6/7/2018

Histamine

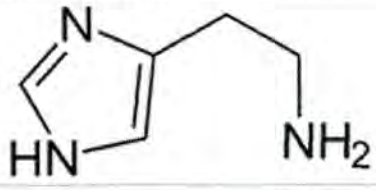
From Wikipedia, the free encyclopedia

For the use as an immunostimulant drug, see Histamine dihydrochloride.

Histamine is an organic nitrogenous compound involved in local immune responses as well as regulating physiological function in the gut and acting as a neurotransmitter.[2] Histamine is involved in the inflammatory response. As part of an immune response to foreign pathogens, histamine is produced by basophils and by mast cells found in nearby connective tissues. Histamine increases the permeability of the capillaries to white blood cells and some proteins, to allow them to engage pathogens in the infected tissues.[3]

Contents

Histamine



IUPAC name

2-(1*H*-imidazol-4-yl)ethanamine

Identifiers	
CAS number	51-45-6
PubChem	774
ChemSpider	753
UNII	820484N8I3
KEGG	D08040
MeSH	Histamine
ChEBI	CHEBI:18295
ChEMBL	CHEMBL90
IUPHAR ligand	1204
ATC code	L03AX14 (http://www.whocc.no/atc_ddd_index/?code=L03AX14),(2HCl) V04CG03 (phosphate)
Jmol-3D images	Image 1 (http://chemapps.stolaf.edu/jmol/jmol.php?model=n1cc%28nc1%29CCN)
SMILES	
InChI	
Properties	
Molecular formula	$C_5H_9N_3$

Properties

Histamine forms coloured hygroscopic crystals that melt at 84 °C, and are easily dissolved in water or ethanol, but not in ether. In aqueous solution, histamine exists in two tautomeric forms: N^{π}-*H*-histamine and N^{τ}-*H*-histamine. The imidazole ring has two nitrogens. The nitrogen farthest away from the

side chain is the 'tele' nitrogen and is denoted by a lowercase tau sign. The nitrogen closest to the side chain is the 'pros' nitrogen and is denoted by the pi sign. The position of the nitrogen with the hydrogen on it determines how the tautomer is named. If the nitrogen with the hydrogen is in the tele position, then histamine is in the tele-tautomer form. The tele-tautomer is preferred in solution.

Histamine has two basic centres, namely the aliphatic amino group and whichever nitrogen atom of the imidazole ring does not already have a proton. Under physiological conditions, the aliphatic amino group (having a pK_a around 9.4) will be protonated, whereas the second nitrogen of the imidazole ring ($pK_a \approx 5.8$) will not be protonated.[4] Thus, histamine is normally protonated to a singly charged cation.

Molar mass	111.15 g mol^{-1}
Melting point	83.5 °C (182.3 °F; 356.6 K)
Boiling point	209.5 °C (409.1 °F; 482.6 K)
Solubility in water	Easily soluble in cold water, hot water[1]
Solubility in other solvents	Easily soluble in methanol. Very slightly soluble in diethyl ether.[1] Easily soluble in ethanol.
Acidity (pK_a)	imidazole: 6.04 NH_2: 9.75
Except where noted otherwise, data are given for materials in their standard state (at 25 °C (77 °F), 100 kPa)	
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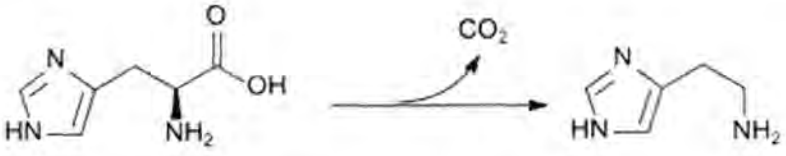
Infobox references	

Synthesis and metabolism

Histamine is derived from the decarboxylation of the amino acid histidine, a reaction catalyzed by the enzyme L-histidine decarboxylase. It is a hydrophilic vasoactive amine.

Tautomers of histamine

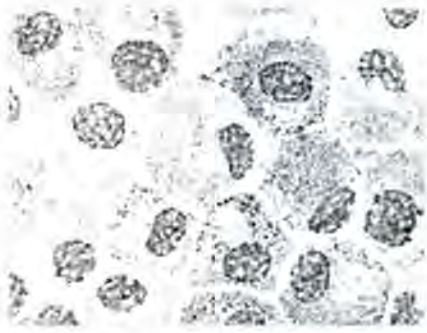


Conversion of histidine to histamine by histidine decarboxylase

Once formed, histamine is either stored or rapidly inactivated by its primary degradative enzymes, histamine-N-methyltransferase or diamine oxidase. In the central nervous system, histamine released into the synapses is primarily broken down by histamine-N-methyltransferase, while in other tissues both enzymes may play a role. Several other enzymes, including MAO-B and ALDH2, further process the immediate metabolites of histamine for excretion or recycling.

Bacteria also are capable of producing histamine using histidine decarboxylase enzymes unrelated to those found in animals. A non-infectious form of foodborne disease, scombroid poisoning, is due to histamine production by bacteria in spoiled food, particularly fish. Fermented foods and beverages naturally contain small quantities of histamine due to a similar conversion performed by fermenting bacteria or yeasts. Sake contains histamine in the 20–40 mg/L range; wines contain it in the 2–10 mg/L range.[5]

Storage and release


Mast cells.

Most histamine in the body is generated in granules in mast cells and in white blood cells called basophils and eosinophils. Mast cells are especially numerous at sites of potential injury — the nose, mouth, and feet, internal body surfaces, and blood vessels. Non-mast cell histamine is found in several tissues, including the brain, where it functions as a neurotransmitter. Another important site of histamine storage and release is the enterochromaffin-like (ECL) cell of the stomach.

The most important pathophysiologic mechanism of mast cell and basophil histamine release is immunologic. These cells, if sensitized by IgE antibodies attached to their membranes, degranulate when exposed to the appropriate antigen. Certain amines and alkaloids, including such drugs as morphine, and curare alkaloids, can displace histamine in granules and cause its release. Antibiotics like polymyxin are also found to stimulate histamine release.

Histamine release occurs when allergens bind to mast-cell-bound IgE antibodies. Reduction of IgE overproduction may lower the likelihood of allergens finding sufficient free IgE to trigger a mast-cell-release of histamine.

Mechanism of action

Histamine exerts its effects by binding to G protein-coupled histamine receptors, designated H_1 through H_4.

In binding to the H_2 receptor, histamine is protonated at the end-chain amine group. This amine group interacts with aspartic acid in the transmembrane domains of the receptor. The other nitrogens interact with threonine and aspartic acid in different transmembrane domains; collectively, this is referred to as a three-pronged interaction. Bringing the transmembrane domains close to each other, it initiates a signal transduction cascade.[6]

It should be noted that all of the known physiological reactions of histamine are a series of weak interactions; the histamine backbone remains unchanged.[6]

Histamine receptors in insects, like *Drosophila melanogaster*, are ligand-gated chloride channels that act to reduce neuronal activity.[7] Histamine-gated chloride channels are implicated in the transmission of peripheral sensory information in insects, especially in photoreception/vision. Two receptor subtypes have been identified in *Drosophila*: HCl_A and HCl_B.[8] There are no known GPCRs for histamine in insects.

Histidine

From Wikipedia, the free encyclopedia

Not to be confused with histamine.

Histidine (abbreviated as **His** or **H**)[2] is an α-amino acid with an imidazole functional group. It is one of the 23 proteinogenic amino acids. Its codons are *CAU* and *CAC*. *Histidine* was first isolated by German physician Albrecht Kossel in 1896. Histidine is an essential amino acid in humans and other mammals. It was initially thought that it was only essential for infants, but longer-term studies established that it is also essential for adult humans.[3]

Contents

L-Histidine

IUPAC name	
Histidine	
Other names	
2-Amino-3-(1*H*-imidazol-4-yl)propanoic acid	
Identifiers	
CAS number	71-00-1
PubChem	773
ChemSpider	6038
UNII	4QD397987E
DrugBank	DB00117
KEGG	D00032
ChEBI	CHEBI:57595
ChEMBL	CHEMBL17962
Jmol-3D images	Image 1 (http://chemapps.stolaf.edu/jmol/jmol.php?model=O%3DC%28O%29%5BC%40%40H%5D%28N%29Cc1cncn1)
SMILES	
InChI	
Properties	
Molecular formula	$C_6H_9N_3O_2$
Molar mass	155.15 g mol^{-1}
Solubility in water	4.19g/100g @ 25 °C [1]
Hazards	
MSDS	External MSDS
NFPA 704	
Supplementary data page	
Structure and properties	*n*, ε_r, etc.
Thermodynamic data	Phase behaviour Solid, liquid, gas
Spectral data	UV, IR, NMR, MS

Except where noted otherwise, data are given for materials in their standard state (at 25 °C (77 °F), 100 kPa)

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Infobox references

Chemical properties

The conjugate acid (protonated form) of the imidazole side chain in histidine has a pK_a of approximately 6.0. This means that, at physiologically relevant pH values, relatively small shifts in pH will change its average charge. Below a pH of 6, the imidazole ring is mostly protonated as described by the Henderson–Hasselbalch equation. When protonated, the imidazole ring bears two NH bonds and has a positive charge. The positive charge is equally distributed between both nitrogens and can be represented with two equally important resonance structures.

Aromaticity

The imidazole ring of histidine is aromatic at all pH values.[4] It contains six pi electrons: four from two double bonds and two from a nitrogen lone pair. It can form pi stacking interactions,[5] but is complicated by the positive charge.[6] It does not absorb at 280 nm in either state, but does in the lower UV range more than some amino acids.[7][8]

Biochemistry

The imidazole sidechain of histidine is a common coordinating ligand in metalloproteins and is a part of catalytic sites in certain enzymes. In catalytic triads, the basic nitrogen of histidine is used to abstract a proton from serine, threonine, or cysteine to activate it as a nucleophile. In a histidine proton shuttle, histidine is used to quickly shuttle protons. It can do this by abstracting a proton with its basic nitrogen to make a positively charged intermediate and then use another molecule, a buffer, to extract the proton from its acidic nitrogen. In carbonic anhydrases, a histidine proton shuttle is utilized to rapidly shuttle protons away from a zinc-bound water molecule to quickly regenerate the active form of the enzyme. Histidine is also important in haemoglobin in helices E and F. Histidine assists in stabilising oxyhaemoglobin and destabilising CO-bound haemoglobin. As a result, carbon monoxide binding is only 200 times stronger in haemoglobin, compared to 20,000 times stronger in free haem.

Certain amino acids can be converted to intermediates of the TCA cycle. Carbons from four groups of amino acids form the TCA cycle intermediates α-ketoglutarate, succinyl CoA, fumarate, and oxaloacetate. Amino acids that form α-ketoglutarate are glutamate, glutamine, proline, arginine, and histidine. Histidine is converted to formiminoglutamate (FIGLU). The formimino group is transferred to tetrahydrofolate, and the remaining five carbons form glutamate. Glutamate can be deaminated by glutamate dehydrogenase or transaminated to form α-ketoglutarate. [9]

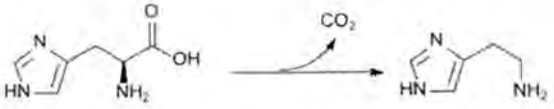
NMR

As expected, the ^{15}N chemical shifts of these nitrogens are indistinguishable (about 200 ppm, relative to nitric acid on the sigma scale, on which increased shielding corresponds to increased chemical shift). As the pH increases to approximately 8, the protonation of the imidazole ring is lost. The remaining proton of the now-neutral imidazole can exist on either nitrogen, giving rise to what is known as the N-1 or N-3 tautomers. NMR shows that the chemical shift of N-1 drops

slightly, whereas the chemical shift of N-3 drops considerably (about 190 vs. 145 ppm). This indicates that the N-1-H tautomer is preferred, it is presumed due to hydrogen bonding to the neighboring ammonium. The shielding at N-3 is substantially reduced due to the second-order paramagnetic effect, which involves a symmetry-allowed interaction between the nitrogen lone pair and the excited pi* states of the aromatic ring. As the pH rises above 9, the chemical shifts of N-1 and N-3 become approximately 185 and 170 ppm. It is worth noting that the deprotonated form of imidazole, imidazolate ion, would be formed only above a pH of 14, and is therefore not physiologically relevant. This change in chemical shifts can be explained by the presumably decreased hydrogen bonding of an amine over an ammonium ion, and the favorable hydrogen bonding between a carboxylate and an NH. This should act to decrease the N-1-H tautomer preference.[10]

Metabolism

The amino acid is a precursor for histamine and carnosine biosynthesis.



Conversion of histidine to histamine by histidine decarboxylase

The enzyme histidine ammonia-lyase converts histidine into ammonia and urocanic acid. A deficiency in this enzyme is present in the rare metabolic disorder histidinemia. In Actinobacteria and filamentous fungi, such as *Neurospora crassa*, histidine can be converted into the antioxidant ergothioneine.[11]

Supplementation

Supplementation of histidine has been shown to cause rapid zinc excretion in rats with an excretion rate 3 to 6 times normal.[12][13]

Additional images

Histidine

The histidine-bound heme group of succinate dehydrogenase, an electron carrier in the mitochondrial electron transfer chain. The large semi-transparent sphere indicates the location of the iron ion. From PDB 1YQ3 (http://www.rcsb.org/pdb/explore/explore.do?structureId=1YQ3).

See also

- Imidazole
- Aromatic amino acids
- Urocanic aciduria
- Carnosinemia
- Beta-alanine
- Diphthamide
- Pauly reaction

References

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External links

- Histidine MS Spectrum (http://gmd.mpimp-golm.mpg.de/Spectrums/a4fc4f0c-0812-4f61-94fd-a79c61419670.aspx)
- Histidine biosynthesis (early stages) (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/His1.html)
- Histidine biosynthesis (later stages) (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/His2.html)
- Histidine catabolism (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/His3.html)
- Food Sources of Histidine (http://nutrient.javalime.com/nutrient.php/512)