New discovery could help oral medicines work better

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Credit: University of Minnesota

A team of researchers from the University of Minnesota and The Dow Chemical Company have discovered a new method for customizing ingredients that help oral medications dissolve in the body and be

absorbed into the bloodstream. The materials discovered in this study could allow life-saving drugs to work faster and more efficiently.

The University of Minnesota and Dow have filed a patent on the discovery that may also lower the cost to produce new medications.

The research study is now online and is published in the current issue of the American Chemical Society's *ACS Central Science*, a leading journal in the chemical sciences.

One of the biggest challenges for pharmaceutical companies when developing oral medications is to ensure that the body will fully absorb the drug molecules. Many therapeutic structures do not easily dissolve on the molecular level, which means they are less effective. In that case, the dose must be increased for patients, which may increase side effects.

"A way to explain the differences in solubility of medicines is to think of how sugar easily dissolves in water and is rapidly absorbed by your digestive system, whereas sand doesn't dissolve in water and if swallowed, would pass right through the digestive system," said Theresa Reineke, a chemistry professor in the University of Minnesota's College of Science and Engineering and lead researcher on the study.

Drug companies add substances, called excipients, to help the medicines dissolve in the stomach and intestinal fluid, but there have been few improvements in recent years to this decades-old technology. The process outlined in the study is a major breakthrough that revolutionizes the process of making drug structures more soluble in the body so that they are better absorbed.

Funded by Dow, researchers examined two medications—phenytoin, an anti-seizure drug, and nilutamide, a drug used to treat advanced-stage prostate cancer. The team used automated equipment at Dow to

synthesize long-chain molecules. Their efficiency as excipients with these drugs were then tested with facilities at the University of Minnesota, including the Characterization Facility located in the University's College of Science and Engineering. One particular excipient discovered by this research allowed these insoluble drugs to fully dissolve in simulated intestinal fluid in a test tube. When they tested phenytoin with the new excipient in rat models, it promoted drug absorption three times better than the previous formulation.

"While we were pleased with the results with these specific drugs, the most important thing is that we have developed a high throughput methodology for excipient development that could be used by many companies to create other life-saving medicines," Reineke said.

"It takes about $1 billion dollars and 10 to 15 years for a pharmaceutical company to develop a new drug, but then they sometimes find marketable formulations are limited by solubility," said Steven Guillaudeu, a lead R&D manager at Dow and co-author of the study. "The methodology our team has created could help drug companies advance their pipeline compounds by using a better method to improve solubility and therefore bioavailability. The approach could have a major impact on the multibillion-dollar industry."

The research discovery is one result of a five-year collaboration between Dow and the University of Minnesota for research partnerships to develop new chemical solutions, improve research facilities, and train the next generation of scientists.

"This discovery is a perfect example of what can happen when industry and academia come together," said Frank Bates, a Regents Professor in the University's Department of Chemical Engineering and Materials Science and co-author of the study. "This research has yielded something that could have a huge effect on human health and lower the cost of

medications."

More information: Jeffrey M. Ting et al, High-Throughput Excipient Discovery Enables Oral Delivery of Poorly Soluble Pharmaceuticals, *ACS Central Science* (2016). DOI: 10.1021/acscentsci.6b00268

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