

Pharmacology Of Autocoids and Their Antagonists

Autocoids and Their Antagonists

Introduction

- Autocoids are locally acting, biologically active substances that are synthesized and released in response to various stimuli and act near their site of synthesis.
- The term "autocoid" is derived from Greek words meaning "self-remedy," highlighting their local action and regulatory roles.
- Autocoids are involved in:
 - Inflammation
 - Pain
 - Allergic reactions
 - Smooth muscle tone modulation
 - Gastrointestinal function
 - Platelet aggregation
 - Neurotransmission
- They exert effects by acting on specific G-protein coupled receptors (GPCRs) or other receptor types on target cells.
- Their actions are short-lived and locally confined, unlike hormones which act at distant sites.
- Examples of autocoids:
 - **Biogenic amines:** Histamine, 5-hydroxytryptamine (5-HT or serotonin)
 - **Lipid-derived:** Prostaglandins, thromboxanes, leukotrienes
 - **Peptides:** Bradykinin, substance P
 - **Platelet activating factor (PAF)**
- Autocoid antagonists are drugs that inhibit their synthesis, release, or receptor-mediated actions, used in a wide range of clinical conditions.

Classification of Autocoids

Autocoids can be classified based on their chemical structure or origin:



A. Biogenic Amine Autocoids:

- Histamine
- 5-Hydroxytryptamine (Serotonin)

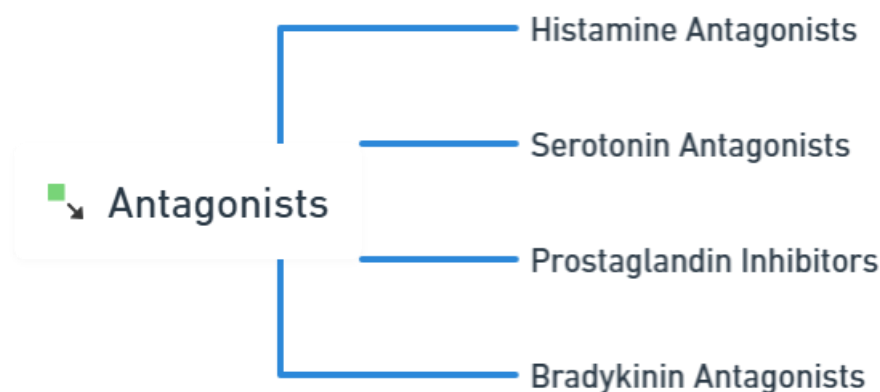
B. Lipid-Derived Autocoids:

- Prostaglandins (PGs)
- Thromboxanes (TXA₂)
- Leukotrienes (LTs)
- Platelet Activating Factor (PAF)

C. Peptide Autocoids:

- Bradykinin
- Substance P
- Vasoactive Intestinal Peptide (VIP)

Antagonists of Autocoids:



1. Histamine Antagonists (Antihistamines):

- H₁ receptor antagonists (e.g., diphenhydramine, loratadine)
- H₂ receptor antagonists (e.g., ranitidine, famotidine)

2. Serotonin Antagonists:

- 5-HT₃ antagonists (e.g., ondansetron)
- 5-HT₂ antagonists (e.g., cyproheptadine)

3. Prostaglandin Inhibitors:

- NSAIDs (e.g., aspirin, ibuprofen) – inhibit cyclooxygenase
- Leukotriene antagonists (e.g., montelukast)
- PAF antagonists (experimental)

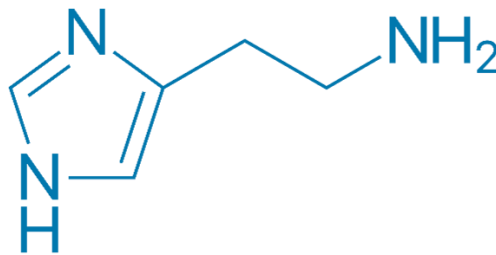
4. Bradykinin Antagonists:

- Icatibant (selective B₂ receptor antagonist)

Histamine

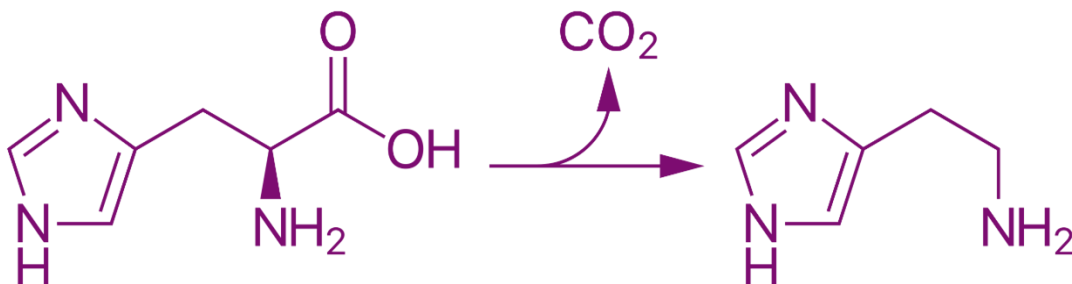
Introduction

- Histamine is a biologically active biogenic amine involved in:
 - Immune responses
 - Allergic reactions
 - Inflammation
 - Gastric acid secretion
 - Neurotransmission



Synthesis and Storage

- Synthesized from histidine by the enzyme histidine decarboxylase



- Stored in:
 - **Mast cells**
 - **Basophils**
 - **Certain neurons** (especially in the CNS)
 - **Enterochromaffin-like (ECL) cells** in the gastric mucosa

Triggers for Histamine Release

- IgE-mediated allergic reactions
- Mechanical or chemical injury
- Certain **drugs** that cause non-IgE mediated release:
 - **Morphine**
 - **Vancomycin**

- Tubocurarine

Histamine Receptors

Histamine exerts effects through four G-protein coupled receptors (GPCRs):

Receptor	Location	Major Functions
H ₁	Smooth muscle, endothelium, brain	Vasodilation, bronchoconstriction, ↑ permeability, sensory nerve stimulation
H ₂	Gastric parietal cells, heart, uterus	↑ Gastric acid secretion, ↑ heart rate, smooth muscle relaxation
H ₃	CNS (presynaptic neurons)	↓ Release of neurotransmitters (modulation of CNS activity)
H ₄	Bone marrow, immune cells	Chemotaxis and immune cell regulation

Mechanism of Action (Histamine Agonist Effects)

H₁ Receptor Activation

- Coupled to Gq protein
- Activates **phospholipase C (PLC)** → ↑ IP₃ and DAG → ↑ intracellular Ca²⁺
- Effects:
 - Bronchoconstriction
 - Vasodilation (via NO)
 - Increased capillary permeability
 - Itching and pain via stimulation of sensory nerves

H₂ Receptor Activation

- Coupled to Gs protein
- Activates **adenylyl cyclase** → ↑ cAMP
- Effects:
 - Increased gastric acid secretion
 - Positive inotropic and chronotropic cardiac effects
 - Smooth muscle relaxation (e.g., uterus, bronchi)

Pharmacodynamics of Histamine

H₁ Receptor Effects

- Flushing, hypotension (vasodilation)
- Edema, wheal formation (↑ permeability)

- Bronchoconstriction
- Itching, pain
- CNS arousal or sedation

H₂ Receptor Effects

- Gastric acid secretion
- Increased heart rate and contractility
- Smooth muscle relaxation

Adverse Effects of Excess Histamine

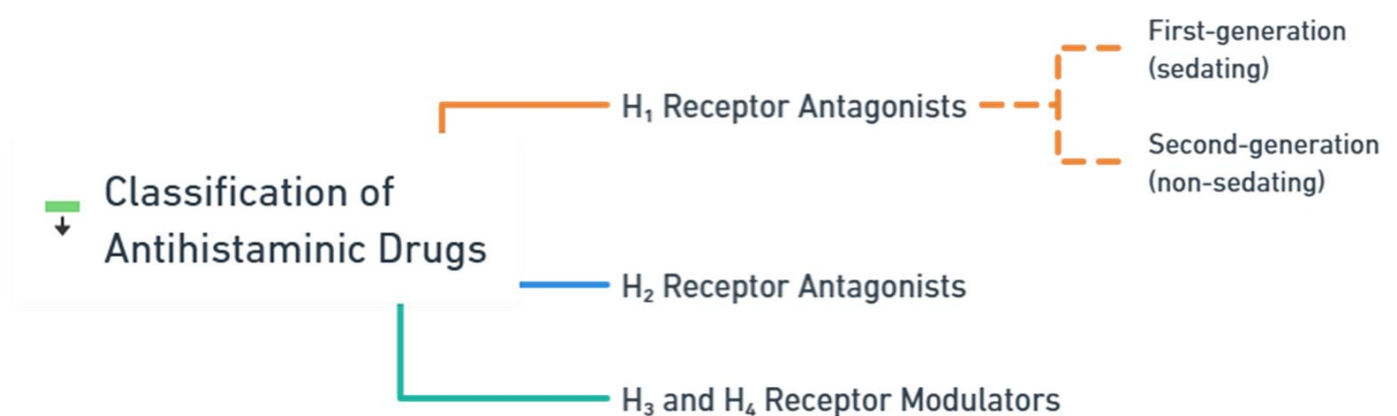
- Flushing
- Headache
- Hypotension
- Bronchospasm
- **Anaphylaxis** (massive histamine release from mast cells)

Antihistaminics

Definition

- Antihistamines are drugs that block the effects of histamine by acting as competitive antagonists or inverse agonists at histamine receptors (mainly H₁ and H₂).

Classification of Antihistaminic Drugs



1. H₁ Receptor Antagonists:

A. First-generation (sedating)

- Diphenhydramine
- Chlorpheniramine
- Hydroxyzine

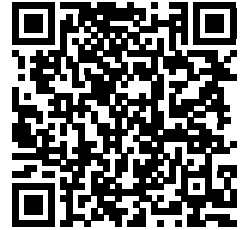


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