Results promising for computational quantum chemical methods for drug development

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New research, led by a Virginia Tech chemist, may someday help natural-products chemists decrease by years the amount of time it takes for the development of certain types of medicinal drugs. The research by T. Daniel Crawford, associate professor of chemistry, involves computations of optical rotation angles on chiral—non-superimposable—molecules. The research titled, The Current State of 'Ab Initio' Calculations of Optical Rotation and Electronic Circular Dichcoism Spectra, appeared recently as the cover article in *The Journal of Physical Chemistry A*.

Many chiral molecules are important for medical treatment for illnesses ranging from acid-reflux to cancer. The term "chiral" means that two mirror images of a molecule cannot be superimposed onto each other. In other words, some are "left-handed" and some are "right-handed."

"Most drugs have this handedness property," Crawford said, "and for many of these drugs, even though both hands can cause a reaction, it is a situation where one hand does a good thing and one does a bad thing." He used thalidomide as an example. A mixture of both hands of the drug was used in the late 1950s and early 1960s to treat morning sickness in pregnant women. Later studies revealed that, while one of the two hands acted as the desired sedative, the other hand was found to cause significant birth defects. Thalidomide was never approved by the FDA in the United States and was eventually taken off the market in Europe.

For chemists, therefore, it is often vital to determine which hand of a molecule they are using. In other words, when you have a sample of a chiral molecule, how do you distinguish between the left and right hand"

This is where a technique called polarimetry comes in to play. By shooting plane-polarized light through a sample of one hand, the chiral molecule in question will rotate to a characteristic angle either clockwise or counterclockwise, and the two hands of a chiral molecule produce opposite rotations.

“So if we figure out the direction and rotation of the light or each hand, we have a frame of reference for determining whether we have the left or right hand of a molecule,” Crawford said.

The problem with this method is that synthesizing the two hands of chiral molecules is often extremely time consuming. “It can take anywhere from weeks to years,” Crawford said.

Crawford’s research applies the theory of quantum mechanics to devise computational methods in order to eliminate having to create a synthetic molecule. “The hope is that this will allow us to calculate things like optical rotation very accurately,” he said. “So when an organic chemist has a molecule and doesn’t know if it is left- or right-handed, we can calculate that directly on the computer.”

Crawford said the ultimate goal in his research is to be able to provide organic chemists with computational tools to determine the handedness of a particular molecule they are working with. He said that such tools could speed up the drug development process by years.

Source: Virginia Tech