

24.1. HISTAMINE AND ANTI-HISTAMINIC AGENTS

24.1.1. Introduction

Histamines are nitrogen-containing organic compounds belonging to the group of amines. Histamines are produced in almost all the cells (present in an animal) during a local immune response. They regulate various physiological functions of the gut. In addition, histamines have also been known to play a role in neurotransmission. Release of histamines is the initiating factor of any inflammatory response. Histamines are synthesised and released by basophils and mast cells (found in the nearby connective tissues) on stimulation (as a part of an immune response against foreign pathogens). They cause increased vascular (capillary) permeability for WBCs and other proteins to facilitate adequate invasion of foreign bodies present within the tissues. Anti-histaminic agents (or **histamine antagonists**) are the drugs that antagonise the action of histamine.

24.1.2. Classification

Following are the **three types** of histamine receptor antagonists:

- 1) **H₁-Antagonists:** These are classical antihistamines blocking the physiological effects of histamine and used in allergic disorders.
- 2) **H₂-Antagonists:** Cimetidine, Ranitidine, and Famotidine are H₂-antagonists reducing gastric HCl secretion and used in peptic ulcer diseases.
- 3) **H₃-Antagonists:** Thioperamide is an H₃-antagonist regulating histamine release from histaminergic neurons of CNS by presynaptic auto-regulatory mechanism. It is not recommended to be used therapeutically.

H₁-antagonists can be classified as follows:

- 1) **First Generation H₁-Antagonists:** They cross the blood-brain barrier readily and produce drowsiness.
 - i) **Ethanolamines:** Diphenhydramine hydrochloride and Dimenhydrinate.
 - ii) **Ethylenediamines:** Pyrilamine maleate and Tripeleennamine hydrochloride.
 - iii) **Alkylamines:** Chlorpheniramine maleate and Brompheniramine maleate.
 - iv) **Piperazines:** Cyclizine hydrochloride and Meclizine hydrochloride.
 - v) **Piperidines:** Cyproheptadine hydrochloride.
 - vi) **Phenothiazines:** Promethazine hydrochloride.
 - vii) **Tricyclic Dibenzoxepins:** Doxepin hydrochloride.

2) **Second Generation H_1 -Antagonists:** They do not cross the blood-brain barrier readily, thus produce less drowsiness.

- i) **Alkylamines:** Acrivastine.
- ii) **Piperazines:** Cetirizine hydrochloride.
- iii) **Phthalazinones:** Azelastine hydrochloride.
- iv) **Piperidines:** Terfenadine, Astemizole, Loratadine, and Fexofenadine.

24.1.3. Individual Compounds

The following drugs are studied in detail:

- 1) Histamine,
- 2) Diphenhydramine,
- 3) Promethazine,
- 4) Cyproheptadine,
- 5) Mepyramine,
- 6) Pheniramine, and
- 7) Chlorpheniramine.