Life Sciences Writing Portfolio
By: Lauren Perna

Going Green with Supercritical Fluid Chromatography

Companies worldwide are implementing green initiatives, and in some sectors, going green means installing solar panels. In the chemistry world, it means making a switch to supercritical fluid chromatography.

Supercritical fluid chromatography (SFC) is a type of normal phase chromatography, designed much like high-performance liquid chromatography (HPLC). The difference is that HPLC uses pressured liquid, whereas SFC uses a supercritical fluid—a highly pressured gas.

HPLC may be a popular and reliable technology, but it has several disadvantages that SFC does not. Most notably, HPLC uses organic solvents that are flammable, toxic, and expensive. In SFC, the most common gas used is CO_2, which is environmentally friendly and inexpensive.

The CO_2 in SFC is recycled, derived from other industries, whereas HPLC generates new CO_2 when the mobile phase is burned. In SFC, the CO_2 is often combined with alcohol, which has lower toxicity than the acetonitrile used in HPLC. Since CO_2 evaporates at the end of the process, the amount of toxic liquid waste is significantly lower in SFC.

SFC is also a cheaper technology due in part to its smaller scale. HPLC is a larger-scale equipment, which means it uses a higher volume of solvent. As we know, these solvents are more toxic, but they are also more expensive. So SFC significantly reduces costs upfront and in the disposal stage.

Supercritical fluid chromatography is also recognized for being a faster, more efficient technology with better resolution. Since supercritical fluids have lower viscosity and higher diffusivity, the flow speed increases and there is better separation. An extraction process may take as little as ten minutes with SFC, whereas other methods could take up to several days.

SFC also offers the advantage of working with a broad range of detectors. This array allows for even better analyses than some of its counterparts.

Companies are recognizing that superfluid chromatography has many clear advantages over high-performance liquid chromatography. At the same time, there is an increasing push to make chemistry greener, all but ensuring that SFC use will rise.

Semi-solids Are Poised For Growth

For decades, the most popular form of drug dosage has consistently remained the oral solid—the tablet, the pill, the capsule. This trend is likely to continue, but the semi-solid market is growing and will continue to over the next five years and beyond. Semi-solid dosage forms are administered topically--coming in the form of creams, ointments, gels, and pastes--but they can also be in the form suppositories or chews.

As the global population ages, we'll see an increase in the demand for SSDs and as drug companies innovate, the semi-solid dose will fill needs that other forms cannot. However, the semi-solid form is not without its challenges. As the SSD market grows, so will the need for companies that know how to handle this form.

An aging population means growth for semi-solids

Demand for semi-solid topical drugs is strong because they are easy to administer and have limited side effects, which improves patient adherence. Patients and clinicians also like that the drug is applied directly to the affected area and that they avoid first-pass metabolism, as can happen with ingested forms. Their ability to cover a wide variety of drug molecules also makes them a popular option.

Given the ease of use, the affordability, and the high level of patient compliance, it's no surprise the home care segment had the largest share of the topical drug delivery market in 2019.
As the population ages, the need for convenient at-home care will only increase, and semi-solid topical drug products will be a crucial part of that care. Skin and eye diseases that accompany aging are becoming more prevalent, as is diabetes. Patients with diabetes often have related dermatological complications that require topical treatments.

The high prevalence of skin and soft tissue infections and burns is also contributing to the rise of the semi-solid market, as is the rise in personalized medicine. Companies are finding the semi-solid can easily deliver customized dosages, created on an individual patient basis.

Challenges that require expertise

Despite being favorable among clinicians, patients, and drug-makers alike, the semi-solid drug form does have its challenges. Most of the difficulties occur in manufacturing and scaling. SSDs are complex products, which means that every step of the manufacturing process--transferring materials, mixing, degassing, filling, storing--can impact the product's characteristics. Once manufacturing is complete, it's essential that the product is stored appropriately and monitored for any issues, as even a slight change in conditions could compromise package integrity.

Scaling is particularly challenging for SSDs because of the differences in equipment at the bench and large-scale levels. Another variable that is difficult to replicate at a large-scale level is temperature. Improper temperature can drastically impact the product's key elements and may even influence the microbial features.

The right equipment and expertise

However, manufacturers can lessen these concerns by using best-in-class equipment and hiring the proper team. The team must have the experience to understand the nuances of SSD manufacturing and the technical expertise to foresee and avoid any significant missteps.

What Orphan Drug Companies Should Look For in a CDMO

In 1983 the United States passed the Orphan Drug Act, which incentivized companies to create products for rare diseases. The program worked; it has led to the development and marketing of over 600 drugs and biologics for rare diseases, with orphan drug revenue topping $127B in 2019.

Those numbers will only continue to rise, as will the need for Contract Development and Manufacturing organizations with orphan drug expertise. Orphan drugs may not require the manufacturing of large volumes like other drugs, but they do require a certain level of skill and quality.

The most important thing is to find a CDMO that is fit for the size and scale of the project. The right fit will ensure a long-term partnership that's mutually attractive from an economic perspective. Many GMP CDMOs that work at the orphan drug scale only focus on the early stage. If you start with one of those companies, you may have to make a costly and time-consuming transfer mid-project.

Often times an orphan drug company will be ready for scale-up, just to be dropped by the CDMO because they were no longer making any money off the project. You can avoid having to transfer the project by finding a CDMO that aligns with your needs and will be your one-stop-shop throughout the whole project.

Part of finding that long-term fit is finding a CDMO that is willing to be flexible and agile. Look for a company that understands what you are trying to do and is willing to create a partnership tailored to your needs.

Many CDMOs have a particular way of doing things and aren't willing to budge, but that can be problematic in working with orphan drugs where one batch could potentially be the world's supply. Because of this, the FDA allows for abbreviated regulatory and validation pathways. These shortened timelines may require alternative approaches, so the CDMO must be able to flex with these adaptations.

Given how unique the regulatory process is for orphan drug companies, it's critical to find a CDMO with experience in commercializing orphan drugs. In the case of another orphan drug company, they realized they had outgrown their CDMO when it became clear the company didn't have the necessary late-stage experience, which threatened to hinder progress.

A company may market itself as a one-stop-shop, but it may not actually have in-depth experience in all stages. That's why it's important to make sure your CDMO is experienced at all stages, especially the critical regulatory stage.