Salvagers of Solubility

High throughput excipient discovery looks set to boost oral bioavailability

A collaboration between The Dow Chemical Company and University of Minnesota has yielded a new method allowing the production of excipients that triple the oral bioavailability of drugs, when compared with commercial excipients (1). To further investigate their work, we speak with Theresa Reineke, a professor at the University of Minnesota and Jodi Mecca, a principal research scientist at Dow.

Why is solubility such a problem for drug developers?

The drug discovery process for new chemical entities has shifted to increasingly less soluble active pharmaceutical ingredients (APIs), which demand new methods and excipients for delivery. Coupled with the need to understand the mechanism of action in both solid and liquid states makes effective formulation a challenging analytical problem. To build a better foundational understanding of the systems, our work has combined the synthesis of polymers, use of industry standard processing (spray drying), and the development of improved analytical tools. As APIs cover a wide range of chemistries, it is unlikely that a single solution will work in all cases, so an integrated development approach offers the best opportunity for developing API specific solutions.

How did you find the solution to insolubility?

Our findings came about through our efforts to understand how variations in polymer chemistry affected drug solubility. We aimed to synthesize well-controlled copolymers that would allow us to study the structure/property relationships and interplay between an active drug and an excipient. During our research, several of the systems showed enhanced results when comparing the copolymers to polymers currently used in the field. An example of this was the NIPAm-DMA copolymer, which was highlighted in our recent publication (1). Through the application of high throughput (HTR) synthesis and API supersaturation screening, we found that the performance could be tailored to the excipient during API development, while working within a defined design space. A couple of graduates from the University of Minnesota collaborated with visited Dow where they were able to quickly synthesize an array of copolymers with a variety of monomers and compositions using HTR semi-continuous parallel polymerization reactors, then screen them using a parallel super-saturation test.

How long have you been developing high throughput capabilities?

Dow has been developing high throughput capabilities for close to two decades, and as part of those efforts we were able to miniaturize and parallelize the supersaturation test that allowed more rapid screening with the additional benefit of reduced volume materials. Techniques like these let researchers probe a larger experimental design space, and approach analytical questions more holistically.

What’s next for your research?

Our next steps revolve around the initial research focused on understanding the role of polymer chemistry, and its relation to solubility enhancement. A key discovery from our work was that nano- and microstructures of polymer systems during dissolution play a critical role in solubility enhancement. We’re building upon this finding by designing systems with controllable structures to more systematically probe these effects.

The University of Minnesota continues to be a strong partner to Dow, particularly when it comes to the areas of organic and analytical chemistries, polymers, and reaction engineering. As such, we remain focused on the future, looking for scientific breakthroughs and technologies.

Reference