ACOUSTIC MIXING FORMS COCRYSTALS

PHARMACEUTICALS: Green, scalable method to produce cocrystals relies on sound waves

IDEALLY, THE ACTIVE INGREDIENT of an oral medication should readily form crystals, dissolve quickly in the digestive tract, and be rapidly absorbed in the body. If a compound can't do those things on its own, scientists can help it by crystallizing the compound with one or more other compounds, forming cocrystals with the desired properties.

Now, researchers report that vigorously combining compounds using intense sound waves—a technique known as resonant acoustic mixing—could provide a green and scalable way to produce pharmaceutical cocrystals (*Org. Process Res. Dev.* 2014, DOI: 10.1021/op4003399).

Traditionally, chemists have produced cocrystals either by crystallizing the compounds together out of a solution or by grinding the chemicals together mechanically with a mortar and pestle or a ball mill. Mechanical methods limit the use of solvents and are therefore more environmentally friendly. But they are also difficult to carry out on the multikilogram scales needed in the pharmaceutical industry.

Jerry S. Salan, CEO of Nalas Engineering Services, in Centerbrook, Conn., thought of a way around this roadblock. He knew that resonant acoustic mixing produces enough force to combine and coat powders, so he wondered whether that force also could produce cocrystals. Acoustic mixers use high-intensity sound waves to transfer mechanical energy to the materials being mingled. The waves vibrate the materials inside a sample vial with forces 10 to 100 times that of gravity.

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As a proof of concept, researchers at Nalas placed the anticonvulsant drug carbamazepine and the coformer compound nicotinamide along with a small amount of solvent into a resonant acoustic mixer. After one hour, the combination readily formed cocrystals that matched the quality of those formed by other methods. The researchers successfully produced cocrystals on a variety of scales, using 100 mg, 1.5 g, and 22 g of the solid starting materials.

Resonant acoustic mixing provides a way of screening cocrystallization conditions with various compounds and doesn't need a lot of solvent, says Nalas's David J. am Ende. Commercially available resonant acoustic mixers come in capacities up to 200 L, which should be sufficient for pharmaceutical-scale operations, the researchers say.

Over the past decade, pharmaceutical companies have realized that cocrystallization could offer a way to make better medicines, says Mike Zaworotko of the University of Limerick, in Ireland. "This paper addresses one of the major hurdles of how to make cocrystals on a larger scale," he says. Further research will be needed to confirm that the process will scale up and to determine if this technique will apply to a range of compounds, he adds.

Nalas has filed a provisional patent for the cocrystallization process. It is seeking a commercial partner to help carry out additional studies needed to scale up the method.—SARAH WEBB, *special to C&EN*

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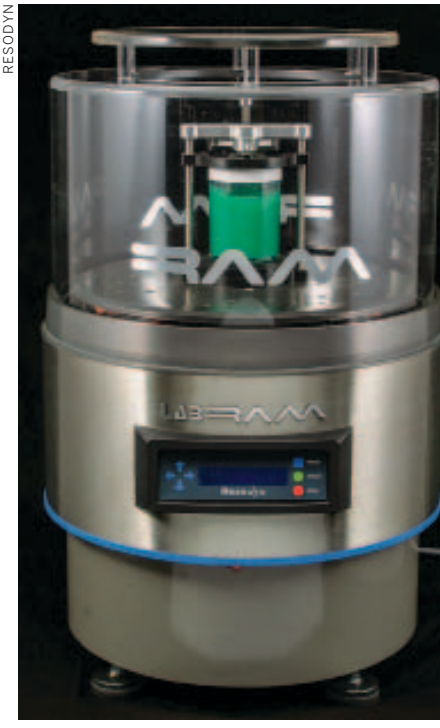

Combining pharmaceutical compounds in a resonant acoustic mixer like this one forms cocrystals in multigram quantities.

BIOTECHNOLOGY Scotland unveils national center to advance sector and create jobs

Scotland has big ambitions for biotech. The country has just opened a national center for industrial biotechnology that it says will help create 1,500 jobs in the sector across Scotland within five years.

Located at the University of Strathclyde, in Glasgow, the center is expected to play a key role in the country's plan to achieve annual biotech sales of up to $5 billion by 2030. That compares with about $300 million today.

Drawing on expertise from 12 of Scotland's universities and one research institute, the center will conduct research around pharmaceuticals, biobased chemicals, and bioenergy, and it will support the development of biotech firms. Scottish government agencies will provide $16 million in initial funding to pay for facilities, equipment, and staff. The agencies predict that the center will attract $70 million more within the next five years in industry and public backing.

Although the center's initial funding is somewhat lightweight, its leadership is anything but. Chemical industry veteran Ian Shott is the chairman. He calls the center "a collaboration of businesses and higher education institutions with the ambition to be truly distinctive, world leading, and responsive to the market and technology needs of industry."

Creating a center to catalyze biotech activity "is a tried-and-true method already implemented with great success elsewhere in Europe," observes Milos Todorovic, an analyst at the market research firm Lux Research. However, the center is being formed at a time of uncertainty for Scotland as the country prepares to vote this year on whether to split from the U.K.—ALEX SCOTT