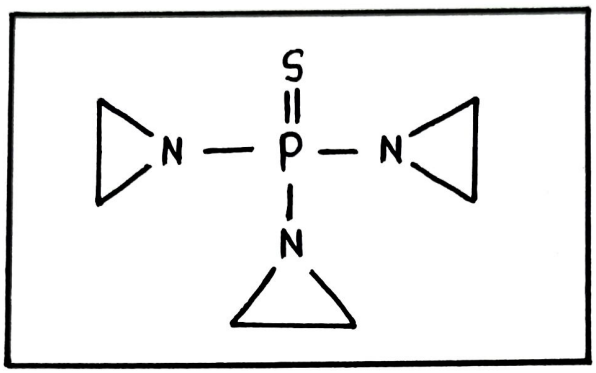
- Busulfan adds alkyl groups to the DNA.
- It preferentially reacts with the N7 position of guanine in DNA, forming covalent bonds.
- These cross-linkages prevents the synthesis & function of DNA.

Uses

- It is used in the treatment of granulocytic leukemia
- It is also a component of pre-transplant conditioning regimen in bone marrow transplantation.

⑥ THIOTEPA

- It belongs to the class of Ethylenimine.
- It produces high toxicity.



Mechanism Of Action

- It works by alkylating & breakage of DNA strands & eventually leads to cell death.

Uses

- It is used for treating Breast, Ovarian & Bladder Cancer.
- It is also used in bone marrow transplantation.

ANTIMETABOLITES

- Antimetabolites are belongs to class of anticancer agents that are structurally similar to the metabolites that are essential for synthesis of DNA such as Purine, Pyrimidine & Folic Acid.
- They act either by inhibiting their synthesis, or by competing with them in DNA & RNA synthesis.
- They interferes with normal cell functioning.
- Antimetabolites commonly kill the cell in S Phase.

CLASSIFICATION

Antimetabolites are classified as follows :

① Folate Antagonist
- Methotrexate *

② Purine Antagonist
- Mercaptopurine *
- Thioguanine
- Azathioprine

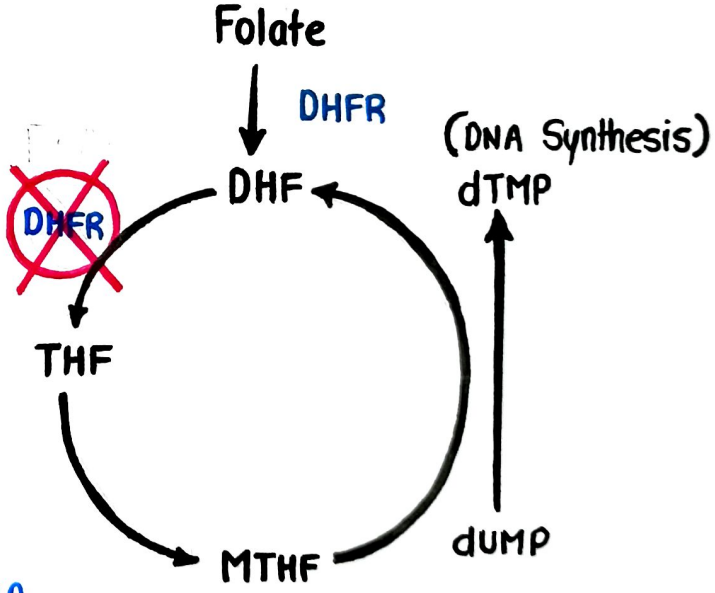
③ Pyrimidine Antagonist
- Fluorouracil
- Floxuridine
- Cytarabine

FOLATE ANTAGONIST

- Folate Antagonist are also referred to Antifolic Acid or Antifolics.
- It is a type of drug that interferes with the metabolism of Folic Acid (Vitamin B9), an essential nutrient required for synthesis of DNA.
- These drugs are particularly effective in treating rapidly dividing cancer cells, but can also affect healthy cells.

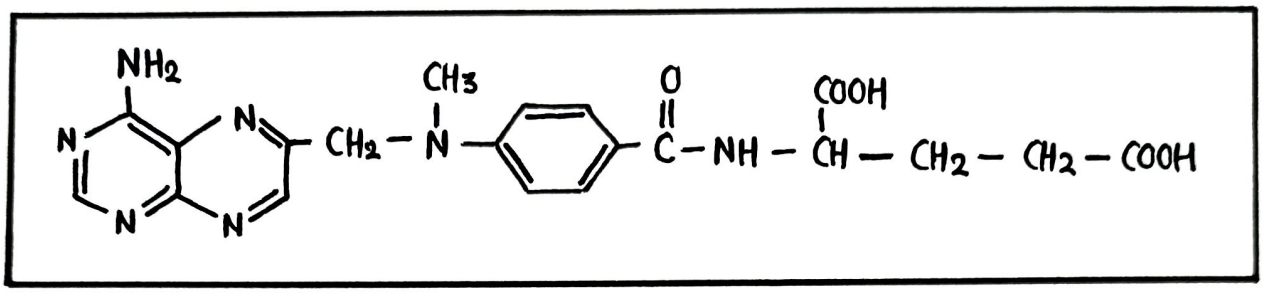
MECHANISM OF ACTION

- Folic Acid is an essential dietary factor.
- Folate Antagonists, such as Methotrexate, specifically inhibit the enzyme Dihydrofolate Reductase (DHFR).
- DHFR is responsible for converting DHF into THF, a reduced form of Folate that is essential for synthesizing Purine & dTMP that are necessary for DNA & RNA production.
- They mostly kill cells in the S Phase



① METHOTREXATE

- Methotrexate is one of the oldest & highly effective Antineoplastic drugs.
- It also has immunosupressant properties.



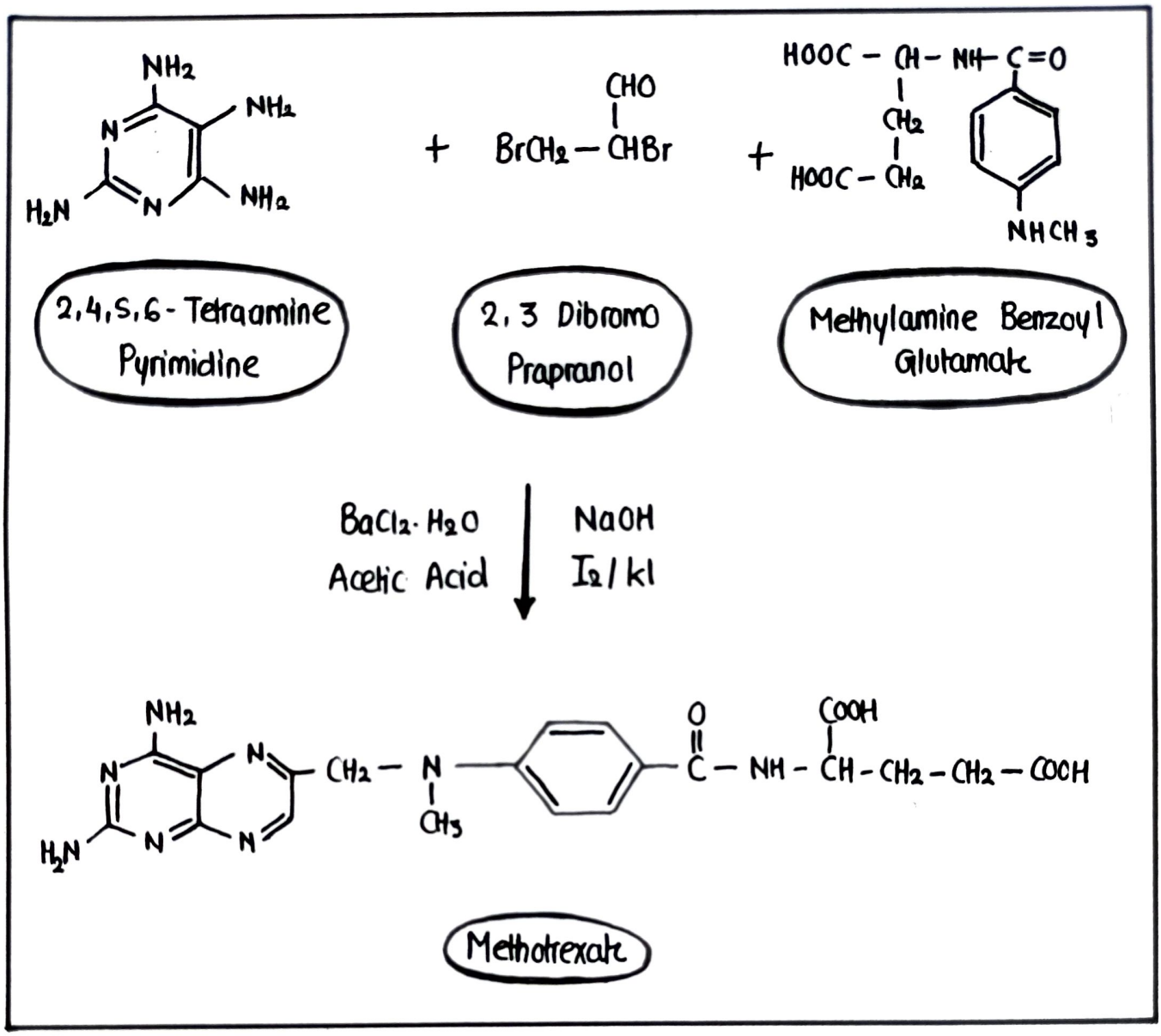
Mechanism Of Action

- Methotrexate act by preventing the synthesis of Folic Acid.
- It binds strongly to Dihydrofolate Reductase (DHFR), an enzyme required for conversion of DHF to THF, which is essential for synthesis of DNA.
- Methotrexate, By blocking DHFR, disrupts the production of DNA, thereby slowing down the growth of rapidly dividing cancer cells.

Properties

- It is yellow / orange crystalline powder
- It is hygroscopic in nature.
- It is soluble in water & slightly soluble in alcohol.

Synthesis



Uses

- It is used in the treatment of lymphocytic leukamia.
- It is used in the treatment of Breast cancer, lung cancer head & neck cancer with combination of other drugs.

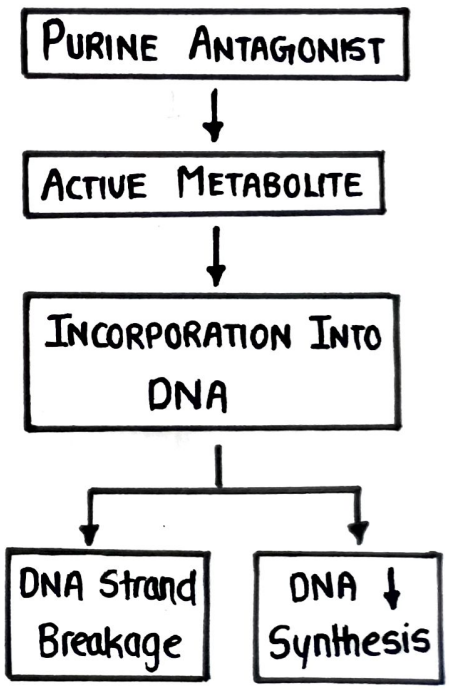
PURINE ANTAGONIST

- A Purine Antagonist belongs to the class of antimetabolites under Anticancer Agents that interferes with the synthesis & function of Purines, which are essential building blocks of DNA & RNA.
- Few drugs belonging to class of Purine Antagonist are as follows:

① Mercaptopurine *
② Thioguanine
③ Azathioprine

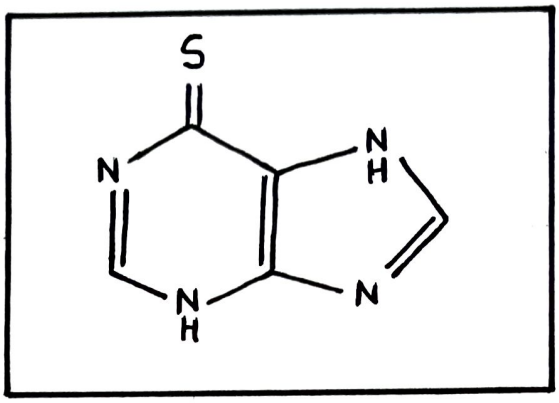
MECHANISM OF ACTION

- Purine Antagonists such as 6-Mercaptopurine and 6-Thioguanine are structurally similar to natural purine bases (Adenine, Guanine)
- Once inside the cell, these drugs are converted into active metabolites, which can be incorporated into growing DNA or RNA strands during S-Phase
- This incorporation results into faulty nucleic acids (DNA & RNA), leading to dysfunctional or incomplete genetic information, which inhibit cell's ability to function properly.
- They also interfere with IMP Dehydrogenase and other enzymes involved in conversion of Inosinic Acid (IMP) to adenine & guanine nucleotides.



② MERCAPTOPURINE

- Mercaptopurine is a purine antagonist antimetabolite under Antineoplastic Agents having immunosuppressant properties.
- It prevents purine metabolism, thus inhibits nucleic acid synthesis



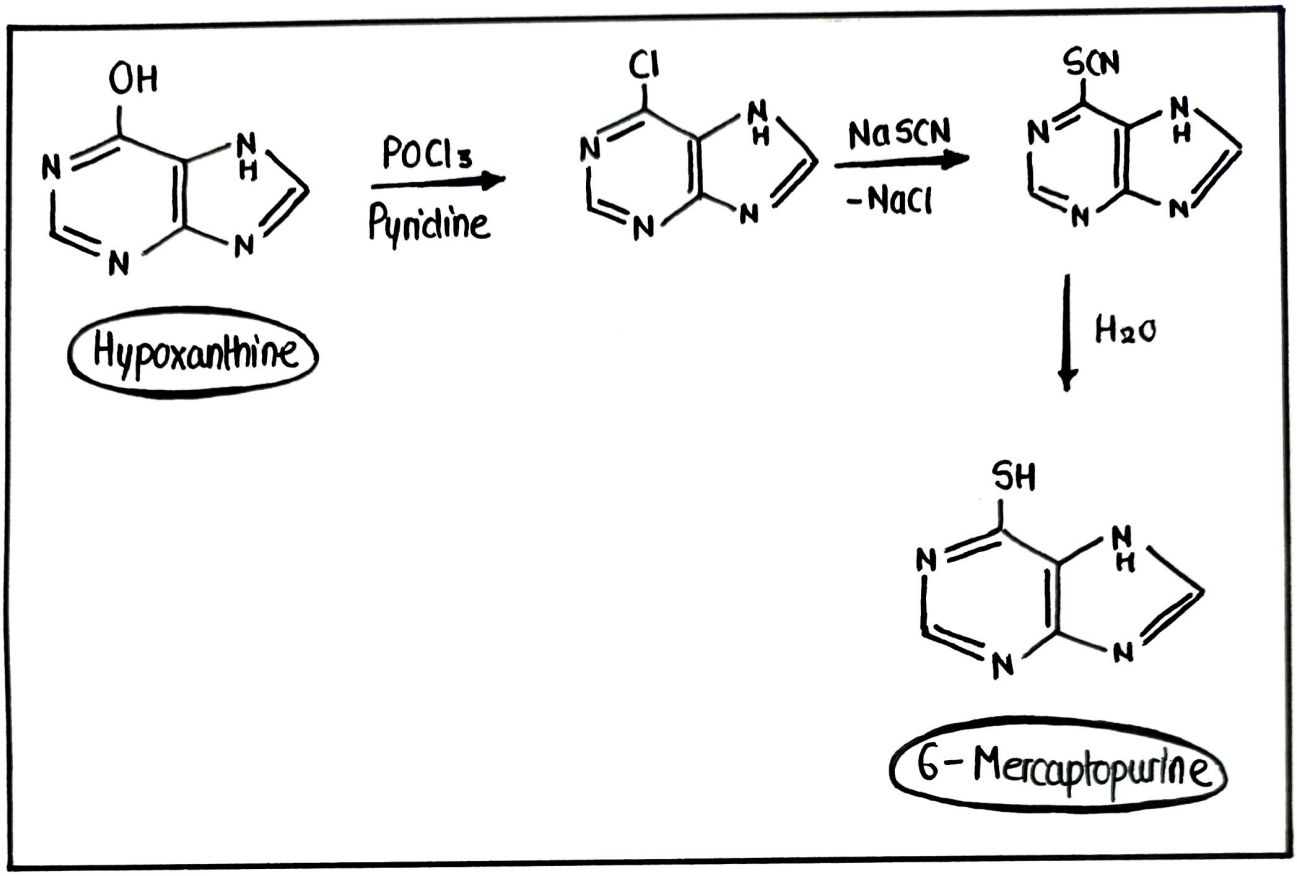
Mechanism Of Action

- Mercaptopurine inhibits the synthesis of Purine Nucleotides.
- Once administered it converted into its active metabolites such as Thioinosine monophosphate (TIMP) and thioguanine nucleotides (TGNs) with the help of Hypoxanthine - Guanine Phosphoribosyltransferase (HGPRT)
- These active metabolites inhibits the conversion of IMP to Adenine & Guanine nucleotides which are essential for DNA & RNA synthesis.
- 6-MP also works by incorporating into DNA & RNA causing further disruption of nucleic acid function & contributing to cytotoxic effects on cancer cells.

Properties

- It is yellowish crystalline powder
- It is insoluble in water & slightly soluble in alcohol.

Synthesis

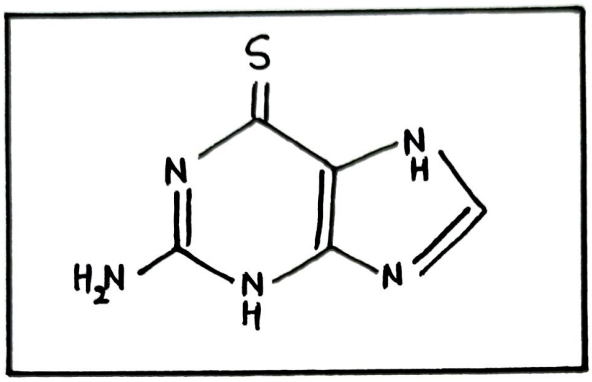


Uses

- It is useful in acute leukaemia.
- It can be used in the treatment of Non-Hodgkin's Lymphoma.
- It is also used in certain types of Autoimmune Disorders.

③ THIOGUANINE

- Thioguanine is a purine analogue under Antimetabolites.
- It is used in the therapy of acute leukaemia.



Mechanism Of Action

- Thioguanine, after administration converted into its active metabolites and interferes with Purine Synthesis.
- It acts by three mechanism

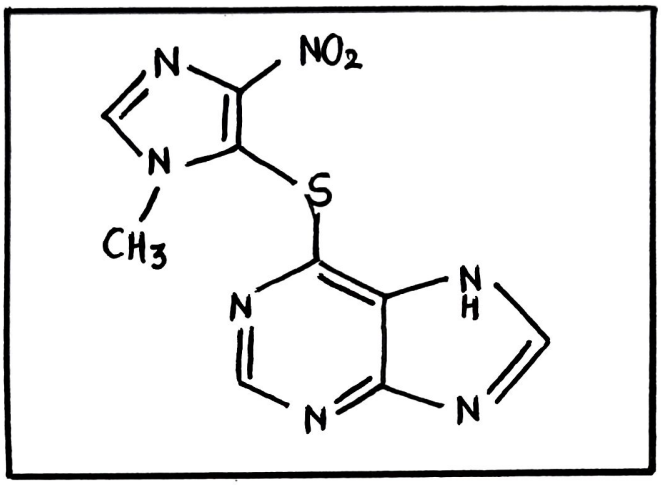
(i) Feedback inhibition of de novo purine synthesis
(ii) Inhibition of inter conversion of purine nucleotide
(iii) Incorporation into DNA & RNA.

Uses

- It is used in the treatment of acute leukamia, especially in combination with cytarabine.

④ AZATHIOPRINE

- Azathioprine is a purine analogue and prodrug of Mercaptopurine
- It is also used as an immunosuppressive agent in organ transplantation.



Mechanism Of Action

- Azathioprine inhibits the purine synthesis.
- Its metabolites are incorporated into DNA & RNA.
- It prevents the synthesis of DNA, RNA & proteins.

Uses

- The use of azathioprine as an antineoplastic agent is less common compared to its immunosuppressive applications.
- It is used mainly in autoimmune disorders.

PYRIMIDINE ANTAGONIST

- Pyrimidine Antagonist are a class of Antimetabolites drugs under Antineoplastic Agents that interferes with the synthesis of Nucleic Acids by mimicking Pyrimidine Bases, that are essential components of DNA & RNA.
- The drugs under Pyrimidine Antagonist includes :

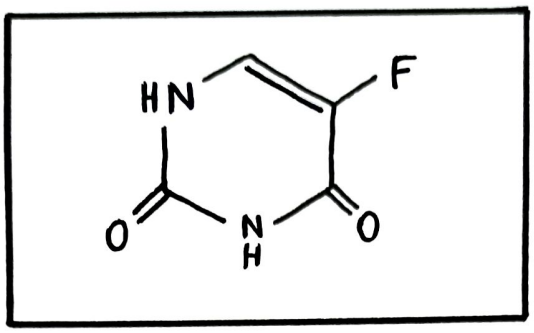
① Fluorouracil
② Cytarabine
③ Floxuridine

MECHANISM OF ACTION

- These drugs inhibit enzymes involved in de novo synthesis of pyrimidines.
- For example : drugs like 5- Fluorouracil inhibit thymidylate synthase, an enzyme crucial for converting uridine into thymidine, a necessary component of DNA.
- Some pyrimidine antagonist can be incorporated into DNA or RNA, disrupting normal nucleic acid function.
- By inhibiting DNA synthesis & repair mechanism, these drugs eventually leads to cell death, especially in rapidly dividing cancer cells.

⑤ FLUOROURACIL

- It is a pyrimidine analogue which is an antineoplastic Antimetabolite



Mechanism of Action

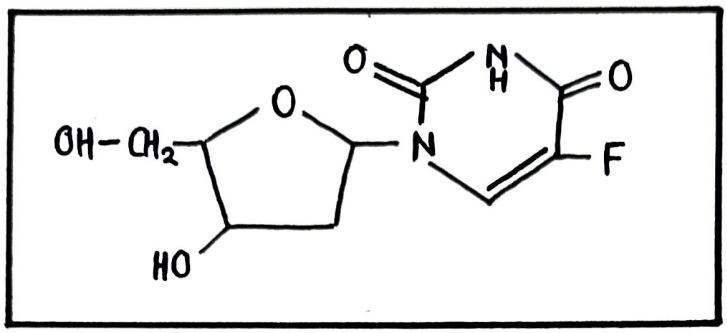
- It inhibits the enzyme Thymidylate synthase that results in inhibition of formation of thymidine from uracil.
- This leads to inhibition of DNA & RNA synthesis & cell death.

Uses

- It is used in the treatment of various types of cancers such as colorectal, breast & skin cancers.

⑥ FLOXURIDINE

- Floxuridine belongs to the class of Pyrimidine Antagonist which on metabolism converted to 5- Fluorouracil.



Mechanism Of Action

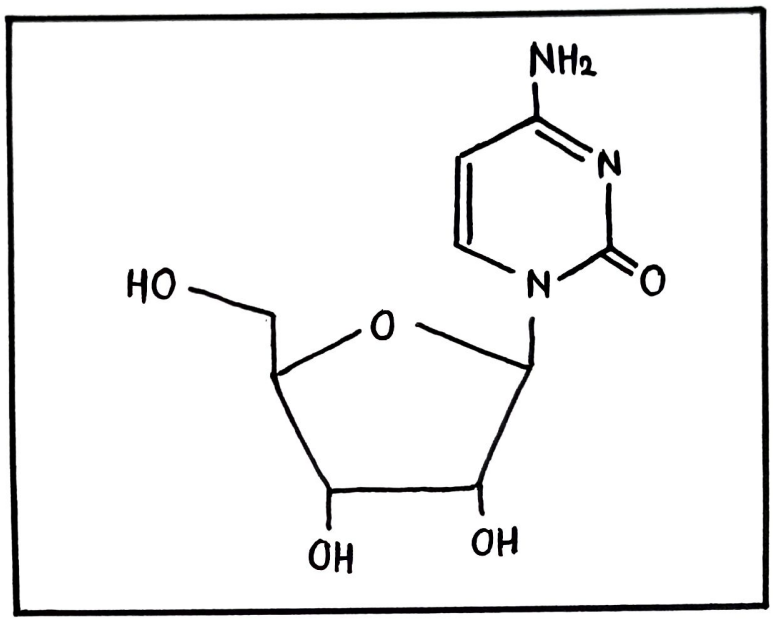
- Floxuridine metabolises into the active 5- Fluorouracil.
- Along with DNA synthesis it also inhibits RNA formation by incorporating into it & producing a false RNA.

Uses

- It is used for management of gastrointestinal adenocarcinoma metastatic to livers.

⑦ CYTARABINE

- Cytarabine belongs to the class of Pyrimidine Antagonist under Antineoplastic Antimetabolite



Mechanism Of Action

- The exact mechanism of action of Cytarabine is not fully understood, however it is believed that it acts through inhibition of DNA Polymerase enzyme by incorporating into DNA

Uses

- It is used for the treatment of acute myeloid leukamia, & various other types of leukamia.

ANTIBIOTICS

- Antibiotics are the drugs that are obtained from Microorganisms.
- They have been recently recognized as an important class of Antineoplastic Agents.
- These are class of drugs known for their ability to inhibit cancer cell growth.
- In our syllabus, we have to study about following drugs :

① Dactinomycin
② Daunorubicin
③ Doxorubicin
④ Bleomycin

MECHANISM OF ACTION

- Antibiotics used as antineoplastic agents works through several mechanism to combat cancer cells.
- Here are following ways :

① Intercalation Into DNA

- Antibiotics such as Doxorubicin & Daunorubicin insert themselves between DNA base pairs, which interferes with normal function of DNA.
- This intercalation disrupts DNA replication & transcription, leading to cell cycle arres and apoptosis (programmed cell death).

② Inhibition Of Topoisomerases

- In addition to intercalation, it inhibits topoisomerase II, an enzyme crucial for DNA replication & repair.
- This inhibition causes DNA strand breakage and impairs the repair process, leading to cell death.

③ Formation Of Free Radicals

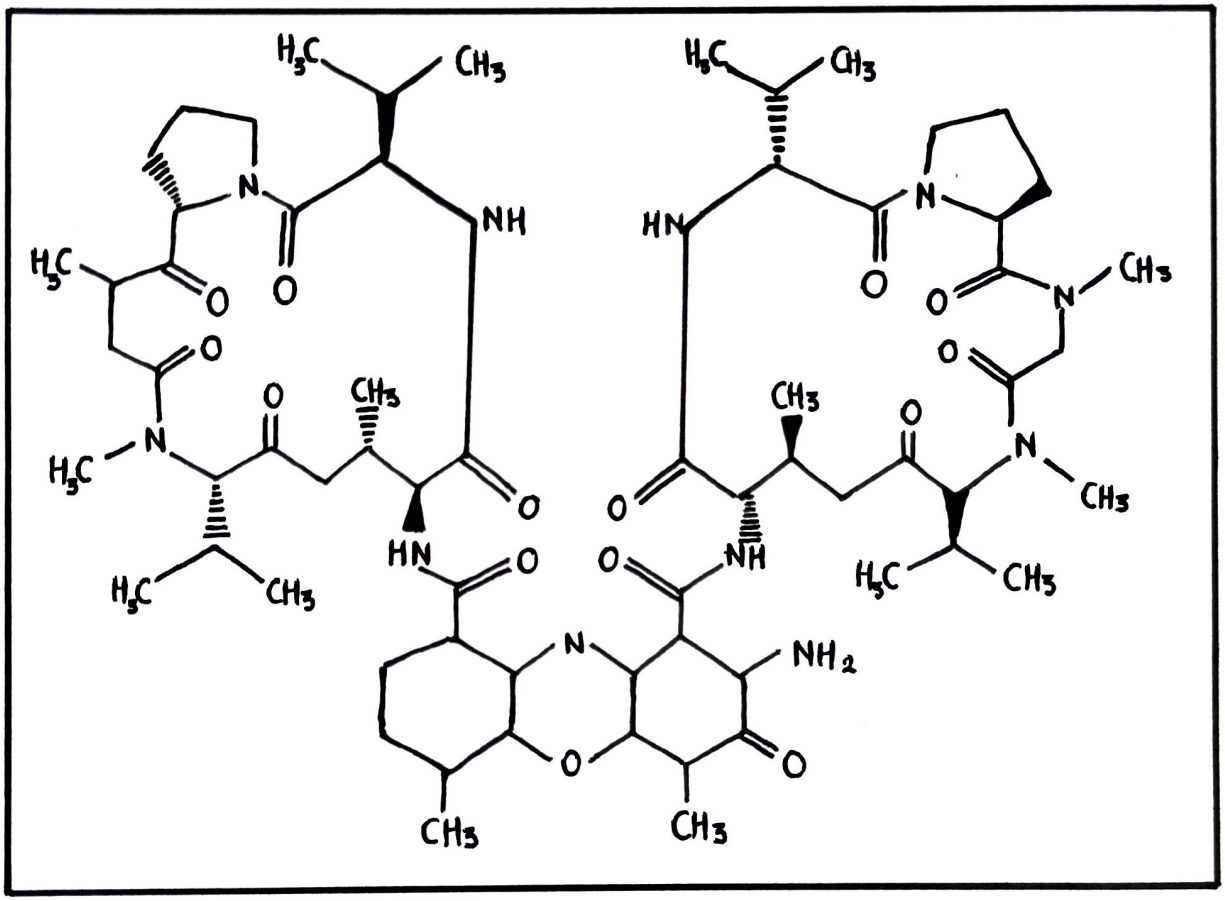
- Antibiotics such as Bleomycin generates Free Radicals, which cause oxidative damage to DNA, leading to single & double strand breakage.
- This damage inhibits DNA replication and transcription, resulting in cell death.

④ Cross Linking of DNA

- Some Antibiotics creates cross-links between DNA strands, which prevents DNA from separating properly for replication & transcription.
- This leads to apoptosis and inhibits tumour growth.

① DACTINOMYCIN

- Dactinomycin, also known as actinomycin D, is an anticancer antibiotic used in treatment of various cancers.
- Dactinomycin having L-threonine, D-valine, L-proline, N-Methyl glycine and L-N methyl valine amino acids.



Mechanism Of Action

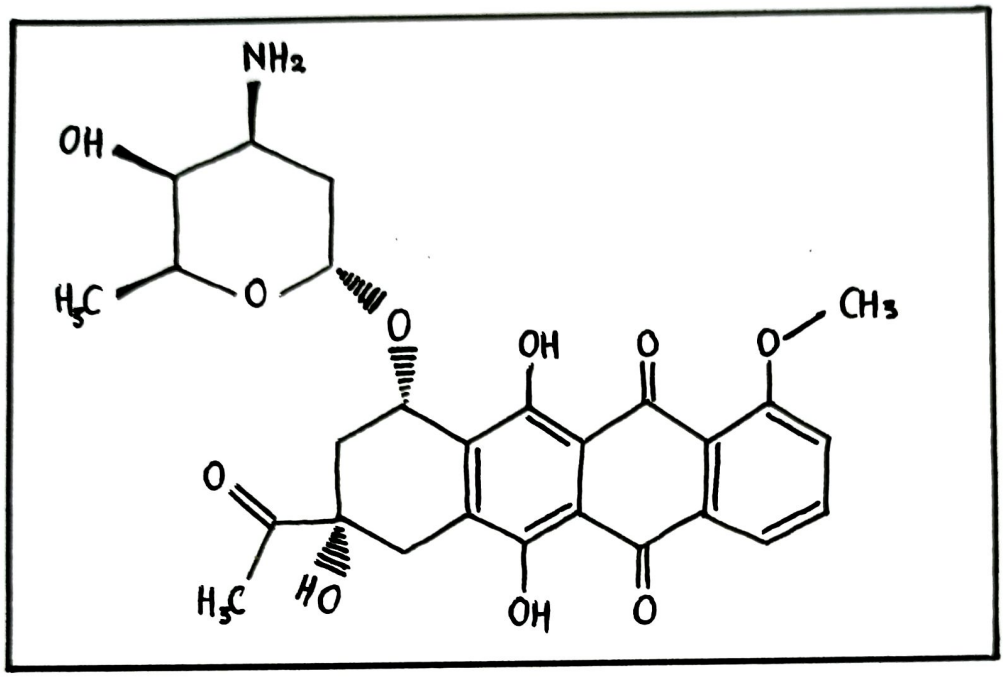
- Dactinomycin is an antineoplastic antibiotic that works by binding to DNA and interfering with its transcription process.
- It intercalates b/w Guanine & Cytosine base pairs in DNA.
- It also inhibits RNA polymerase enzyme required for synthesis of RNA

Uses

- It is used in treatment of various types of cancers.

② DAUNORUBICIN

- Daunorubicin is a toxic anthracycline aminoglycoside antineoplastic agent obtained from Streptomyces Peucetius.



Mechanism Of Action

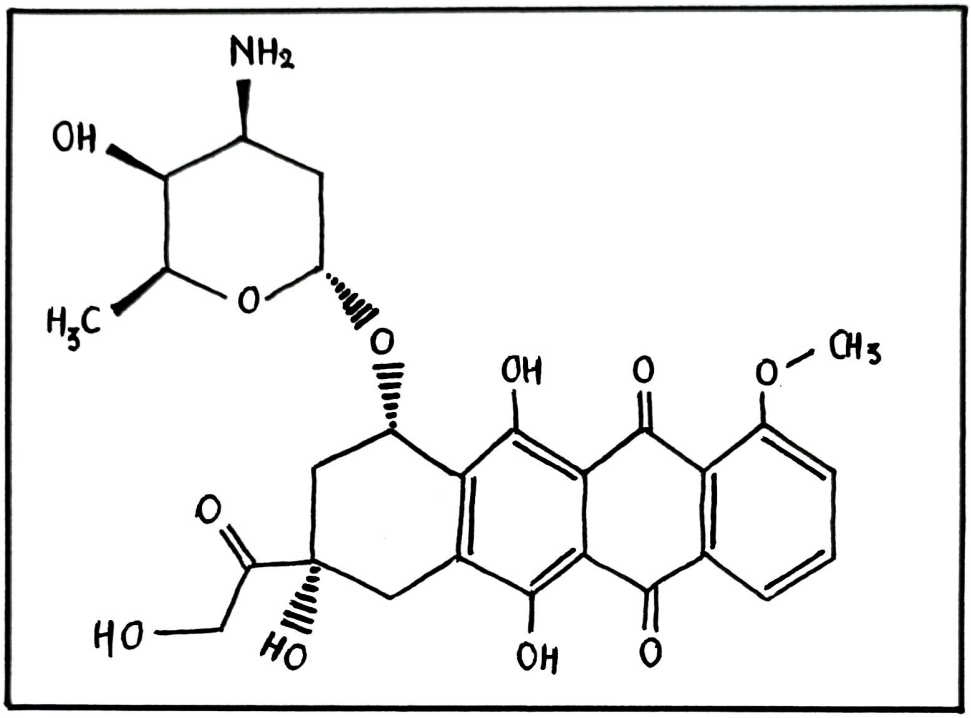
- It damages DNA by intercalating between Base Pairs resulting in uncoiling of the helix, inhibiting DNA & RNA synthesis.
- Daunorubicin may also act by inhibiting Polymerase Activity, affecting regulation of gene expression and generating free radicals.

Uses

- These drugs are used for the treatment of acute myclocytic leukaemia, & acute lymphoblastic leukaemia.

③ DOXORUBICIN

- It is an anthracycline antibiotic with antineoplastic activity & isolated from Streptomyces Peucetius.



Mechanism Of Action

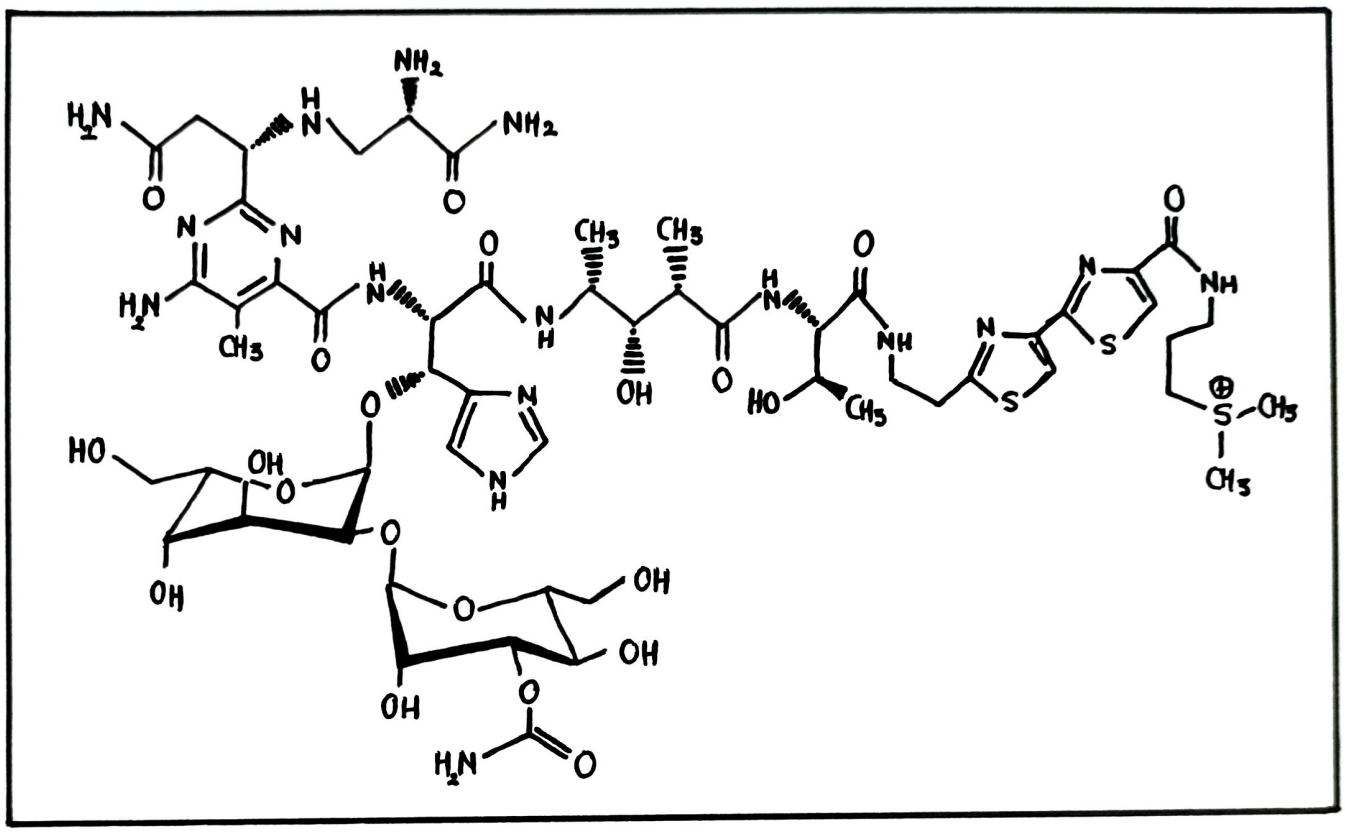
- Doxorubicin act by forming complexes with DNA through intercalation between base pairs.
- It also inhibits the active of Topoisomerase -II.

Uses

- Doxorubicin used in combination with other medications to treat certain types of bladder, breast, lungs, stomach & ovarian cancer.
- It also used in treatment of Hodgkin's & Non-Hodgkin's lymphoma.

④ BLEOMYCIN

- Bleomycin is a complex of related glycopeptide antibiotic obtained from Streptomyces Verticillus & consist of Bleomycin A2 & B2.



Mechanism Of Action

- The exact mechanism of action of Bleomycin is not known, but available evidences indicates that it inhibits DNA synthesis & also RNA & protein synthesis.

Uses

- Hodgkin's Lymphoma
- Non- Hodgkin's Lymphoma
- Testicular, Ovarian Cancer

PLANT PRODUCTS

- Plant Products as Antineoplastic Agents refers to compound derived from plants that have the ability to inhibit or prevent the growth of cancer cells
- These compounds known as phytochemicals, can act in various ways to combat cancer such as disrupting cell division, including apoptosis or interfering with blood supply to tumors.
- Plant derived drugs have fewer or no side effect.

In our syllabus, we have to study about :

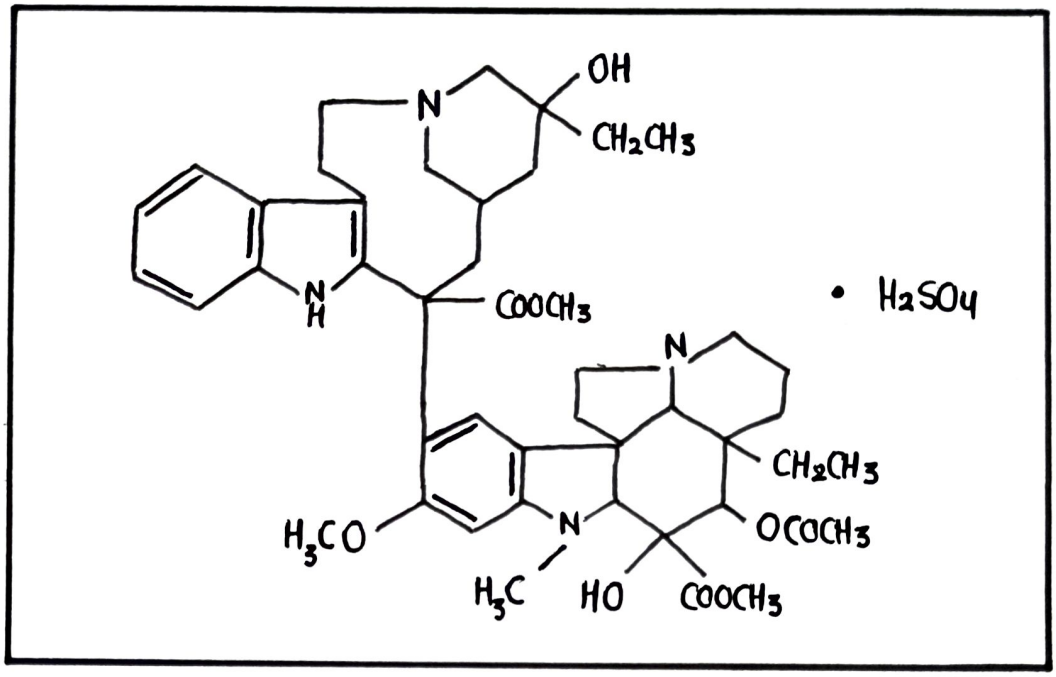
① Vinblastin Sulphate
② Vincristin Sulphate
③ Etoposide

Mechanism Of Action

- Plant products as antineoplastic agents work through various mechanism to target and kill cancer cells.
- Plant poooducts such as Vinblastin & Vincristine inhibit the polymerization of tubulin into microtubules, disrupting spindle formation & blocking cell division.
- Drugs such as Etoposide Inhibits topoisomerase II, an enzyme crucial for DNA strands breakage and cell death.

① VINBLASTIN SULPHATE

- Vinblastin sulphate is the sulphate salt of Vinblastine, a natural alkaloid isolated from the plant Cathrantus Roseus with antineoplastic properties.



Mechanism of Action

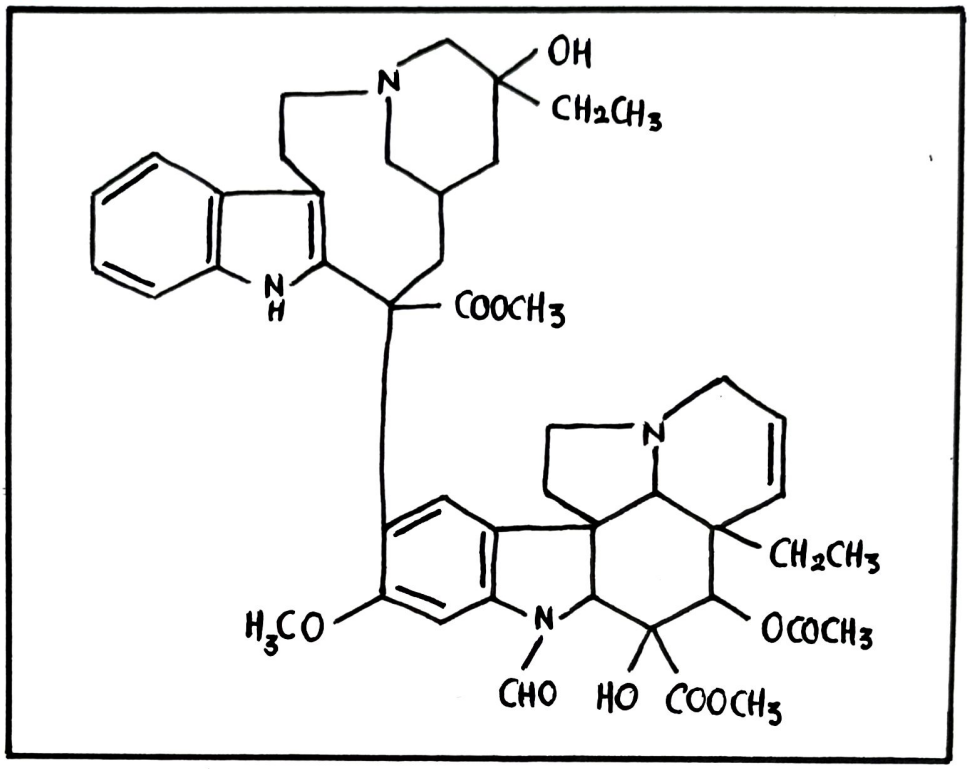
- Vinblastine binds to tubulin & inhibits microtubule formation, resulting in disruption of mitotic spindle.
- The chromosomes fails to move apart during mitosis & lead to metaphase arrest.

Uses

- Hodgkin's Lymphoma
- Non-Hodgkin's lymphoma
- Lymphocytic Lymphoma

② VINCRISTINE SULPHATE

Vincristine was first isolated in 1961
It is given intravenously.



Mechanism Of Action

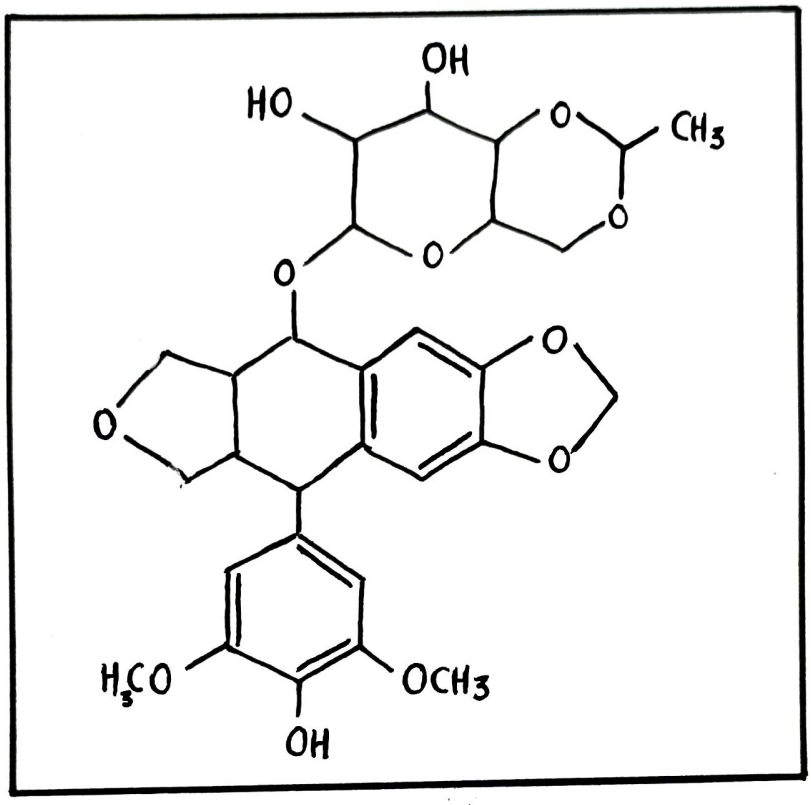
- It binds to tubulin protein, prevents polymerization and assembly of microtubules, and causes mitotic spindle destruction
- The chromosomes fails to move apart during mitosis & lead to metaphase arrest.

Uses

- Acute Myeloid Leukaemia
- Hodgkin's Disease
- Lung Cancer etc.

③ ETOPOSIDE

Etoposide is a semisynthetic derivative of podophyllotoxin. It possess potent antineoplastic property.



Mechanism Of Action

- It forms complex with topoisomerase II enzyme and causes breakage of DNA strand.

Uses

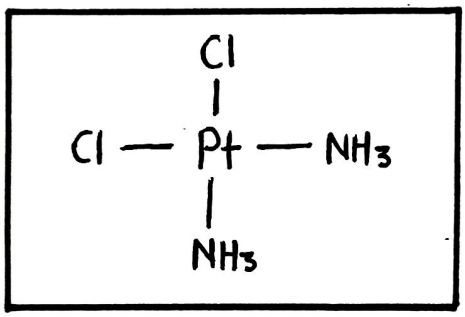
- Testicular Cancer
- Lung Cancer
- Bladder Cancer
- Hodgkin's Lymphoma etc.

MISCELLANEOUS

- Miscellaneous antineoplastic agents refer to a group of cancer drugs that do not fit completely into the typical categories of chemotherapy due to their unique MOA.
- Some of them are as follows :

① CISPLASTIN

- Cisplastin is a platinum based chemotherapy drug known for its antineoplastic activity



Mechanism Of Action

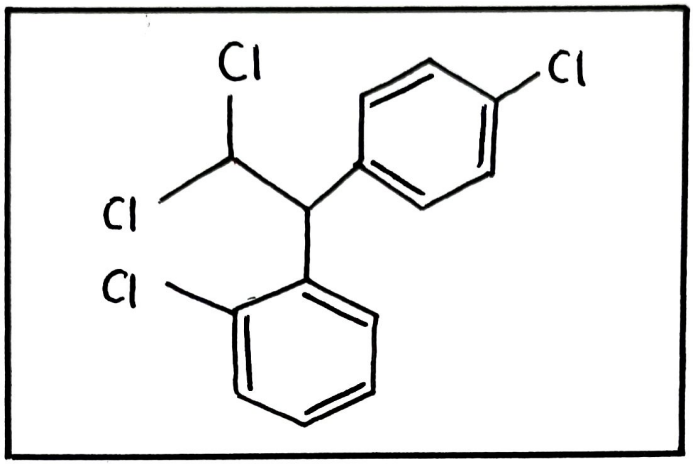
- Cisplastin works by damaging the DNA of cancer cells, by DNA crosslinking, leading to cell death.

Uses

- Testicular Tumour
- Ovarian Tumours
- Bladder Cancer

② MITOTANE

- Mitotane is the derivative of dichlorodiphenyldichloroethane having anticancer properties.



Mechanism of Action

- The exact MOA of Mitotane is not known, but according to present data it affects the Adrenal Cortex by inhibiting steroid production, leading to destruction of adrenal cancer cells.

Uses

- Cancer of Adrenal Gland (Adrenocortical Carcinoma)

THANK YOU

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