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GISTAMIN: THE DRIVING FORCE BEHIND ALLERGIC REACTIONS

Shukrullayeva Dilnoza
Eshpulatova Malikabonu
Tasahkent State Medical University

Abstract
This article provides a detailed examination of histamine, its role in the human body, and its medical significance. It explores the primary source of this compound—synthesized from the amino acid histidine—and its storage in mast cells. The article discusses histamine and its fractions (endogenous and exogenous), highlighting its involvement in various medical conditions such as allergies, asthma, and urticaria. Based on histamine's effects in the body, the article also covers antihistamines and their therapeutic properties. Additionally, it presents information on various antihistamine drugs, their mechanisms of action, and the characteristics of first-, second-, and third-generation antihistamines. The article also provides important insights into foods that may cause histamine intolerance and their impact on the body.

Keywords: Histamine, antihistamines, allergic reactions, mast cells, H1 receptor, H2 receptor, H3 receptor, histaminosis, histidine, immunoglobulin E.

Introduction

The human body possesses complex and precisely coordinated defense mechanisms in response to external influences. At the center of these systems stands histamine—a small yet powerful biological compound. Initially studied as a simple chemical mediator, this molecule later attracted attention for its significant role in the interactions between the immune, nervous, and vascular systems. When a foreign substance enters the body or under certain conditions, histamine is released from cells and triggers a cascade of reactions across multiple systems within a short period. These processes ensure the body mounts a rapid and strong response to external threats. An in-depth analysis of the mechanisms of histamine's action, its interaction with receptors, and its overall physiological effects enables a comprehensive understanding not only at the clinical level but also at the molecular level.

Main Body

Histamine is a derivative of imidazole and belongs to five-membered heterocyclic compounds containing two heteroatoms. In the human body, it is synthesized from the amino acid histidine through the action of a specific enzyme—histidine decarboxylase. Histamine is released into the bloodstream primarily during allergic attacks; otherwise, it remains stored within histiocytes.
Histamine acts as a pathogenic factor behind short-term, elementary, and atypical reactions in response to irritants in the human body. It plays a central role in the development of

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hypersensitivity reactions—especially allergies—by being released from monocytes (a type of leukocyte).

During allergic reactions, mast cells undergo degranulation—histamine is released from intracellular granules into the extracellular space and becomes active. This is a complex, multi-stage process triggered by sensitization, a condition in which the body becomes more sensitive to specific substances. These substances, or allergens, are usually proteins or carbohydrates found in medications, animal dander, food, or chemicals.

Initially, the immune system does not respond to the allergen but "remembers" it. Through this immunological "memory," antibodies specific to the allergen are produced. In this case, immunoglobulin E (IgE) antibodies bind tightly to the membranes of mast cells. When the antigen re-enters the body, it binds to IgE, triggering mast cell degranulation and the release of large amounts of histamine.

As a result of histamine's action, blood capillaries dilate, and the permeability of their walls increases, allowing plasma to leak into the interstitial space. This leads to swelling and a drop in blood pressure. In response to the decreased blood pressure, the adrenal glands increase the secretion of adrenaline, causing capillary constriction and an increased heart rate. Histamine also induces spasms in the smooth muscles of the bronchi. Swelling forms under the skin, along with redness, itching, and either blotchy or nodular rashes. Body temperature rises moderately. These symptoms typically develop rapidly—within half an hour—so such allergic reactions are classified as "immediate-type hypersensitivity."

In the human body, histamine exists in two main fractions:

1. Endogenous – Synthesized from dietary histidine in the digestive system. Under the influence of gastrointestinal bacteria and enzymes, histidine undergoes decarboxylation and is delivered to cells (such as basophils and mast cells) for intracellular histamine synthesis. This fraction is more active than the exogenous type and is synthesized more rapidly, particularly in spleen and liver tissues.
2. Exogenous – Enters the body through animal-based foods. In high-quality food products, histamine levels are negligible and do not negatively affect a healthy human body. However, if food storage hygiene is compromised, pathogenic microorganisms may proliferate, leading to the accumulation of a toxic fraction of histamine. Vvvvv

Foods that Increase Histamine Production in the Body:	High-histamine foods:
Cow's milk	Vinegar-containing products
Chocolate	Carbonated fermented alcoholic drinks
Alcoholic beverages	Dried meat
Nuts	Dried fruits
Bananas	Nuts
Wheat germ	
Artificial preservatives and colorings	Canned fish

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English Translation:

There are three main groups of specific receptors responsible for the pathogenic effects of histamine:

1. H1 (histamine 1) – Contracts the smooth muscles of the bronchi, intestines, and pulmonary circulation vessels; increases vascular permeability and the secretion of the nasopharyngeal mucosa; enhances the release of hormone-like substances involved in blood pressure regulation.
2. H2 – Increases the secretion of the respiratory tract mucosa; affects class E immunoglobulins by suppressing the function of T-lymphocytes (cells that recognize antigens); stimulates the secretion of digestive glands.
3. H3 – Responsible for suppressing the release of amines in the central nervous system. Here, histamine acts as a neurotransmitter—a substance that ensures the transmission of nerve impulses.

Histamine plays an essential role in all types of allergic reactions. Its high concentration can cause:

- Anaphylactic shock, characterized by a sudden drop in blood pressure, vomiting, loss of consciousness, and convulsions;
- Increased permeability of the vascular walls of small and large arteries, leading to headache, papular (nodular) rashes, skin redness, and swelling of the mucous membranes of the respiratory tract;
- Lowered blood pressure;
- Increased secretion of bronchial mucus and gastric juice;
- Increased synthesis of adrenaline, which raises heart rate and blood pressure;
- Involuntary spasms of the muscles in the bronchi and digestive organs, causing diarrhea, stomach pain, and difficulty breathing.

Histaminosis is a condition characterized by elevated levels of free histamine outside cells. Symptoms of histaminosis include:

- Skin itching;
- Swelling of nasal mucosa and upper respiratory tract;
- Shortness of breath;
- Increased blood pressure;
- Heart rhythm disturbances;
- General weakness, fatigue;
- Sleep disturbances;
- Mild elevation in body temperature;
- Nausea and vomiting;
- Abdominal pain, diarrhea;
- Menstrual cycle irregularities.

Histaminosis is often triggered by certain medications, including:

- Acetylsalicylic acid (aspirin);
- Analgin (metamizole);
- Metoclopramide;

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- Intravenous dextran infusions (e.g., poliglucin, rheopoliglyukin, hydroxyethyl starch);
- Some antibiotics;
- Tricyclic antidepressants.

1nd Generation		
Characteristics	Examples	Side Effects
Easily crosses the blood-brain barrier	Diphenhydramine (Dimedrol)	Drowsiness, decreased attention
Has a sedative effect	Suprastin (Chloropyramine)	Dry mouth, constipation
Short duration of action (4-8 hours)	Tavegil	Psychomotor agitation

2nd Generation		
Characteristics	**Examples**	**Side Effects**
Does not cross the blood-brain barrier	Loratadine	Drowsiness (rare), headache
Less sedative effect	Cetirizine	Dry mouth, itching, or diarrhea
Long-lasting effect (12–24 hours)	Fexofenadine (Allegra)	

3rd Generation		
Characteristics	**Examples**	**Side Effects**
Selective H1-histamine receptor blocker	Claritin (Loratadine)	Drowsiness, headache, or increased appetite (sometimes)
No sedative effect	Zyrtec (Cetirizine)	
Stable and long-lasting effect	Desloratadine	

In recent years, allergic diseases have been recognized as one of the major global public health issues. According to reports from the World Health Organization (WHO), more than 20% of the global population suffers from IgE-related allergic conditions, including allergic asthma, rhinitis, and urticaria. This highlights the hyperactivity of histamine in the immune system and its role as a key mediator in the regulation of allergic reactions.

In addition, there are cases when the body is unable to sufficiently break down histamine. This condition, known as **histamine intolerance**, is estimated to affect approximately 1–3% of the global population. According to scientific reviews by the company Bioiberica, histamine intolerance is more commonly observed among middle-aged women and manifests with a range of general symptoms such as headaches, skin reactions, and digestive problems.

The market for antihistamine drugs—widely used to manage allergic reactions—is also steadily growing. According to data presented by Data Bridge Market Research, the global antihistamine drug market was valued at USD 279.96 million in 2023, and this figure is expected to reach USD 568.16 million by 2031. This corresponds to an average annual growth rate of 9.25%. These

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statistics confirm the clinical importance of histamine and the growing significance of treatments aimed at counteracting its effects in medicine.

Conclusion:

Histamine is an important biologically active compound involved in numerous physiological and pathological processes in the human body. Its precursor, the amino acid histidine, is enzymatically decarboxylated in the body to form histamine. The effects of histamine are wide-ranging, primarily influencing the immune system, central nervous system, and digestive system. Notably, histamine plays an unparalleled role in the development of allergic reactions, being released in large quantities through mast cell degranulation and triggering a chain reaction in the body.

Histamine acts on various tissues in the body through H1, H2, and H3 receptors, causing diverse effects such as vasodilation, bronchial spasms, increased heart rate, skin itching, shortness of breath, and even severe conditions like anaphylactic shock. Therefore, histamine is central not only to normal physiological functions but also to pathological processes.

Moreover, factors influencing histamine levels in the body—such as diet, medications, and the state of the microbiota—can lead to clinical conditions like histaminosis and histamine intolerance. Because the symptoms of these conditions resemble those of allergies, they are often misdiagnosed, resulting in improper treatment.

The aforementioned statistical data further confirm the relevance of diseases related to histamine and the importance of medications aimed at managing them. Thus, knowledge about histamine and its receptors, histidine metabolism, and counteracting agents—namely antihistamines—holds a significant place in modern medicine, not only in allergology but also within the contexts of pharmacology, immunology, and diseases of the digestive system.

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