NMR spectroscopy method provides faster way to determine chiral structure of molecules

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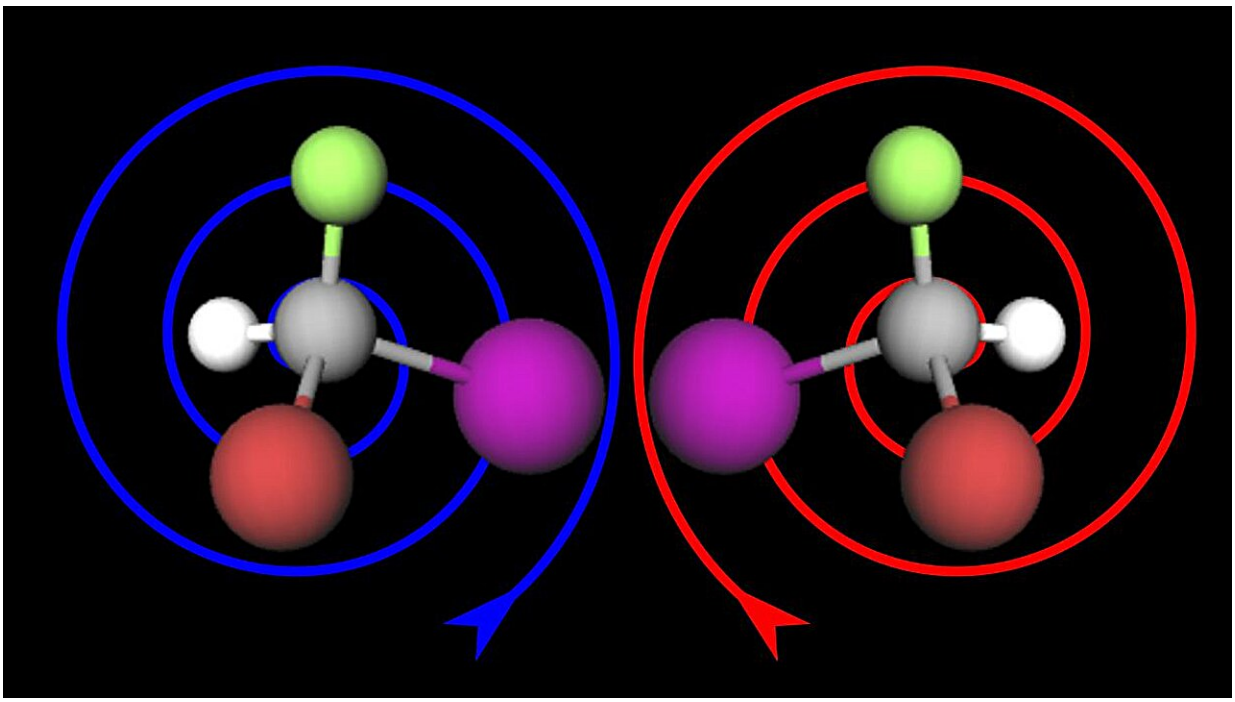

Depending on whether the atoms in a molecule are arranged in a left-handed or right-handed manner, the effects they produce can vary greatly, for example in drugs. Credit: Sagar Wadhwa, KIT

Researchers from Karlsruhe Institute of Technology (KIT) and Voxalytic GmbH have developed a new method that allows, for the first time, the

elucidation of the chiral structure of molecules—the exact spatial arrangement of the atoms—by nuclear magnetic resonance (NMR) spectroscopy.

This important step in the development of new drugs used to be a time-consuming process before now. The new method could now become a standard tool for the chemical and pharmaceutical industries. The research is published in *Advanced Materials*.

The chirality of a molecule refers to its basic structure: Some molecules, so-called enantiomers, occur in pairs and are mirror images of each other. They differ in the way a left and a right glove do. Depending on whether the twisted structure of a molecule is left-handed or right-handed, its influence on biochemical and chemical reactions is different. Despite the mirror-image arrangement, the properties vary or even counteract each other.

With drugs, this can have devastating consequences: When children were born with physical deformities in Germany and England in 1960, the active ingredient called Contergan or Thalidomid was the cause. The drug had been administered to pregnant women for the treatment of pregnancy disorders. It was subsequently banned.

Since then, it is compulsory for pharmaceutical companies to check whether the active ingredients, which are often chiral, are not converted to their opposite enantiomer in the human body.

Method facilitates search for active ingredients

Now a joint team of KIT and Voxalytic GmbH (a spin-off from KIT and the University of Freiburg), led by Professor Jan Korvink, Director of the Institute of Microstructure Technology at KIT, has succeeded in measuring the chiral molecular structure directly using nuclear magnetic

resonance (NMR) spectroscopy.

Although NMR spectroscopy is the only method to elucidate chemical structures down to atomic resolution at ambient temperature, it had so far been "blind" to the chirality of molecules. In order to measure the twists of a molecule, the optical method that has been used can recognize the sense of rotation, but not at atomic resolution.

"We are very excited about the opportunity to turn this method into a convenient tool for the industry and have had the concept patented," says Korvink.

This could make chirality elucidation a future standard method of NMR analysis, as Dr. Sagar Wadhwa from Voxalytic, who wrote his doctoral thesis on this topic, explains. "This will make work easier for chemists who do research into the production of specific enantiomers."

Dr. Dominque Buyens, biochemist and postdoctoral researcher at KIT, adds, "We will study the new method in the context of drug development. It could significantly accelerate drug screening."

More information: Sagar Wadhwa et al, Direct Chiral Discrimination with NMR, *Advanced Materials* (2024). DOI: 10.1002/adma.202408547

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