Anti-Gout Drugs

Definition:- *A gout is a disease in which plasma urate concentration get increased (Hyperuricaemia). Uric acid is a product of purine metabolism at low pH has low water solubility.*

Causes:-

Overthinking of alcoholic beverages, especially beer, or purine rich foods.

Drugs like thiazides, furosemide, levodopa, clofibrate reduce uric acid excretion by kidney and produce gout.

Antigout Drugs:- *These are the drugs which are used in the treatment of gout; are called as antigout drugs.*

Pharmacotherapy of gout:- *1. Inhibiting uric acid synthesis (Allopurinol) 2. Increasing uric acid excretion (Probencid)*

3. Inhibits leucocytes migration towards joints (Colchicine)

4. Providing general NSAIDs action (Glucocorticoids)

Classification:-

1. Acute goout:- *Acute gout is a painful condition that often affects only one joint.*

EX:- NSAIDs,, Colchicine, Glucocorticoids.

2. Chronic gout:- *Chronic gout is a repeated episodes of painn and inflammmation.*

Ex:- Probencid, Allopurinol, etc.

Common Mechanism Of Action:- *An antigouut agents that competitively inhibits reabsorption of uric acid at th proximal convulated tubule. Also, inhibits renal tubular secretion of weak organic acids, such as penicillins.*

1) NSAIDs Drugs:-

Various drugs used are indomethacin, naproxen, diclofenac etc given at high and repeated dose to terminate attack.

Produces responses slow as compared to colchicine ;but well tolerated so more preffered than colchicine.

But not recommended for long term management due to risk of toxicity.

Naproxen,piroxicam inhibits chemotactic migration of leucocytes into the inflamed joints.

Side effects:-Nausea, vomitting, diarrhea, decreased appetite, hypersensitivity etc.

Therapeutic Use:-

1.In the treatment of both acute as well as chronic gout. 2.In the treatment of inflammaion and pain.

2) Colchicine:-

Alkaloid from autumn crocus found as antigout in 1763 and isolated as pure form in 1820

Not having anti-inflammatory or analgesic activity;but used specifically in the treatment of gouuty inflammation.

It is used in the treatment of acute as well as chronic gout.

MOA:-

It deacreases the migration of granulocytes towards joints and also inhibits the synthesis and release of leukotrienes

Adverse effect:- Diarrhea, nausea, abdominal pain, vomiting etc.

Therapeutic use:-

Used to prevent gout attack.

3) Corticosteroid:-

Intra-articular injection of soluble steroids supress symptoms of acute gout.

Corticosteroids deacrease the pain,swelling,redness,and inflammation of gout.

But corticosteroids are used only for patients suffering bfrom renal failure or peptic ulcer (Because NSAIDs are contraindicated).

Risk of rebound of attack is observed on drug withdrawl.

Example:- Prednisolone 40-60mg.given once a day.

Adverse Effects:-

-Fluid retension
-Upset stomach
-High blood pressure etc.

4) Probencid:-

The medication is used to prevent gout and gouty arthritis.

Probencid belongs to a class of drugs known as Uricosurics.

It lowers high levels of uric acid in your body by helping the kidneys to get rid of uric acid.

Probencid should not be used in children younger than 2 years.

Adverse Effects:-

-Diarrhea
-Nausea
-vomiting
-Abdominal pain etc.

5) Sulfinpyrazone :-

It is a pyrazolone derivative related to phenyl butazone having consistent uricosuric action.

Not having anti-inflammatory or analgesic activity but used specially in the treatment of gouty inflammation.

MOA OF Sulfinpyrazone:-

It inhibits tubular reabsorption of uric acid.

Also,inhibits platelet aggregation.

Adverse Effect:-

Gastric irritation so contraindicated in patients with peptic ulcer.

Rashes and other hypersensitivity reactions.

Use:- Used in the treatment of chronic gout 100-200mg.BD

6) Allopurinol:-

This hypoxanthine analogue was synthesized a purine antimetabollite for cancer chemotherapy it had no antineoplastic activity.

It has substrate as well as inhibitor of Xanthine oxidase ,the enzyme responsible for uric acid synthesis.

Adverse Effect:-

-Hypersensitivity.
-Headache.
-Liver damage.
-Nausea.

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SUBJECT : Pharmacology–II

TOPIC : Anti-Gout Drugs.

CLASS : Third year B.pharm

ACADEMIC YEAR : 2021-2022

ANTI-RHEUMATIC DRUG

➢ RHEUMATOID ARTHRITIS (RA) :-

- Rheumatoid arthritis (RA) is a chronic, symmetrical, Inflamantory autoimmune disease that initially affects small joints, progressing to larger joints, and eventually the skin, eyes, heart, kidney, and lungs.
- The first line drugs used in the treatment of RA are NSAIDs that help in relieving pain, swelling, morning stiffness, immobility, but do not show complete cure.

➢ OSTEOARTHRITIS (OA) :-

- Osteoarthritis is a degenerative disease that worsens over time, often resulting in chronic pain.
- Joint pain and stiffness can become severe enough to make daily tasks difficult.

➢ ANTI-RHEUMATIC DRUG :-

- Anti-rheumatic drugs are specific anti - inflammatory or analgesics, used to suppress the rheumatoid process and also bring the remission. These drugs do not include corticosteroids.
- They can be used along with the NSAIDs and are also called as Disease Modifying Anti -Rheumatic Drugs (DMARDs) or Slow Acting Anti-Rheumatic Drugs (SAARDs).

➢ CLASSIFICATION:-

1) **Disease Modifying Antirheumatic Drugs (DMARDs).**
   - i) Immunosuppressants – Methotrexate, Azathioprine, and Cyclosporine.
   - ii) Sulfasalazine.
   - iii) Chloroquine or Hydroxychloroquine.
   - iv) Leflunomide.
   - v) Gold sodium thiomalate and Auranofin.
   - vi) D-Penicillamine
2) **Biologic Response Modifiers (BRMs).**
   - i) TNF Inhibitors: Etanercept, Infliximab, and Adalimumab.
   - ii) IL-1 Antagonist: Anakinra
3) **Adjuvant Drugs: Corticosteroids – Prednisolone.**

➢ ACTION OF ANTI-RHEUMATIC DRUG :-

Sr. No.	Anti-rheumatic drug	Mechanism of action	Pharmacological action	Uses	Adverse effects
1.	Methotrexate	Inhibition of enzyme	MTX becomes polylutamated once inside the cell	Treat certain type of cancer	Feeling sick, Headaches
2.	Azathioprine	Inhibit purine synthesis	Redues the no. of circulating monocytes	To prevent the organ rejection in people	Loss of appetite,fatigue
3.	Gold salt	Inhibit lymphocyte proliferation	Lupus erthematous	Used to treat arthritis	Renal damage,stomatitis
4.	penicillamine	Inhibiting the synthesis and reduses of IL-I	Leave the body through the urine	Used in Wilson's disease	Stomach pain, nausea, vomiting

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SUBJECT:- Pharmacology-II.

TOPIC NAME:- Anti-rheumatic drug.

CLASS:-T.Y.B.Pharmacy.

ACADEMIC YEAR:-2021-2022.

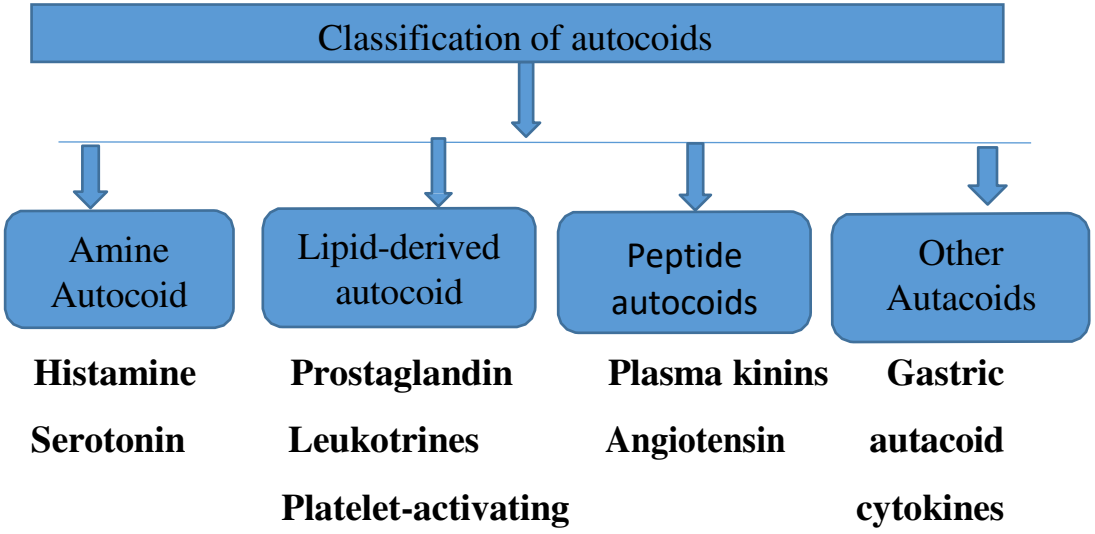
AUTOCOIDS AND RELATED DRUGS

DEFINITION:-The term autacoids derived from Greek; autos-self, akos – healing substance or remedy.

They have also been called 'Local Hormone'. Autacoids involve in a number of physiological and pathological process. These are diverse substance produced by a wide variety of cell in the body having intense biological activity. But generally act locally at site of synthesis and release

Some autacoids in addition serve as a transmitter or modulator in the nervous system, but there role at many site is not precisely know. A number of useful drugs act by modifying their action or metabolism.

• CLASSIFICATION:-

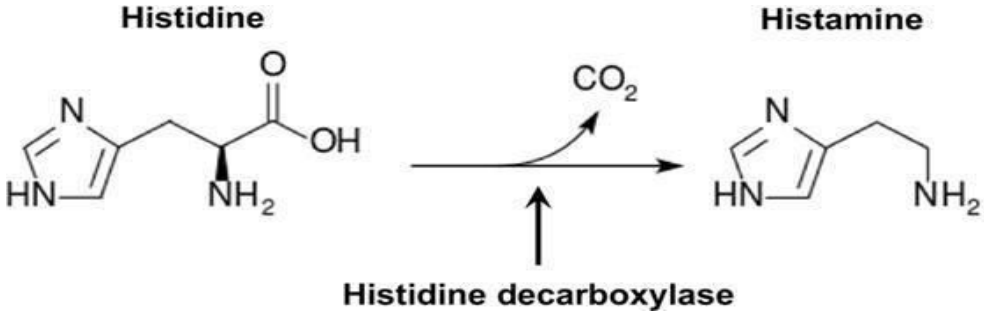


HISTAMINE:-

Histamine is a chemical messenger that mediates a wide range of cellular response including allergic and inflammatory reactions gastric acid secretion and neurotransmission in parts of the brain.

Histamine has no clinical application but agents that interfere with the action of histamine have imp therapeutic application.

- **SYNTHESIS:-**



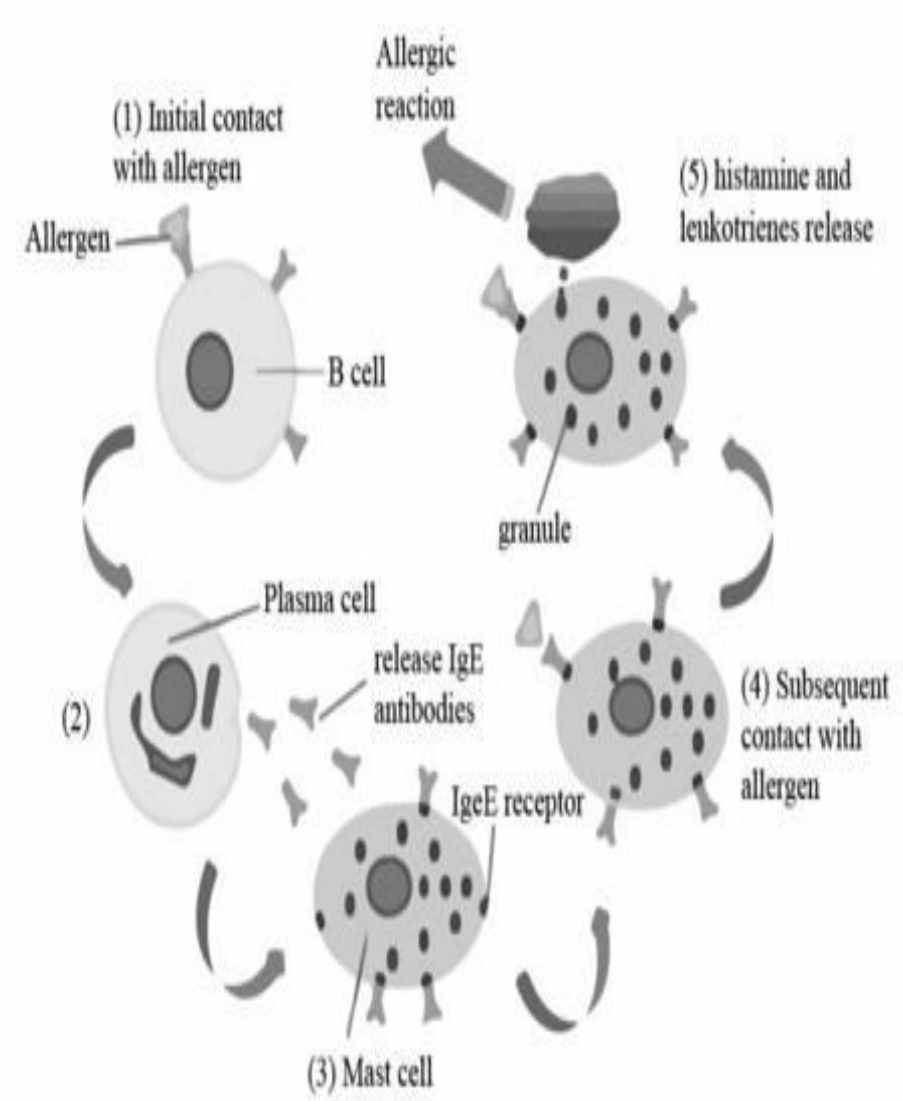
- **LOCATION:-**

- In human histamine is found in nearly all tissue of the body, where it is stored primarily in the granules of tissue mast cells.

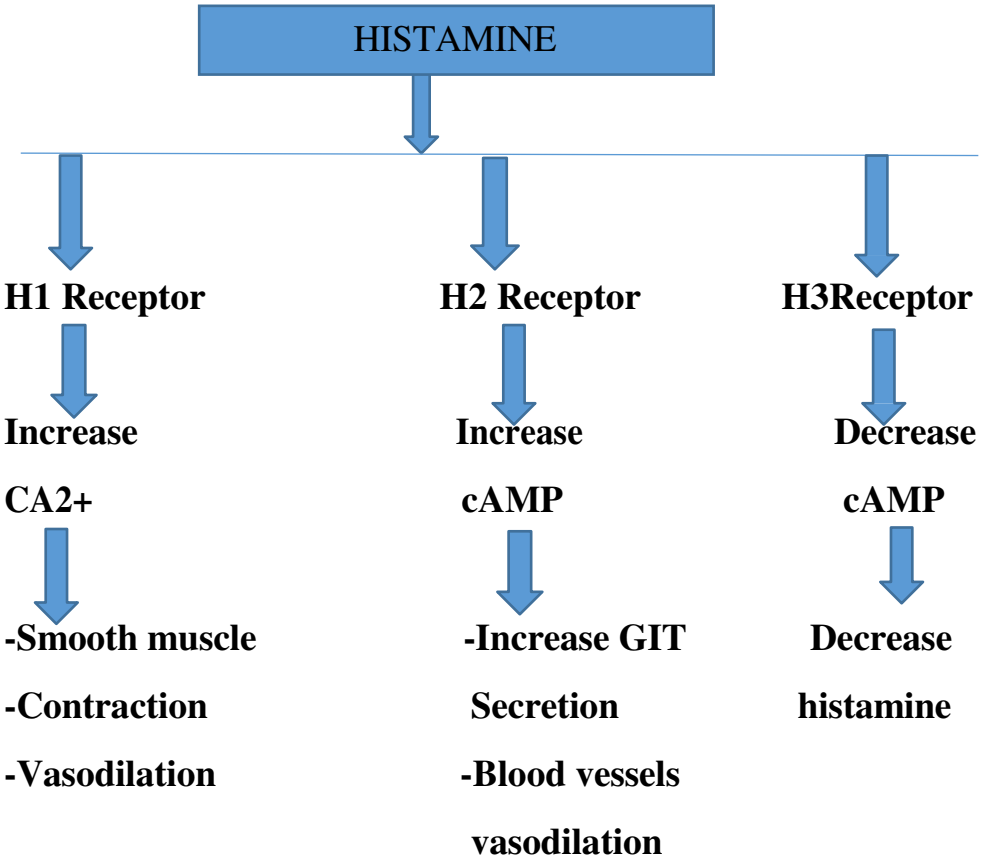
- The blood cells called basophils also harbor histamine containing granules.

- Histamine occur in practically all tissue but it is unevenly distributed with high amount found in lung, skin and the gastrointestinal tract - It found at high concentration in mast cells or basophils. Histamine also occur as a component of venoms and in secretion from insect stings.

● **RELEASE OF HISTAMINE:-**



● **MECHANISM OF HISTAMINE:-**



• ANTAGONIST OF HISTAMINE:

CLASS	EXAMPLE
•H1 ANTAGONIST	Antazoline, Mepyramine, Chloropyramine
FIRST GENERATION:-	
1.Ethylenediamine	Doxylamine, Bromazine, Clemastine
2.Ethanolamine	Pheniramine, Chlorphenamine.
3.Alkylamines	Cyclizing, Meclizine
4.Piperazine	Promethazine,Cyproheptadine
5.Tricyclic	
SECOND GENERATION	
1.Piperidine	Fexofenadine
2.Miscellaneous	Loratadine, Cetirizine

CLASS	EXAMPLE
• H2 ANTAGONIST	Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole,
• H3 ANTAGONIST	Burimamide, Ipromidine, Theoperamide
• H4 ANTAGONIST	Thioperamide

H1 ANTAGONIST

MECHANISM OF ACTION:-

The primary mechanism of antihistamine

action in the treatment of allergic disease is believed to be competitive antagonism of histamine binding of cellular receptor which are present on the nerve ending smooth muscles

USES:-

1. In allergic conditions
2. It is used in the treatment of rhinorrhea.
3. It is also used in the treatment of urticarial.
4. In a conditions like cold and flu, it is very effective to treat.

ADVERSE EFFECT:-

Sedation

Dizziness

Tinnitus

Blurred vision

Euphoria

Anxiety

Insomnia

H2 ANTAGONIST-

MECHANISM OF ACTION:-

H2 antagonist decrease gastric and secretion by reversible binding histamine H2 receptor located on the gastric parietal cells

USES:-

1 It is used in allergic rhinitis and urticarial

2 It is used in motion sickness.

3 It is use as pre-anesthic medication.

4. it also used in duodenal and gastric ulcer.

ADVERSE EFFECT:-

Headache

Drowsiness

Joint or muscle pain

Breast swelling and tenderness

Confusion in elderly people

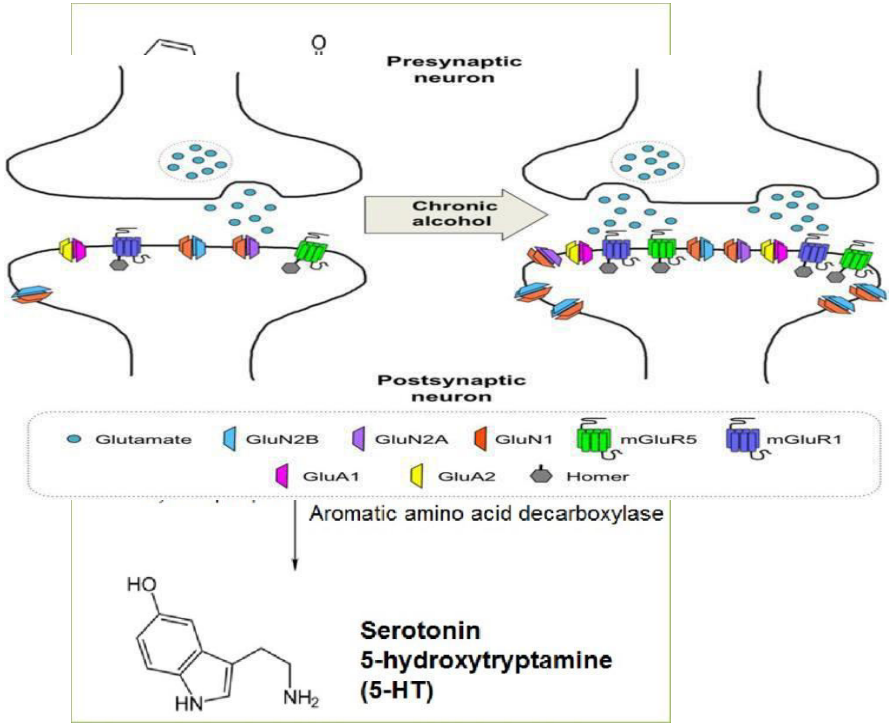
Trouble urination

A rash

● 5 HYDROTRPTAMINE [5HT, SEROTONIN]:-

Serotonin was the name given to the vasoconstriction substance which appeared in the serum when blood clotted and enteramine to smooth muscles contractive cells of the gut mucosa.

● SYNTHESIS:-



● **STORAGE:-** 5-HT is stored within storage vesicles and its uptake at the vesicular membrane by vesicular monoamine transporter[VMAT-2].

● 5-HT ANTAGONIST:-

● CYPROHEPTADINE:-

It primarily blocks 5-HT2A receptors and has additional H1-antihistamine, anti-cholinergic and sedative properties like other histaminic, it is a good antipruritic but anti-5-HT action has no role in these condition. It increase appetite and has been used in children and poor eater to promote weight gain

● MECHANISM OF ACTION:-

Cyproheptadine appears to exert its antihistamine and antiserotonin effects by competing with free histamine and serotonin for binding at their respective receptors.[9] Antagonism of serotonin on the appetite center of the hypothalamus may account for cyproheptadine's ability to stimulate the appetite

● USES OF CYPROHEPTADINE:-

1 It is used to relive allergy symptom.

2 It use in hay fever.

3 It is also used to relive the itching of allergy skin condition.

● ADVERSE EFFECT OF CYPROHEPTADINE

1 Dry mouth , nose, and throat

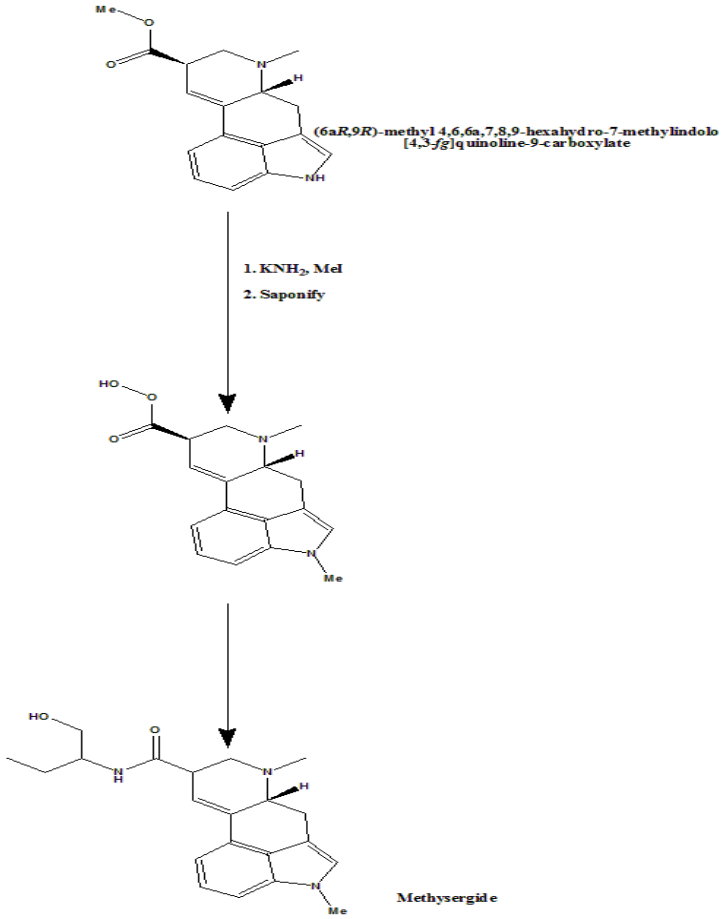
2 Drowsiness

3 Nausea

● **DOSES** - 4 mg orally 3 times a day.

● METHYLSERGIDE:-

It is chemically related to ergot alkaloids. Methylseride is a potent 5-HT antagonist with some tissue specific agonistic action as well but is non selective acts on 5-HT receptor also. It also used for migraine, prophylaxis, and carcinoid.



MECHANISIM OF ACTION:-

Methysergide is serotonin antagonist acts on central nervous system (CNS), which directly stimulates the smooth muscle leading to vasoconstriction. Some alpha-adrenergic blocking activity has been reported. Suggestions have been made by investigators as to the mechanism whereby Methysergide produces its clinical effects, but this has not been finally established, although it may be related to the antiserotonin effect.

● USES OF METHYLSERGIDE:-

1 It uses in treatment of migraine headaches

2 It is not used to treat migraine attacks

3 It is also use to treat episodic

● ADVERSE EFFECT OF METHYLSERGIDE:-

1 Nausea

2 Vomiting

3 Heart burn

4 Abdominal pain

5 Constipation

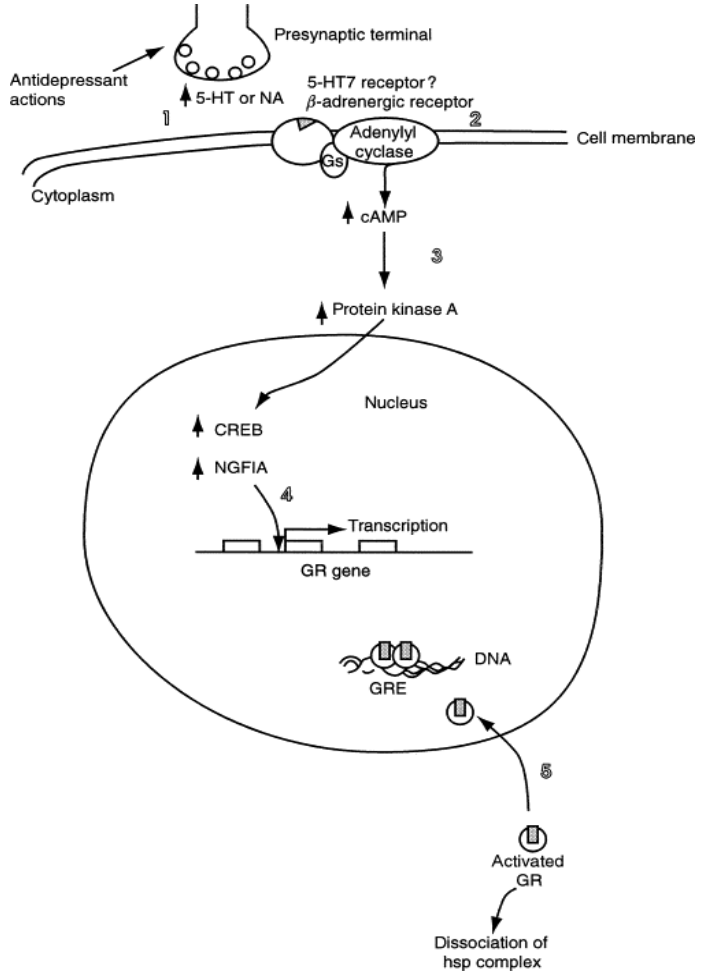
● DOSES –

4 to 8 mg daily orally.

● KETANSERIN

It has selective 5-HT_2 receptor blocking property with negligible action on 5-HT, 5-HT_3, & 5-HT_4, Receptor and no.

● MECHANISM OF ACTION: -



Ketanserine it is new antihypertensive agent with affinity to serotonin (5HT_2) receptor and higher concentration also to alpha1-adreno receptor.

● USES OF KETANSERIN:-

1 It is used in cardiac surgery.

2 It is used in treatment of hypertension

● ADVERSE EFFECT OF KETANSERINE

1 Drowsiness

2 Fatigue

3 Headache

4 Dry mouth

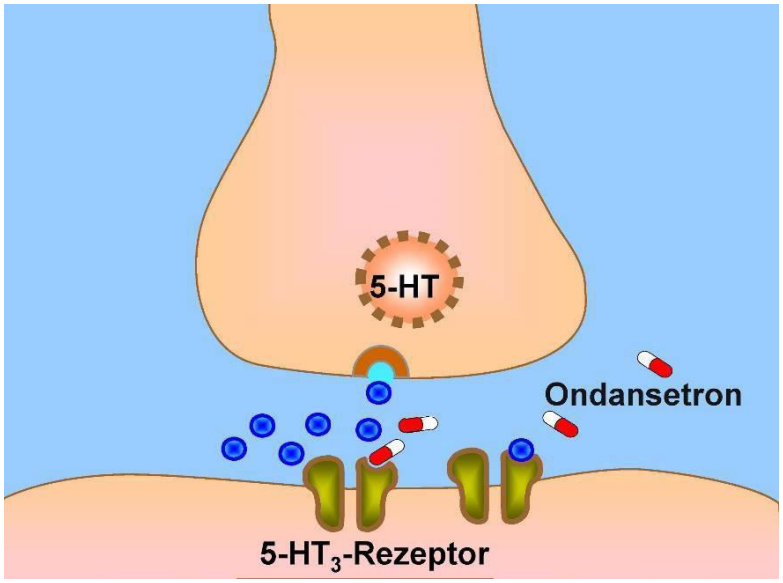
● DOSES –

Adult 20 mg increases 40 mg after 2-4 week

• ONDANSETRON

It is highly potent and selective antagonist at 5-HT_3 receptor antagonist. Its antiemetic action were first revealed by its ability to antagonize retching and vomiting induced by chemotherapy and radiotherapy in animal and man.

MECHANISM OF ACTION:-



Ondansetron is a selective 5-HT_3 receptor antagonist. It blocks the depolarizing action of 5-HT through 5-HT receptor on vagal afferent in the GIT & in the brain.

USES:-

1. It is used in cancer treatment
2. In pregnancy
3. Gastro-entertities

ADVERSE EFFECT:-

Constipation

Abdominal dysfunction

DOSE:- 0.15 mg IV

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3)Lippincort Wiliams & Wilkins Pharmacology 4th Edition page no -519-527

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TOPIC:- Autacoids and related drugs

CLASS:- T.Y.B. Pharm

ACADEMIC YEAR:- 2021-2022

AUTOCOID HISTAMINE

- Chemical messenger that mediates a wide range of cellular responses, including allergic and inflammatory reactions, gastric acid secretion, and neurotransmission in parts of the brain.
- Plays an important role in gastric acid secretion.

Location of Histamine

- Occurs in practically all tissues.
- High amounts found in lung, skin, and the GIT.
- Found at high concentration in mast cells or basophils.
- Occurs as a component of venoms and in secretions from insect stings.

Synthesis of Histamine

- Histamine is an amine formed by the decarboxylation of the amino acid histidine by histidine decarboxylase

Release of Histamine

- Immunologic Release
- Chemical and Mechanical ReleaseChemical and mechanical mast cell injury causes degranulation and histamine release

Role in allergy and anaphylaxis

- contraction of smooth muscle.
- stimulation of secretions.
- dilation and increased permeability of the capillaries.

Mechanism of Action of Histamine

Histamine

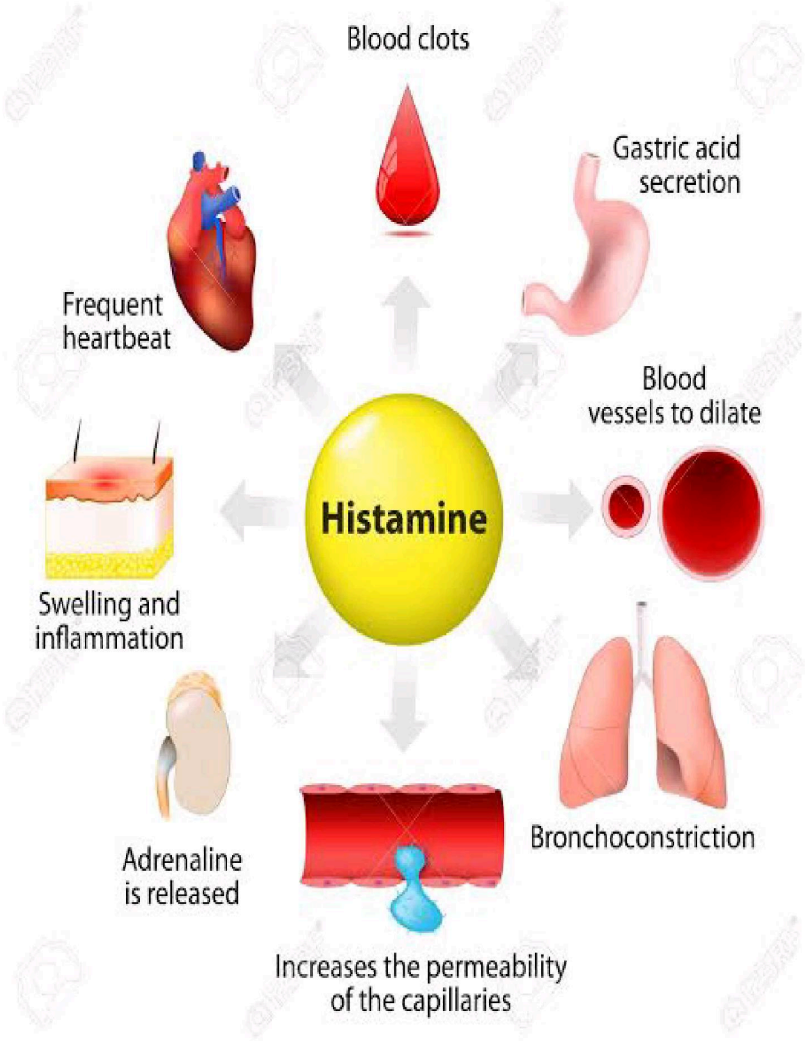
H1 Receptor → Ca^{2+}

- Smooth muscle contractions.
- Increase capillary permeability.
- Vasodilation.
- Sensory nerve endings pain and itching.

H2 Receptor → cAMP

- Increase gastric acid secretion.
- Blood vessels - vasodilation.
- Increase capillary permeability.

Pharmacological Action



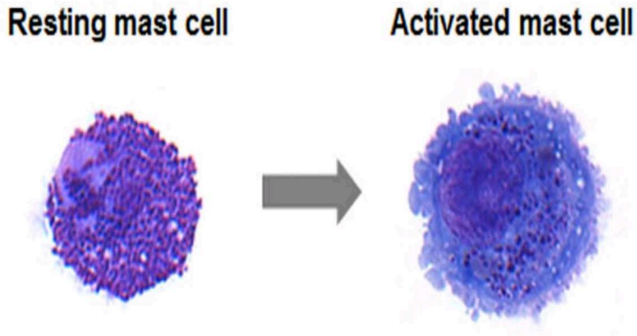
Role of mediators

- Symptoms associated with allergy and anaphylactic shock result from the release of certain mediators from their storage sites.
- Difference between these two situations results from differences in the sites from which mediators are released and in their rates of release.

mediator of allergy, inflammation, gastric acid secretion

Adverse effects of histamine release

- Itching, Urticaria
- Flushing Hypotension
- Tachycardia Bronchospasm
- Angioedema Wakefullness
- Increased acidity (Gastric acid secretion)



ANTIHISTAMINES

There are more types of receptors H1, H2, H3, and H4. H1 and H2 receptor are widly expect and are the target of clinicaly use full drug

A. H1 Receptor blockers

- These compounds do not influence the formation or release of histamine; rather, they block the receptor mediated response of a target tissue.

Example of H1 Antihistamines

- Loratadine
- Desloratadine
- Cetrizine
- Chlorpheniramine
- Diphenhydramine
- Promethazine
- Levocetrizine
- Cyclizine

Mechanism of Action: H1 Antagonists

- Displaces histamine from the H1 receptor, which is a G-protein coupled receptor.
- Histamine leads to formation of IP3 and a release of stored Ca++, followed by a cascade of other events.
- H1 receptor blockade prevents this activity and leads to a decrease in Ca++ inside of the cell.

Pharmacokinetics

- Absorption : Oral, parenteral routes
- Distribution : Throughout body.Enter Brain Newer compounds penetrate poorly
- Metabolism : Metabolized by Liver
- Excretion : Excreted in Urine

Uses

use in treatment of,

- allergic and inflammatory reaction
- motion sickness and nausea
- somnifcients
- vertigo

Adverse effects

- sedation
- dry mouth
- over dose may hypotension
- over dose may include hallucinations
- over dose may include collapse and several respiratory system.

B. H2 Receptor blockers

- Block the actions of histamine at all H2 receptors.
- Chief clinical use is to inhibit gastric acid secretion.secretio
- Effective against nocturnal acid secretion.

Examples of H2 Receptor blockers

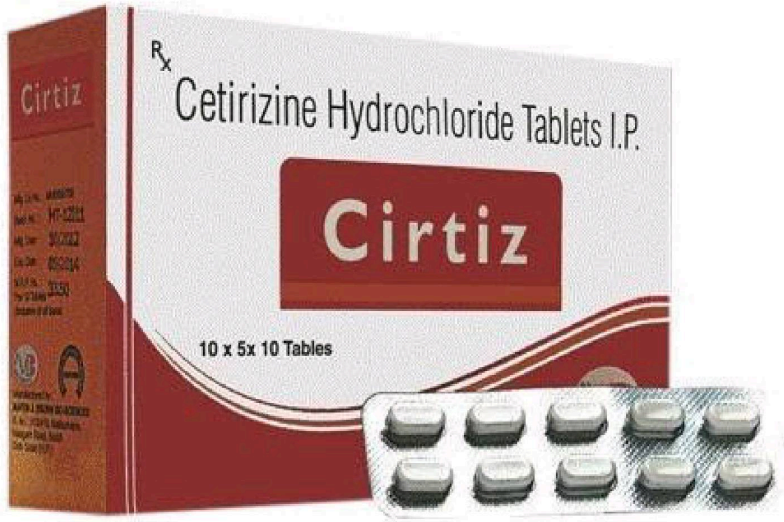
- Cimetidine
- Ranitidine
- Famotidine
- Nizatidine

Mechanisms of Action: H2 Antagonists

- Displaces histamine from the H2 receptor, a G-protein coupled receptor, Because histamine activates cAMP, H2 blockers lead to a decrease in cAMP and a concomitant decrease in Ca++

Adverse Effects

- Diarrhea
- Dizziness
- Somnolence
- Headache
- Rash
- Constipation
- Vomiting



Uses

- Duodenal ulcer
- Gastric ulcer
- Gastroesophageal reflux disease
- Used prior to surgery in patients with GI obstruction to elevate gastric p
- Antacid

AUTOCOID PROSTAGLANDINS

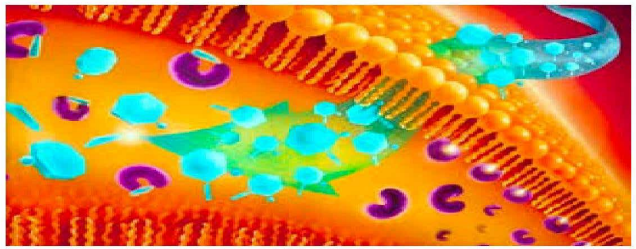
- Prostaglandins (PGS) and related compounds that is Prostacyclines (PGI), Thromboxanes (TXA), Leukotrienes (LT) and Lipoxins are collectively known as "eicosanoids."
- Most are produced from arachidonic acid, a 20-carbon polyunsaturated fatty acid derivative they act on the tissue in which they are synthesis and rapidly metabolites to inactive product site of action.
- The eicosanoids are considered "local hormones.
- They have specific effects on target cells close to their site of formation.
- They are rapidly degraded, so they are not transported to distal sites within the body.

Examples

Misoprostol, latanoprost, and alprostadil are some examples of prostaglandins

Uses

- termination of pregnancy
- menstrual regulation
- control of postpartum hemorrhage
- glaucoma
- stomach ulcers
- labor induction



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