TAKE A DEEP BREATH!

Inhalable medication is essential with lung diseases. But not every active ingredient can be processed into a respirable medication. Now, a new thin film freezing (TFF) process developed by the University of Texas at Austin can tame even difficult substances. The US companies TFF Pharmaceuticals and Experic are collaborating on new powder formulations and processes for encapsulating TFF inhalable powders.

Anyone who has ever tried to pour the contents of a saucepan into a narrow bottle opening will have a rough idea of the efficiency of oral delivery of many pulmonary drugs. Frequently, only around ten percent of the active ingredients reach their target. One of the reasons for this is the poor solubility of many drugs in water. This makes it difficult for the body to absorb the active ingredients, reducing efficiency. Delivery through dry powder inhalers is much more efficient and targeted, explains John Koleng, Vice President of Product Development and Manufacturing at TFF Pharmaceuticals. "The patient takes a deep breath, and the tiny particles of the engineered powder containing the active substance directly reach the deep pulmonary tissues without major loss. This only works with fine powders whose particles are aerodynamically smaller than about five micrometers. This rules out many highly effective substances from the start." Researchers at the University of Texas at Austin have succeeded in identifying a solution to this problem. They developed a technology which converts a coarse powder into a light and respirable one. TFF Pharmaceuticals has secured a license for the patented thin film freezing process technology.

FROZEN AND CONDITIONED

"Thin film freezing is a particle engineering process," explains Koleng. "We dissolve the drug in a solvent and then drop the liquid onto a stainless-steel drum cooled with liquid nitrogen, where the droplets are rapidly frozen. The frozen product is then freeze-dried to remove the solvent thus yielding the TFF powder." At the end of the process, the originally coarse and compact powder has been converted to brittle matrix particles that are highly porous, have a large surface area and a low bulk density. After conditioning, the result is a fine powder. This way, a dry powder inhaler is used to deliver up to 75 % of the active ingredient to the lungs where it is intended to act.

"With TFF technology, a coarse powder can be converted into a light and respirable one."

John J. Koleng, Ph.D., R.Ph.
Vice President of Product Development and Manufacturing at TFF Pharmaceuticals

LEVERAGING COMMON POTENTIAL

TFF Pharmaceuticals works closely with Harro Höfliger and its partner, Experic, in evaluating TFF manufactured powders and their subsequent encapsulation for use with a dry powder inhaler. Experic is a contract manufacturing and development organization that manufactures and packages clinical trial materials and specialty supplies primarily for small,

Experic, Avector/Adobe Stock

Since the beginning of 2019, the US company Experic has been offering contract services for the manufacturing, packaging, labeling and global logistics of clinical trial materials and specialty commercial supplies. Experic is focused on the small, midsize, and specialty pharmaceutical customer.

medium and specialty pharmaceutical customers. Justin Lacombe, Chief Scientific Officer at Experic, explains: "As a CDMO partner, we manufacture powders for TFF Pharmaceuticals and carry out tests with our Harro Höfliger filling machines. In this way we can test formulations for compatibility with the encapsulation machines at an early stage of development. This supports early success with initial clinical manufacturing and facilitates feedback that enables successful scale-up."

INFINITE POSSIBILITIES

The thin film freezing particle engineering process has a lot of potential, and TFF Pharmaceuticals and Experic are working together to develop new applications. One of these is TFF Pharmaceuticals' inhaled tacrolimus product, currently in Phase 2 trials. Tacrolimus is a natural compound that acts as an immunosuppressant. Inhaled tacrolimus is being studied as an alternative to oral tacrolimus for lung transplant patients where direct to lung delivery could potentially maintain the efficacy of the oral therapy while reducing side effects

"As a CDMO partner, we manufacture TFF powders and carry out filling tests with our Harro Höfliger machines."

Justin Lacombe, Ph.D.
Chief Scientific Officer at Experic

and drug-drug interactions. However, TFF developers are not just looking at repurposing existing drugs. Koleng explains that around one third of the most important drugs available worldwide are difficult to dissolve in water and that thin film freezing technology is suitable for many of them, as well as for combination therapies and the growing segment of biologics. "Inhalable powders are the future," he says, adding: "They can be accurately measured, don't require cold chain storage and distribution, and are significantly easier to handle than sterile syringes. We can give them a boost with TFF technology."

HOW THIN FILM FREEZING WORKS

1. Formulation: The thin film freezing process involves first combining a drug or drugs in a liquid carrier system, which can include agents designed to promote dispersion and avoid aggregation, as well as excipients to promote delivery to the target site.

2. Freezing: Controlled freezing the liquid material on the surface of a cryogenic drum results in brittle matrix particles: highly porous, large surface area, low-density particles

3. Drying: The frozen solvent is then removed by sublimation to yield a dry powder material that can be aerosolized to facilitate delivery to the lungs, nose, eyes and topically through the skin.

4. Finishing: The brittle matrix particles are then further processed to facilitate creation of the final dosage form for the targeted route of administration.