New method enables design, production of extremely novel drugs

January 23 2008

A new chemical synthesis method based on a catalyst worth many times the price of gold and providing a far more efficient and economical method than traditional ones for designing and manufacturing extremely novel pharmaceutical compounds is described by its University at Buffalo developers in a review article in the current issue of *Nature*.

The chemistry, the basis of a new biotech startup company called Dirhodium Technologies, LLC in Buffalo, has the potential to improve dramatically the design and production of new drugs based on small molecule organic compounds, which comprise the great majority of new drug applications.

"If you tend to make things by methods that have been around for 100 years, there's a decent chance that you'll make something that's already known or is very close to something that is," said Huw M.L. Davies, Ph.D., UB Distinguished Professor in the Department of Chemistry and lead author on the Nature paper. "But if you use an entirely new strategy like the one we developed, virtually every reaction you run will result in a new structural entity. That's critical to drug development."

The chemical strategy Davies developed depends on the use of proprietary catalysts his company manufactures.

Minute amounts of the rhodium-based catalyst can have a major impact, he explained, with 1 gram capable of producing 10 kilograms of a pharmaceutical product.

"So it's like a bit of 'golden dust' to get everything going," said Davies, a researcher at UB's New York State Center of Excellence in Bioinformatics and Life Sciences and president and chief executive officer of Dirhodium Technologies.

"As rhodium metal costs 10 times the price of gold, the catalyst is a high-value material," he said.

Available through chemical supply companies, the reagents are being used by pharmaceutical scientists in both industry and academia.

Already, one major pharmaceutical company is using the reagents to synthesize a compound now in clinical trials.

"Demand for our catalysts has gone from gram to kilogram quantities, from fractions of an ounce to multiple pounds," said Davies.

So far, the new synthesis strategy has generated compounds that have potential activity against a broad range of disease states, from cancer to central nervous system disorders, such as depression, to inflammatory and microbial diseases and medications for treating cocaine addiction.

"This method is like an enabling technology, making available new targets and materials that previously were out of range," said Davies.

Its ability to result in never-before-seen chemical structures is making Davies' collaborations with scientists in partner institutions on the Buffalo Niagara Medical Campus especially fruitful.

"We're using this as a platform for drug discovery, collaborating through the Center of Excellence with biologists at UB, Roswell Park and Hauptman Woodward Medical Research Institute," said Davies.

Davies' company is one of 10 life sciences spinoffs based in the Center of Excellence, which has the dual mission of promoting life sciences research while facilitating economic development in Upstate New York.

In addition to helping drug companies design novel leads for new products, the new chemistry also allows pharmaceutical companies to synthesize efficiently and economically large quantities of novel compounds.

Through catalysis, the chemical synthesis method the UB researchers developed allows for highly unusual functionalizations of carbon-hydrogen bonds, Davies explained.

"The method allows you to transform a molecule from a simple structure to a much more elaborate, drug-like material," he said, "so it goes from a cheap building block to a potential drug-like candidate. Without a catalyst, it won't happen."

A major advantage of Davies' chemical strategy is that the resulting compounds are produced selectively as single mirror images.

Pharmaceutical companies prefer to develop new chiral drugs (chiral meaning "handed") as a single isomer because opposite mirror images can have different biological effects and may be harmful.

"A small amount of our catalyst can be used to generate large amounts of the active mirror image of the pharmaceutical ingredient," Davies said.

Source: University at Buffalo

Citation: New method enables design, production of extremely novel drugs (2008, January 23)