Source : www.thehindu.com Date : 2021-10-10

# EXPLAINED

Relevant for: Science & Technology | Topic: Science and Technology- developments and their applications and effects in everyday life

Asymmetric approach: Benjamin List and David W.C. MacMillan were chosen for nding an ‘ingenious’ way to build molecules that can be used to make everything from medicines to food avourings. | Photo Credit: AP

**The story so far:** The 2021 Nobel Prize in Chemistry has been awarded to German scientist Benjamin List of the Max Planck Institute and Scotland-born scientist David W.C. MacMillan of Princeton University “for the development of asymmetric organocatalysis”. Developed by the duo in 2000, this novel technique of catalysis is an efficient, “precise, cheap, fast and environmentally friendly” way to develop new molecules.

Catalysis is a term used to describe a process in the presence of a substance (the catalyst) that controls and influences the rate and/or the outcome of the reaction. The substance — the catalyst — which helps in achieving this remains intact and is not consumed during the reaction and neither becomes a part of the final product. The catalyst is subsequently removed so as not to add impurity to the final product. Catalysts are often used to produce new and functional molecules that are utilised in drugs and other everyday substances. For example, catalysts in cars transform toxic substances in exhaust fumes to harmless molecules. When silver is put in a beaker along with hydrogen peroxide, the latter suddenly breaks down to form water and oxygen. The silver, which initiated the reaction, does not get consumed or affected by the reaction.

Editorial | Simple, but brilliant: On 2021 Nobel Prize in Chemistry

The Nobel release points out that in 1835, the renowned Swedish chemist Jacob Berzelius started to see a pattern. “He listed several examples in which just the presence of a substance started a chemical reaction, stating how this phenomenon appeared to be considerably more common than was previously thought. He believed that the substance had a *catalytic force* and called the phenomenon itself *catalysis*.”

Two very different catalysts —metals and enzymes— were routinely used by chemists before Dr. List and Dr. MacMillan developed the asymmetric organocatalysts. As the name denotes, metal catalysts often use heavy metals. This makes them not only expensive but also environmentally unfriendly as sufficient care needs to be taken to ensure the final product does not contain even traces of the catalyst. There are several other challenges when metal catalysts are used. The heavy metals used in these catalysts are often highly sensitive to the presence of oxygen and moisture. Hence, industrial application of this class of catalysts required equipment that ensured no contact with either oxygen and moisture, which made the process expensive.

In the case of enzyme catalysts, the problem arises from their very large sizes. They are often 10,000 times larger than the actual target medicine and can take just as long to make. Enzymes, which are proteins found in nature, are wonderful catalysts. Our bodies also contain thousands of such enzyme catalysts which help make molecules necessary for life. Many molecules exist in mirror images — left-handed and right-handed. But the molecules of interest will be one of the two mirror images. Many enzymes engage in asymmetric catalysis, which help in producing only one mirror image. They also work in a continuous fashion — when one enzyme is finished with a reaction, another one takes over. In this way, they can build complicated molecules with amazing precision.

Unlike enzyme catalysts which are huge, asymmetric organocatalysts are made of a single amino acid. They are not only environmentally friendly but also quicken the reaction and make the process cheaper. Most importantly, asymmetric organocatalysts allow only one mirror image of the molecule to form as the catalysts are made from a single, circular amino acid. Chemists often want only one of these mirror images, particularly when producing drugs.

Organic catalysts have a stable framework of carbon atoms, to which more active chemical groups can attach. These often contain common elements such as oxygen, nitrogen, sulphur or phosphorus. This means that these catalysts are both environmentally friendly and cheaper to produce.

Organocatalysts can allow several steps in the molecule production process to be performed in an unbroken sequence. This is achieved by cascade reactions in which the product of the first reaction step is the starting material for the subsequent one, thus avoiding unnecessary purification operations between each reaction step. This helps in considerably reducing waste in chemical manufacturing. Before organocatalysts could be used, it was often necessary to isolate and purify each intermediate product to prevent the accumulation of a large volume of unnecessary byproducts. This led to loss of some of the substance at every single stage of the process.

Ever since the two laureates developed the novel concept of asymmetric organocatalysis, the field has witnessed rapid development. Since 2000, the asymmetric organocatalysis research area has flourished. A huge number of cheap and stable organocatalysts, which can be used to drive a huge variety of chemical reactions and applications, has been developed. This period is referred to as the ‘organocatalysis gold rush’. Currently, the area is “well established in organic chemistry and has branched into several new and exciting applications”.

Besides helping the generation of novel molecules used in various industries, pharmaceutical companies have used asymmetric organocatalysis to “streamline the production of existing pharmaceuticals”. Thanks to a multitude of catalysts that can break down molecules or join them together, “they can now carve out the thousands of different substances we use in our everyday lives, such as pharmaceuticals, plastics, perfumes and food flavourings”. The fact is, according to the release, it is estimated that 35% of the world’s total GDP in some way involves chemical catalysis.



Going by past experience, the FDA might greenlight the vaccine for young children in a matter of weeks. The company expects to submit data of children 2–4 years and 6 months to 1 year by the end of the year.

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