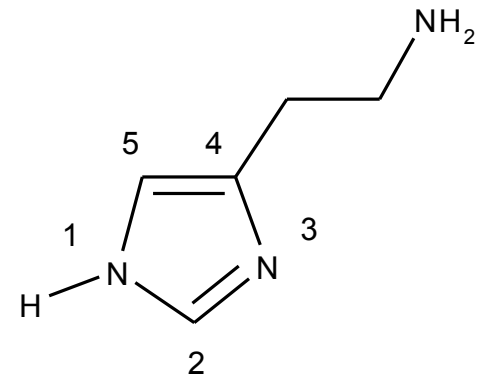


Antihistamines

Histamine

- chemical messenger that mediates many cellular responses
 - inflammation
 - allergic reaction – H1
 - gastric acid secretion - H2
 - neurotransmission – H3



Histamine

Release of histamine

- stimuli causing histamine release
 - „storage“ cell destruction
 - injury
 - action of histamine liberators
 - foreign proteins
 - drugs – curare, morphin
 - allergy, anaphylaxis

Mechanism of action

- binding to specific receptors on the cell surface
- variety of responses
- H1-H2 – important ligands
- H3-H4 – no usefull ligands
- metabotropic type

Actions of histamine – H1

- **exocrine secretion**
 - increase of nasal and bronchial mucus production
→ respiratory symptoms of allergic reaction
- **bronchial smooth muscle**
 - bronchoconstriction → symptoms of asthma
- **intestinal smooth muscle**
 - constriction → cramps and diarrhoea
- **sensory nerve endings** → itching

Actions of histamine – H1+2

- **cardiovascular system**
 - lowers blood pressure reducing peripheral resistance
 - positive chronotropism
- **skin**
 - rapid dilation and increased permeability of capilars
 - itching, swelling, pain, bladders

Actions of histamine – H2

- **stomach**

- stimulation of hydrochloric acid secretion

- **direct vasodilatation**

- slower but persistent for a longer time

Actions of histamine – H3

- **CNS**

- inhibition of histamine release from histaminergic neurons – autoreceptors
- probably play an important role in satiety regulation

Histaminergic drugs used in therapy

- **histamine** – for diagnosis
- **betahistine** (analog) in Menier's disease
H1 partial agonist/H3 antagonist
- **betazol** – H2 agonist (increases gastric secretion)

Treatment possibilities

- histamine – no clinical importance
- **mast cells stabilize agents**
 - sodium cromoglycate, nedocromil
- **H1 antihistamines**
 - 1st gen. - diphenhydramine, promethazine, fenistil
 - 2nd gen. - cetirizine, loratadine
 - 3rd gen. - levocetirizine, desloratadine
- **H2 antihistamines**
 - cimetidine, ranitidine, famotidine

H1

Pharmacodynamics

- Competitive antagonism - H1
- No effect on H2 – limited influence on blood vessels
- Older compounds have anticholinergic, anti-5-HT and antiadrenergic effects

- Block the allergy symptoms:
 - **partially** bronchoconstriction
 - rapid dilatation of blood vessels
 - increased membrane permeability
 - itching

1st generation

Pass BBB – sedative effect

- diphenhydramine (hypnotic) (Psilo-Balsam)
- moxastine (Kinedryl tbl)
- clemastine (Tavegyl tbl)
- dimetinden (Fenistil roll on)
- promethazine (Prothazin tbl) – originally antipsychotic drug
- bisulepine (Dithiaden tbl)
- azelastine (Allergodil nas spr)

2nd generation

Do not pass BBB

- Cetirizine
- Loratadine
 - Both suitable for long-term therapy and small children (from 1 year)

3rd generation

Do not pass BBB; less/no effect on QTc

- Levocetirizine – Xyzal
- Desloratadine – Aeries
- Fexofenadine - Ewofex

Use

- non-complicated allergical symptoms
- local treatment – insect sting
- allergic itching
- allergic rhinitis
- motion sickness and nausea
- sedatives
- anaphylactic shock – i.v.

Adverse effects

- sedation
- inhibition of other receptors – cholinergic type M
- atropin-like effect
 - dry mouth