The possibilities and challenges of spray drying

Spray drying has been used in the pharmaceutical industry for years for the drying of APIs, but the process also offers a range of particle engineering possibilities. Henrik Schwartbach explains why spray drying is garnering new interest and slowly but surely becoming part of the pharmaceutical industry's standard toolbox.

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How is spray drying performed and what advantages does the process offers over alternatives?

In its basic form, spray drying is a very simple process where droplets/particles are dried while suspended in the drying gas, turning a liquid feed into a dry powder in a single continuous process step. The basic spray drying process has three essential steps: atomisation, where the droplets are formed; drying gas and droplet contact, where the liquid feed is turned into droplets; and finally powder recovery, where the dried particles are separated from the drying gas stream.

The source of the excellent performance of spray dryers is also the source of their main limitation. A spray dryer is a suspended particle dryer, where the droplets/particles need to be dried before they hit the interior wall of the drying chamber to avoid deposits of wet and sticky particles. Drying the particles while suspended requires that drying is very fast and that droplet trajectories are kept away from the drying chamber wall for as long as possible.

Fast drying is achieved through two means: effective and uniform atomisation of the feed, thereby creating a very large feed surface area; and by ensuring effective mixing of the droplets with the drying gas. The available drying time is a result of the size of the drying chamber and the flow pattern. Additionally, the process requires small droplets to work. The smaller the dryer, the smaller the maximum droplets that can be dried, and drying times are short (at least for spray drying in its basic form), which sets a limit to how low a residual solvent level can be achieved in the final product. Consequently, the spray drying process is most limited at the small-scale. Scale up, however, offers more opportunities and improved process robustness.

The fast drying, the short residence time and predictable temperature exposure — caused by the effective mixing of the droplets with the drying gas — results in a lenient drying process that can be adjusted for a broad range of process conditions, including the drying of heat sensitive materials such as live vaccines and complex proteins. Just as importantly, spray drying is a highly reproducible process that can be predictably scaled up to nearly any scale of production — spray drying processes can be designed for batches of a few grams of solids, all the way up to very large instruments that can continuously produce more than 10 metric tons of powder per hour.

Apart from drying, spray drying offers a range of particle engineering possibilities. By altering the process parameters (and/or spray dryer configuration), spray drying can produce complex powders that meet exact powder properties in terms of particle size and shape, bulk density, dispersability, polymorphism, flow properties and so on. An example could be the manufacture of a polymer-stabilised, amorphous and solid dispersion of an API for direct compression into tablets, without an intermediate granulation or mixing stage. In this case, the process conditions are chosen to produce a homogenous, free flowing and non-dusty powder of good density from a

The author says...

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- Being a highly reproducible process, spray drying can be scaled up to nearly any production size.
- Although spray drying and lyophilisation are supplementary technologies, spray drying is generally more flexible, efficient and economical.
- Spray drying does not perform as well at the small laboratory scale; therefore, extra care is required in development to avoid false negative results.

liquid feed containing the necessary components of the final tablet in solution and/or suspension. The fast drying at low temperatures (below the glass transition temperature of the solids) will intentionally favour the amorphous form of the API/ polymer mixture. In other cases, the requirement may be completely different; for example, powders for inhalation must have a small aerodynamic size, resulting from the small geometric size and low density.

Modern spray dryers can be built for operation with a wide range of (flammable) solvents as well as water, for congealing of melts, for contained processing of potent compounds, for aseptic processing, for agglomeration with integrated fluid beds and more.

In short, spray drying is a very versatile lenient drying process that turns a liquid into a powder in a single process step at any scale with particle engineering possibilities that makes spray drying worth considering even when drying is not otherwise required.

Why has there been a renewed interest in spray drying from the pharmaceutical industry?

Spray drying has played a role in the pharmaceutical industry for many years, mainly in the drying of APIs — particularly excipients. To a large degree, new interest in spray drying has been driven by the use of spray drying as an enabling technology; for example, the production of amorphous solid dispersions can greatly improve the performance of poorly soluble APIs. Such processes, based on organic solvents, are ideally suited for spray drying and produce results that generally surpass those of alternative technologies. Interest has also spread to other areas where spray drying may be more economical or where the particle engineering possibilities are better than the traditional methods of production. However, the interest in spray drying is mostly for new compounds, which naturally slows the adoption of spray drying into the pharma industry.

How does spray drying compare with lyophilisation?

Spray drying is generally more flexible, more efficient and more economical in terms of installation, investment and operation for the same evaporative capacity compared with lyophilisation; for instance, the evaporative capacity of a normal sized pharmaceutical spray dryer can match the evaporative capacity of 5–7 large freeze dryers. In many cases, however, the two technologies are supplementary. For small batches of difficult-to-dry powders to be supplied in vials, lyophilisation has an advantage, whereas spray drying has an advantage if free flowing powders are required. However, there are probably several freeze dryer installations that could be replaced with a modern spray dryer.

How do you see spray drying fitting into the manufacturing process?

Spray drying is most likely to be an additional technology that can supplement the technologies already used for drying and/or particle formation. One example of where spray drying can be used is where lyophilisation is less effective; for instance, for large volume products or for where particle engineering is required. In most case where spray drying is used, lyophilisation is not a viable alternative, but there are alternative processes such as crystallization, high-shear mixing/granulation, fluid bed drying/ granulation and more.

What should manufacturers avoid when considering spray drying for drying and/or particle engineering technology?

Any feed that cannot be atomised will obviously not work. Frequently this problem can be solved by simple dilution or a better solvent, but this is not always the case — high molecular weight polymers are examples of this. Highly thermoplastic and hygroscopic materials may create heavy deposits or not come out of the dryer at all. Also, if the product melts at the temperature required to dry it to a non-sticky material then it is not usually suitable for spray drying. However, this problem can often be solved by replacing or reducing the problematic material in the formulation (e.g., if it is an excipient, or by adding a benign excipient as a drying aid).

Are there any disadvantages/ challenges associated with spray drying?

There are few available pharmaceutical spray drying facilities in the market for product and process development purposes. This can be a serious issue, especially during the planning of clinical trials when there is a need for production, but a risk of losing an investment in a new plant. Another challenge is that, although spray drying is a proven technology, there is still limited knowledge about the technology in many pharmaceutical companies. Hopefully this will inspire the pharmaceutical companies to seek external expertise at an early stage of development. At the very small scale (laboratory scale), spray dryers are not performing as well as they do at the larger scale and extra care is required in early development to avoid false negative results.

What kind of future do you predict for spray drying?

Spray drying is slowly but surely becoming part of the pharma industry's standard. The flexibility of the technology will surely find many more uses in the coming years. **PTE**

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