The geometry of histamine revealed by Russian scientists

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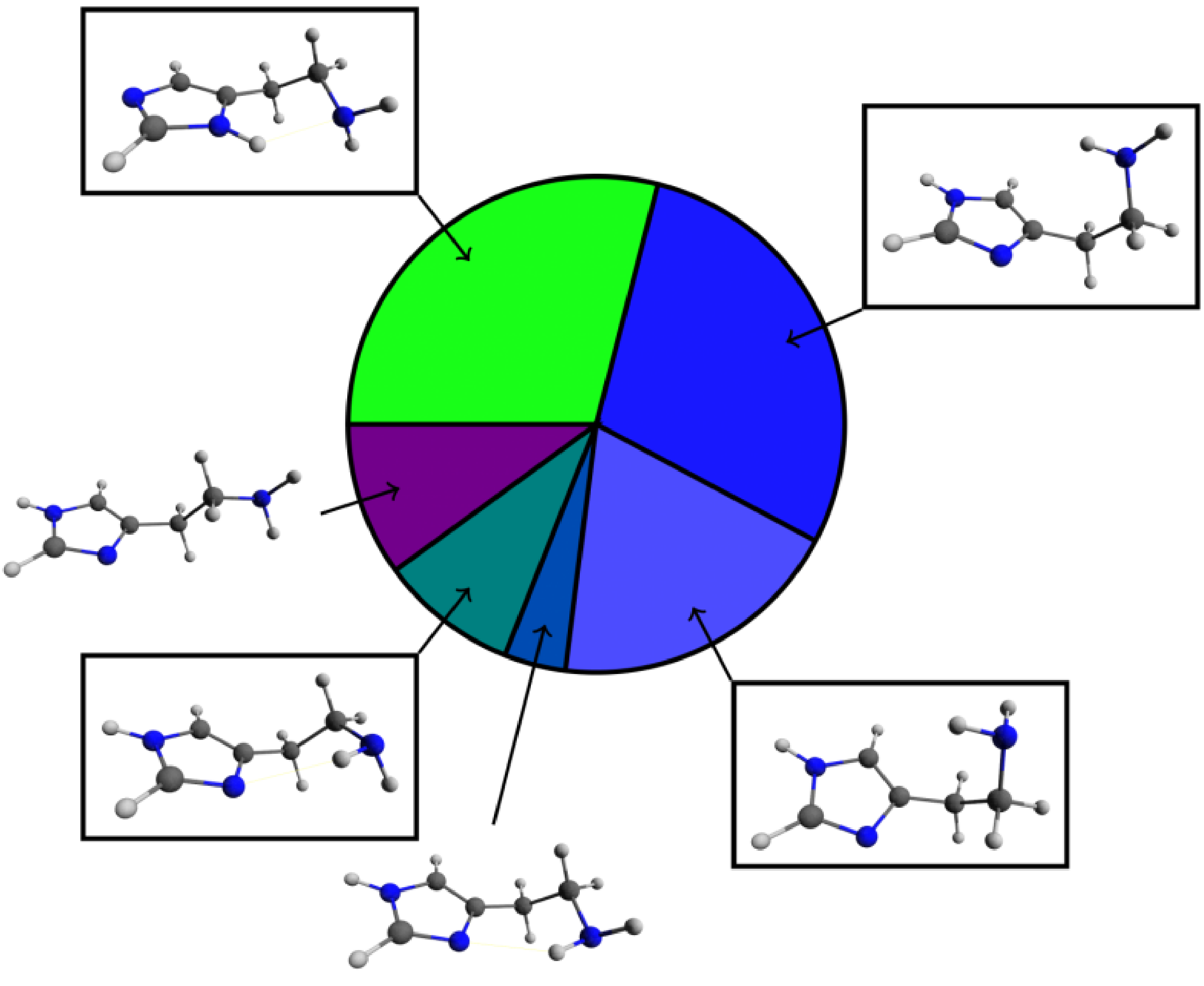

The six most stable conformers composing histamine in the gas phase. Credit: Denis Tikhonov et al., *Phys. Chem. Chem. Phys.*

A group of scientists from Lomonosov Moscow State University studied histamine molecules in the gas phase using an electron beam. The study involved both experiment and calculations, and the results have been published in *Physical Chemistry Chemical Physics*. The authors specialize in the study of bioactive compounds and medicines.

Histamine is a biologically active substance involved in the regulation of many functions of organisms. It is the cause of several pathological conditions, in particular allergic reactions.

The allergic action of histamine is expressed via interaction with several receptors located on the cell surface. Histamine is often compared to a key and receptors to locks—unlocking activates a number of different physiological processes, including headaches, skin rashes, diarrhea, and even anaphylactic shock. Modern antiallergic medicines—antihistaminic drugs—compete with histamine for the receptors, preventing the "key" from getting close to the "lock." Unfortunately, the geometry of histamine is still poorly understood, and determining its structure is important for assessing its properties and potential.

"It's very hard to get data on the geometric structure of histamine," says co-author Leonid Khaikin, a lead researcher at the Laboratory of the Chemical Faculty of Lomonosov MSU. "This is due to the fact that in this case, the geometry of the individual conformers constituting histamine is determined by so many factors influencing each other."

The experimental method used by researchers from Moscow State University was gas electron diffraction. Basically, it uses a beam of fast electrons in high vacuum passing through the vapor of the investigated substance. Electrons are scattered by collisions with the molecules, and the resulting diffraction pattern is recorded.

"This pattern can be used to understand the geometry of the molecule.

One can compare it to a fingerprint, which helps to determine its owner," Khaikin explains. "In other words, the diffraction pattern obtained is characteristic of histamine, and by analyzing this picture, we can infer the geometric characteristics of the molecule encrypted in the pattern. The problem was also in the fact that such a 'fingerprint' could be left by more than one 'finger' (histamine conformer). Therefore, we had to carry out multiple quantum-chemical calculations and to use reported spectroscopic data for vibrational and rotational spectra, and so on."

Purely analytical work came after the experiment. According to Khaikin, analysis of the obtained diffraction pattern was the most time-consuming and difficult part of the study, taking several months of hard work. As a result, MSU scientists were able to adjust all the available experimental and theoretical data on the structure of histamine. It was also possible to predict theoretically the mechanism of so-called tautomerization of histamine, a spontaneous transition of the molecule from one structural state to another. It has helped to reconcile the data observed in different experiments.

The results can now be used in different reference databases of structural and spectral data, for further development of theoretical concepts of structural chemistry and evaluation of the reactivity of the compounds. As often happens with the results of fundamental science, it will likely take a long time before researchers find practical application of these results in medicine. Quite possibly, knowledge about the mechanism of histamine molecule transition from one structural state to another might help to find more effective drugs against allergies.

Provided by Lomonosov Moscow State University