New technique to make drugs more soluble: System makes amorphous particles out of almost anything

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Before Ibuprofen can relieve your headache, it has to dissolve in your bloodstream. The problem is Ibuprofen, in its native form, isn't particularly soluble. Its rigid, crystalline structures—the molecules are lined up like soldiers at roll call—make it hard to dissolve in the bloodstream. To overcome this, manufacturers use chemical additives to increase the solubility of Ibuprofen and many other drugs, but those additives also increase cost and complexity.

The key to making drugs by themselves more soluble is not to give the molecular soldiers time to fall in to their crystalline structures, making the particle unstructured or amorphous.

Researchers from Harvard John A. Paulson School of Engineering and Applied Science (SEAS) have developed a new system that can produce stable, amorphous nanoparticles in large quantities that dissolve quickly.

But that's not all. The system is so effective that it can produce amorphous nanoparticles from a wide range of materials, including for the first time, inorganic materials with a high propensity towards crystallization, such as table salt.

These unstructured, inorganic nanoparticles have different electronic, magnetic and optical properties from their crystalized counterparts, which could lead to applications in fields ranging from materials engineering to optics.

David A. Weitz, Mallinckrodt Professor of Physics and Applied Physics and an associate faculty member of the Wyss Institute for Biologically Inspired Engineering at Harvard, describes the research in a paper published today in *Science*.

"This is a surprisingly simple way to make amorphous nanoparticles from almost any material," said Weitz. "It should allow us to quickly and easily explore the properties of these materials. In addition, it may provide a simple means to make many drugs much more useable."

The technique involves first dissolving the substances in good solvents, such as water or alcohol. The liquid is then pumped into a nebulizer, where compressed air moving twice the speed of sound sprays the liquid droplets out through very narrow channels. It's like a spray can on steroids. The droplets are completely dried between one to three microseconds from the time they are sprayed, leaving behind the amorphous nanoparticle.

At first, the amorphous structure of the nanoparticles was perplexing, said Esther Amstad, a former postdoctoral fellow in Weitz' lab and current assistant professor at EPFL in Switzerland. Amstad is the paper's first author. Then, the team realized that the nebulizer's supersonic speed was making the droplets evaporate much faster than expected.

"If you're wet, the water is going to evaporate faster when you stand in the wind," said Amstad. "The stronger the wind, the faster the liquid will evaporate. A similar principle is at work here. This fast evaporation rate also leads to accelerated cooling. Just like the evaporation of sweat cools the body, here the very high rate of evaporation causes the temperature to decrease very rapidly, which in turn slows down the movement of the molecules, delaying the formation of crystals."

These factors prevent crystallization in nanoparticles, even in materials that are highly prone to crystallization, such as table salt. The amorphous nanoparticles are exceptionally stable against crystallization, lasting at least seven months at room temperature.

The next step, Amstad said, is to characterize the properties of these new inorganic amorphous nanoparticles and explore potential applications.

"This system offers exceptionally good control over the composition, structure, and size of particles, enabling the formation of new materials," said Amstad. " It allows us to see and manipulate the very early stages of crystallization of materials with high spatial and temporal resolution, the lack of which had prevented the in-depth study of some of the most prevalent inorganic biomaterials. This systems opens the door to understanding and creating new materials."

More information: "Production of amorphous nanoparticles by supersonic spray-drying with a microfluidic nebulator" www.sciencemag.org/lookup/doi/ … 1126/science.aac9582

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