HISTAMINE ANTAGONIST

A histamine antagonist is an agent that inhibits action of histamine via histamine receptors. Histamine is a β-imidazoyl ethylamine derivative that is present in essential all mammalian tissues. Histamine is a major component of many venoms & sting secretion. It is produced naturally by immune system & released in response to tissue damage. In Human, histamine mediate allergic & inflammatory response, cause gastric acid release & function as CNS neurotransmitter. John H et al

H_1_ antihistamines are used as treatment for symptoms of allergies such as runny nose. Allergies are caused by an excessive type 1 hypersensitivity response of the body to allergens, such as pollen released by plants. An allergic reaction, which if severe enough can lead to anaphylaxis, results in excessive release of histamines and other mediators by the body. Other uses of H_1_ antihistamines help with symptoms of local inflammation that result from various conditions, such as insect stings, even if there is no allergic reaction. Other commonly used examples of antihistamines include the H_2_ antagonists (Cimetidine) which are widely used for the treatment of acid reflux and stomach ulcers as they decrease gastric acid production. K. Ilango, P et al

Histamine receptor antagonists represent a third approach to the reduction of histamine-mediated responses. For over 60 years, compounds have been available that competitively antagonize many of the actions of histamine on smooth muscle. However, not until the H_2_-receptor antagonist burimamide was described in 1972 was it possible to antagonize the gastric acid-stimulating activity of histamine. The development of selective H_2_-receptor antagonists has led to more effective therapy for peptic disease. Selective H_3_ and H_4_ antagonists are not yet available for clinical use. However, potent and selective experimental H_3_-receptor antagonists, thioperamide and clobenpropit, have been developed. Bertram G et al

H_1_ RECEPTOR BLOCKER
Compounds that competitively block histamine at H\textsubscript{1} receptors have been used in the treatment of allergic conditions for many years, and many H\textsubscript{1} antagonists are currently marketed in the USA. Many are available without prescription, both alone and in combination formulations such as "cold pills" and sleep aids.

**HISTAMINE RECEPTOR**

**H\textsubscript{1} receptor:** Found in smooth muscles of intestine, bronchi, blood vessels, adrenal medulla, endothelial cell and lymphocytes

**H\textsubscript{2} receptor:** Found in myocardial cell and cell membrane of acid secretory cell and mediate the gastric acid secretory action

**H\textsubscript{3} receptor:** Found in presynaptic receptor that influences the release of histamine and other neurotransmitters from neurons

**CLASSIFICATION**

**A. FIRST GENERATION ANTI HISTAMINES**

1. **Amino alkyl ether:** eg. DiphenhydramineHCl, carbonoxamine malate, Bromophenhydramine HCl, Doxylamine succinate, Dimenhydrinate, Clemastine Fumarate
2. **Ethylene diamines:** eg. Tripelennamine Citrate, Pyrilamine Malate, Methapyrilene HCl, & Thonzylamine HCl & Antazoline Phospate
3. **Propylamine derivatives:** eg. Chlorpheniramine malate, Pheniramine malate, Triprolidine HCl, Bromophenaramine Malate, & Dextrbromopheniramine malate
4. **Phenothiazine derivatives:** eg. Promethazine HCl, Trimethazine tartarate & Methdilazine HCl
5. **Piperazine derivative:** eg. Cyclizine HCl, Chlorcyclizine, Meclizine HCl & Buclizine HCl
6. **Dibenzocycloheptanes:** eg. Cyproheptadine HCl, & Azatadine Maleate
7. **Miscellaneous drugs:** eg. Diphenylpyraline HCl, Dimethindene Maleate
B. SECOND GENERATION ANTIHISTAMINES

The Second generation anti histamines bind only to peripheral H₁ receptor & reduce with little or no sedation eg. Cetirizine, Loratadine, FexofenadineHCl & Acrivasine

C. “DUAL ACTING” ANTIHISTAMINES

eg. Azelasine HCl & Ketotifen fumarate

THERAPEUTIC APPLICATION OF ANTIHISTAMINES

- Nasal allergies particularly seasonal allergic rhinitis (Hay fever), vasomotor rhinitis
- Allergy reaction
- Motion sickness & vestibular disturbance
- Nausea, vomiting of pregnancy
- As hypnotic and rarely as local anesthetics
- In treatment of Parkinsonism
- In cardiac arrhythmias
- As anti emetics
- Antiasthamatic
DEVELOPMENT OF NEW ANALYTICAL METHODS:
A regulatory analytical procedure is the analytical procedure used to evaluate a defined characteristic of the drug substance or drug product. An alternative analytical procedure is an analytical procedure proposed by the applicant for use instead of the regulatory analytical procedure.

Analytical chemistry based on TWO aspects

Qualitative analysis: To establish the presence of a given element or functional group in a sample (Inorganic / Organic).
Quantitative analysis: To establish the amount of the given element or compound in given sample.

Methods of Detecting Analysts

Physical means
Mass
Color
Refractive Index
Thermal Conductivity

With Electromagnetic Radiation (spectroscopy)
• Absorption
• Emission
• Scattering

By an electric charge
• Electrochemistry
• Mass spectrometry
VALIDATION OF ANALYTICAL METHOD:

As defined by the USP, method validation provides an assurance of reliability during normal use, and is sometime referred to as “the process of providing documented evidence that the method does what it is intended to do.”

The objective of validation of an analytical method is to demonstrate that the procedure, when correctly applied, produces results that are fit for purpose. To be fit for the intended purpose, the method must meet certain validation characteristics.

In a 1987 guideline (Guideline for Submitting Samples and Analytical Data for Methods Validation), the FDA designated the specifications in the current edition of the USP as those legally recognized when determining compliance with the Federal Food, Drug and Cosmetic Act. can be referred to as the “eight steps of method validation,” as shown in Figure. 1

![Diagram](image_url)  
**FIGURE 1**: The USP eight steps of method validation

Typical validation characteristics, which should be considered, are: selectivity (specificity), linearity, range, accuracy, precision, limit of detection, limit of quantization, ruggedness, robustness and system suitability testing.

Validation is required in following situations
- When totally new process
- New equipment
- Process and equipment which have been altered to suit changing properties
- Process where the end product test is poor and an unreliable indicator of product quality.