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Research Article

Stereo Selectivity of Histaminic Receptors Play an Important Role of Anti-histaminic Activity

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Abstract

The histamine is a natural compound derived from histidine and amino acid which act on different histaminic receptors (H1, H2, H3 and H4), each receptor combined with histamine and give the different actions especially H1 and H2 receptors.

The action of each depends on the specificity of the receptors e.g. the compounds which act on H1 receptor are similar to each other but different than the compounds which act on H2 receptor (due to the difference between two receptors from the area and stereo of the receptors).

Keywords: Histaminic receptors, H1, H2, H3 and H4, chiral carbon, lipid solubility, anti- histaminic activity, H1 antagonists and H2 antagonists.

Introduction

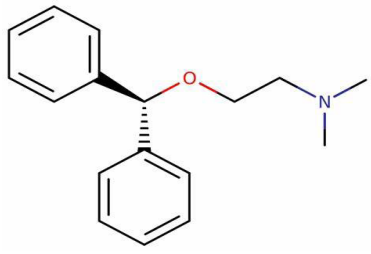
The histamine is a natural body substance resulted from decarboxylation of the amino acid called histidine. The histamine reveal some physiological functions in some tissues in the body where cause vasodilatation and may be release some transient matters which cause hypersensitivity, may increase the acidity due to increase the hydrochloric acid from the stomach. The histamine acts on four receptors which present in the body (stomach H2, mainly skin and others H1, CNS H3 and H4 receptor subtype responsible for the immunity). The more famous of histaminic receptors are H1 and H2 where the physiological activity of the histamine appears obviously at these receptors H1 and H2 where the hypersensitivity (itching, flushing and inflammation of skin, anaphylaxis, catarrhal symptoms) and hyper acidity and peptic ulcer respectively. The examine of H1 and H2 receptors present the difference of compounds which act on these receptors, the compounds act on H1 receptors are diphenhydramine, clemastine, pheniramine, chlorpheniramine, triprolidine, dimethindene, tripelennamine, antazoline, buclizine, hydroxyzine, promethazine, pimethixene, cyproheptadine, ketotifen, terfenadine, fexofenadine, acravastine and cetirizine, while the compounds act on H2 receptor are cimetidine, ranitidine, nizatidine, famotidine, and burimamide.

From the previous drugs we note the chemical structure differences of the H1 antagonists and H2 antagonists explain the stereo selectivity of histaminic receptors, hence the activity of anti-histaminics different according to the receptor.

Chmestiry and Pharmacology

H1 antagonists include the anti-histaminics which used in treatment of hypersensitivity and allergy, also anaphylactic shock. Because the stereo selectivity of the receptor, the H1 antagonist must be contain at least four atoms e.g. Ethylenediamine or ethanolamine these examples four atoms compounds at least.

Diphenhydramine.



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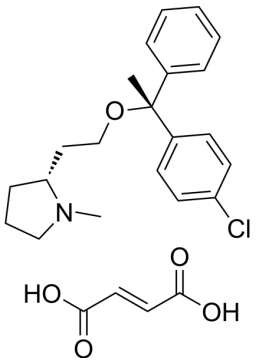
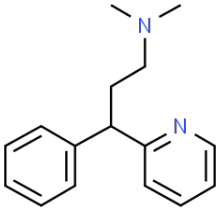
This drug has amine attached to two carbons and oxygen, this compound used in management of hypersensitivity and many types of urticaria.

Clemastine fumerate.



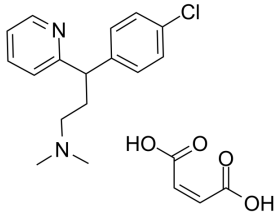
Clemastine fumerate is H1 antagonist explain the stereo selectivity of H1 receptor where it contain chiral carbon and used as other anti-histamine.

Pheniramine maleate.



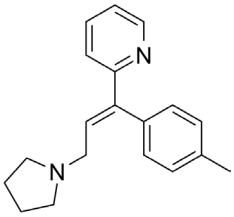
This compound also showed the stereo selectivity of H1 receptor, and also used as anti-allergic (different types) and anti-hypersensitivity.

Chlorpheniramine maleate.



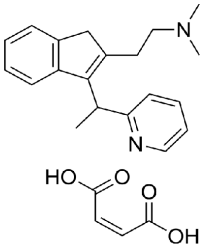
The same pharmacological action of pheniramine maleate but has long duration and high lipid solubility.

Triprolidine.



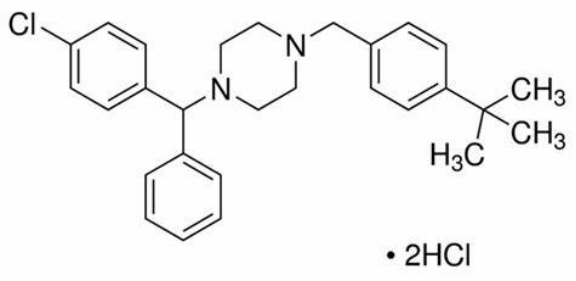
Dimethindene.

This compound is H1 antagonist and has geometrical isomerism.



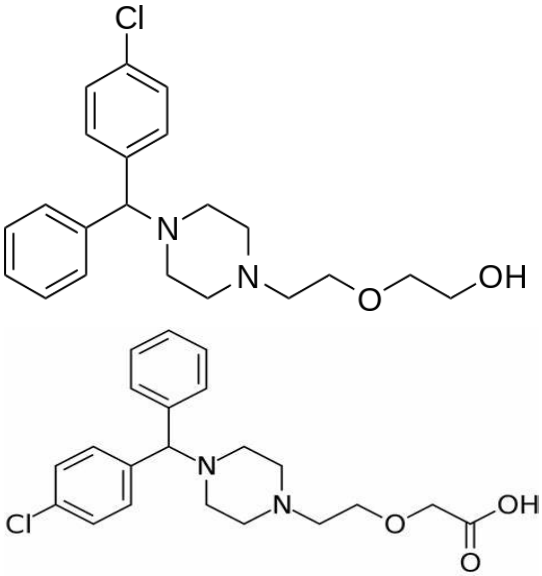
Dimethindene is H1 antagonist and its medicinal uses as previous compounds, also explain the stereo selectivity of histaminic receptor (its levo enantiomer).

Buclizine.



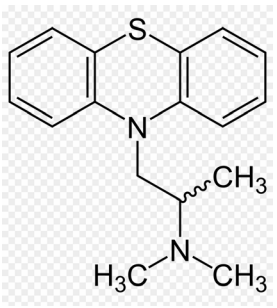
In addition to anti histaminic it's anti-emetic and anti-vertigo activities and has chiral carbon which make it optical active compound, also explain the stereo selectivity of histamine receptors

Hydroxyzine.



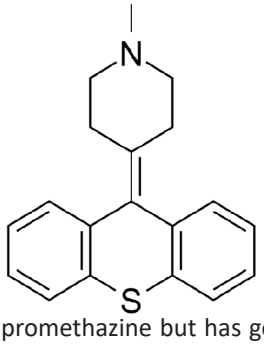
Its optical active compound has H1 antagonist and metabolized into cetirizine which also optical active compound, they are indicated to stero selectivity of the receptors.

Promethazine HCL (phenothiazine derivative).



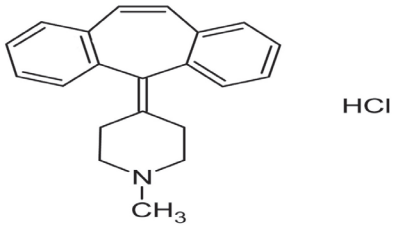
In addition to its H1 antagonist activity it has tranquilizer which potentiate the analgesic activity of analgesics and anti-emetic activity, this drug has optical activity and prove of the stereo selectivity of H1 receptor.

Pimethixene.



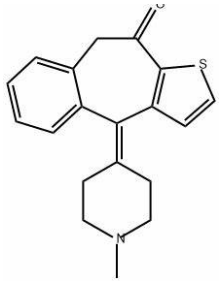
It is analogue of promethazine but has geometrical isomerism.

Cyproheptadine HCL.



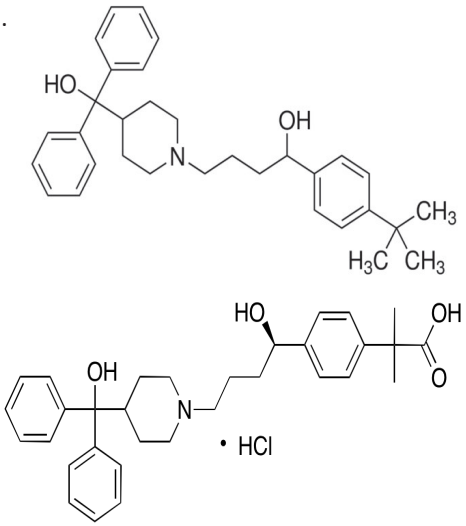
In addition to H1 antagonist it has anti-serotonergic activity (tricyclic anti-depressant and appetite stimulant and has geometrical isomerism).

Ketotifen.



One of these H1 antagonist in addition to mast cell stabilizer so used in prophylaxis against bronchial asthma, not merely but has geometrical isomerism.

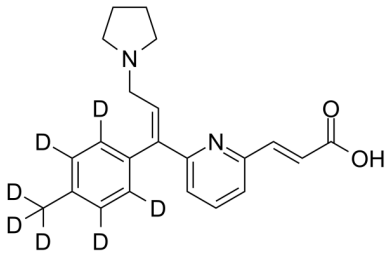
Terfenadine.



One of H1 antagonist which has optical activity, but also has one side effect is cardiac arrhythmia, so it is withdrawn from the market.

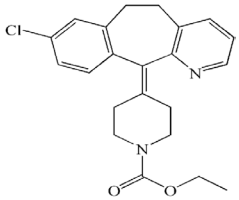
N.B. its metabolite *FEXOFENADINE* not produce cardiac arrhythmia and has H1 antagonist, optical active compound.

Acrivastine.



One of these drugs which has H1 antagonist and has geometrical isomerism.

Loratadine.

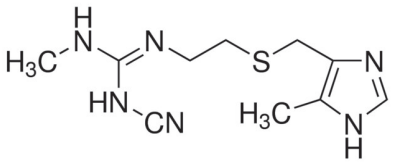


Loratadine non-sedative anti-histaminic and has geometrical isomerism.

N.B. all H1 antagonist has lipid solubility which is indicate to penetrate the cell and reach to the action wanted, these compounds mainly fitted with H1 receptor due to the chemical structure which required for H1 receptor, as well as the optical or geometrical isomerism of them.

All the above characteristics indicate to stereo selectivity of the H1 receptor comparing with H2 antagonists as following.

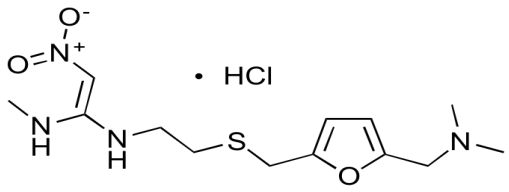
Cimetidine.



One of the H2 antagonists in spite it has chemical structure near to H1 antagonists, this indicates also to stereo selectivity of H2 antagonists, the cimetidine has anti-androgenic activity, inhibit CYP-450 enzymes so delayed the metabolism of drugs which metabolized by CYP-450 and interfere with anti-acids.

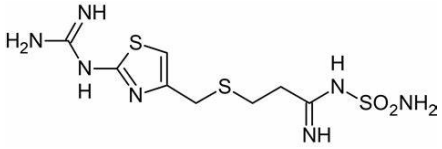
N.B. this drug has imidazole ring which similar to histamine.

Ranitidine.

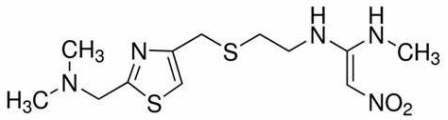


H2 antagonist has furan ring.

Famotidine.

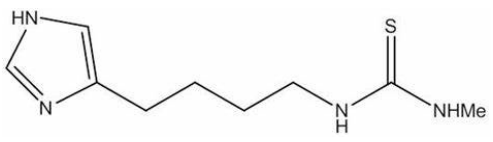


Nizatidine.



N.B. famotidine and nizatidine H2 antagonist and has thiazole ring.

Burimamide.



N.B. the Burimamide is the prototype of H2 antagonist but it has the major side effect (agranulocytosis), so it is not clinically used.

Conclusion

H1 ANTAGONISTS AND H2 antagonists are similar in some chemical features and many of them have stereo chemistry. All of these antagonists either H1 or H2 explain stereo selectivity.

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