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Vacuum Shelf Dryer Provides More-Uniform Cakes

Different approach to endpoint determination leads to greater consistency

By Steve Webb, Eli Lilly and Company

Shelf drying is a common unit operation for reducing the liquid solvent content of solid cakes prior to material storage or downstream processing. Where the use of high temperatures could result in product stability issues, shelf dryers may employ vacuum to evaporate volatiles at low temperatures. Pharmaceutical manufacturing, for one, often requires efficient drying at less than ambient temperatures. The combination of shelf drying and sub-atmospheric pressure allows for efficient volatile material evaporation while maintaining the solid cake at relatively low temperatures. Determining the drying endpoint using in-process conditions that accurately predict the solid-cake moisture content minimizes the potential for a need to stop and restart the operation. We have found in a case study that the absolute pressure during a vacuum shelf drying operation correlates closely with the volatiles’ content of solid cake and, thus, can serve to regulate drying time.

In this case, we must dry a crystalline solid product to a specified solvent content prior to storage and shipping for downstream processing. Technicians load a batch of wet solids that contain 20–40-wt.% solvent into stainless steel pans. The pans then are placed on jacketed shelves within the dryer and thermocouples are inserted into thermowells installed on the pans to measure cake temperature. The dryer is connected to a vacuum pump separated by a block valve that controls the start and end of drying. The vacuum pump runs at capacity throughout drying, with a flow rate of 40–82 acfm depending upon the operat-
ing pressure. The dryer shelf contains recirculated water that is temperature controlled to a specified set point to regulate heat transfer to the pans. Figure 1 shows the dryer and Figure 2 depicts the equipment layout.

Drying starts once the dryer door is sealed and the vacuum supply valve is opened. The shelf transfers conductive heat to the cake. Pressure is measured on piping connecting the dryer to the vacuum pump. The pump runs at full capacity, both removing solvent vapors and continually decreasing the pressure within the dryer. Initial pressure is as high as 7 mm Hg abs., but typically falls to 0.1–0.5 mm Hg abs. by the end of the drying operation. The thermocouples installed into the trays continuously monitor the solid cake temperature. It drops quickly at the start of drying from ambient temperature to between -10°C and -25°C as a result of evaporative cooling. The rate of evaporative cooling is greatest at the start of the drying operation when the cake has its highest volatiles’ content. Temperature soon levels off and then slowly increases for the majority of the process due to the ever-decreasing rate of heat transfer from the solids to the vapor as the drying rate falls. By the end of drying, the cake temperature typically is 5–11°C when controlling the jacket to 12°C.
CONVENTIONAL STRATEGIES

Control of the drying operation endpoint historically has been based on either a fixed time or a final cake temperature within a fixed time range. Both strategies heavily rely upon a defined time or time range to estimate when drying ends. A time-based approach poses inherent issues because factors that impact the drying rate vary from batch to batch and are difficult to control. The most influential factors are batch size or cake thickness, and initial moisture content.

Additionally, the temperature endpoint strategy has proven ineffective for several reasons. The level of leak rate into the dryer can impact the efficiency of solvent removal but is undetectable by the cake temperature alone. The placement of the temperature sensor within the cake also adds variability because the cake temperature changes as a function of its distance from the shelf. In addition, the cake isn’t uniform in initial moisture content, so a single-point temperature measurement within the cake isn’t always representative of the average of the entire cake due to lower or higher rates of localized evaporative cooling. These factors result in unacceptably high variability of endpoint moisture content.

In our case, prior to the vacuum dryer operation, the cake undergoes a forced nitrogen convection process that removes excess liquid solvent. As a result, the solvent contents observed in the process always start and end within the falling rate period of drying; therefore, the drying rate always is a function of the moisture content in the cake as mass transfer laws dictate. For this operation, batches enter the dryer with variable initial solid weights and liquid solvent contents. Batch size and the initial solvent content contribute to the volume of volatiles to be removed; larger or wetter batches generally require longer times to dry in the falling rate period of drying. Bigger batch sizes and, thus, thicker cakes also increase resistance to flow because diffusing vapor must travel a more torturous path to the surface. In addition, higher initial solvent content increases dry-
ing times because a greater ratio of initial solvent content to solid mass results both in a larger volume of solvent to remove and more-extensive evaporative cooling heat transfer occurring from the solids to the vapor. A higher extent of evaporative cooling removes heat from the solids and generates a lower temperature profile throughout the drying process, slowing the drying rate and extending the drying time.

**A DIFFERENT APPROACH**

We decided to try to determine drying endpoint based on product solvent content in the cake by indirectly gauging the vapor mass flow rate via pressure measurement. Assuming a low leak rate into the dryer, the pressure at any given time during drying is proportional to the volumetric flow rate as determined by the vacuum pump pressure/flow curve. In this case study, the vacuum pump capacity far exceeds the drying rate; therefore, the operating conditions all are on a sloped portion of the vacuum pump curve where volumetric flow rate continually decreases as pressure falls. Because the vacuum chamber is well sealed with a minimal leak rate and contains a vapor-producing stream from the cake in the falling rate period of drying, the pressure generated at any time reflects the mass flow rate of solvent vapor from the cake.

To check the assumption that the leak rate is minimal, we measured the pressure impact of the leak rate by running the vacuum dryer process without loading product. The pressure generated by the system at equilibrium primarily is a result of the system leaks, including from the vacuum pump. The leak rate pressure was found to be approximately 0.01 mm Hg abs. ±0.005 mm Hg. Because the pressure associated with leaking accounts for only 1%-15% of the total pressure at the endpoint condition, we felt comfortable treating the contribution of leak rate as minimal and relatively constant. These data support the conclusion that the large majority of flow through the system when drying stems
from solvent vapor evaporative mass transfer from the wet cake, also identified as the drying rate.

The Ideal Gas Law enables calculating the drying mass flow rate from the measured pressure during drying, the volumetric flow rate as determined by the vacuum pump performance curve, and the average cake temperature. The Ideal Gas Law is a good approximation of the actual drying rate as a result of low operating pressures. The drying rate is required to correlate measured pressure and the cake solvent content. However, in this case study, calculating the specific drying rate wasn’t necessary because our desire was to predict the final volatiles’ content in the cake.

The correlation of drying mass flow rate to the actual cake solvent content in the falling rate period of drying is complex and depends upon several factors including the specific cake’s resistance to drying. The unknown geometry of interstitial spaces both between and within the solid particles making up the cake results in complex cake resistances. Therefore, empirical data are required to equate drying rate to a final volatiles’ content and complete the correlation to endpoint pressure.

We experimentally determined the relationship between endpoint pressure and cake moisture content by measuring the final solvent content of the cake for 40 batches using a fixed-time drying endpoint strategy. We plotted the endpoint pressure and volatiles’ content (wt.%) of each batch on an x-y chart and found a linear correlation for the given data range (Figure 3). We used the best-fit linear relationship to approximate an average volatiles’ content that correlates to each endpoint pressure. We fit confidence limits of 99%
The Ideal Gas Law is a good approximation of the actual drying rate as a result of low operating pressures.

(shown in red) to the data to show with high confidence the expected range of volatiles’ contents for each endpoint pressure condition. In this case, we selected a specific endpoint pressure to achieve an average solvent content of 6.25% while limiting the upper range to 6.8%.

Upon implementing this pressure endpoint drying strategy, we produced a set of 56 batches by controlling the endpoint pressure to 0.12 mm Hg absolute. The result was an average final solvent content of 6.26 wt.%, with a range of 5.85–6.73 wt.%, which closely resembles the targeted average and upper limit. Figure 3 shows that the average volatiles’ content with the pressure endpoint drying strategy was predictable by using a linear fit to the fixed time data. Additionally, the range can be predicted because the pressure endpoint drying data remained within the 99% confidence limits set for the fixed time drying data.

We now have implemented the pressure endpoint strategy; drying time (i.e., the time needed to reach the endpoint pressure) varies from -35% to +20% of the previous fixed time. Smaller and initially dryer batches require less time in the dryer while larger and wetter batches need more time. As a result of this strategy, the variability in the final solvent content in the cake has decreased by approximately 50%. These results support the conclusion that using a fixed pressure endpoint can compensate for batch-to-batch variability such as batch size (cake thickness) and initial moisture content.

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Conquer Crystallization Challenges

Question the need for cooling and ensure you have the right data

By Tom Blackwood

Crystallization is easy! You just cool the solution and out drops your product. That’s a delusion as numerous plants can attest. Many products that start out in this manner cause problems in downstream processing. For instance, fine crystals may not separate from the solvent completely and drying may take a long time.

Once the chemists have given you a process — react, cool, separate and dry — they should look at various scenarios and alternative routes to the product. Such alternatives certainly exist. Cooling may not be the optimum way to generate supersaturation.

So, let’s examine five alternative routes that you should suggest to the chemists:

1. Generate enough supersaturation to nucleate the product and slowly grow the crystals to a large size. Sometimes this means an incubation period or even a fines-destruction step to ensure the correct number of nuclei. The crystals should be big enough to separate from the solvent easily and even to allow their washing. With less solvent to evaporate, drying can be more rapid. Often, the equipment required for the downstream processing is less expensive and smaller. Generally, this is a big benefit. However, spending a lot of time in the crystallization process to make a large particle can destroy that advantage.

2. Generate the supersaturation and introduce seeds or artificial nucleation via sonication to control the number of
Process problems often occur because the meta-stable-zone width isn’t well defined or understood.

nuclei. This extra step may make the solvent easier to remove, even with a smaller crystal. This results in less time spent crystallizing while still realizing a reduced drying time.

3. Remove the excess nuclei generated by primary or secondary nucleation via fines destruction, and return that solute to the crystallizer. This will allow operating at a higher supersaturation that will increase growth rate, reduce crystallization time, and maintain the advantages cited in the first route. An optional way to remove excess fines is through Ostwald ripening, where the batch is held at the end of crystallization to re-dissolve fine particles onto larger crystals.

4. Rather than making a large crystal, stick with the fine product and perform multiple crystallizations using the solvent in a cascade manner to wash the crystals or even use liquid/liquid extraction to purify the wash. The fine particles produced can be agglomerated during drying or pelletized through extrusion to give granular product of the desired size.

5. Remove solvent instead of cooling. While cooling works well for many chemicals, some have unusual, if not strange, solubility curves. In such cases, you must remove solvent to generate supersaturation. Also, polymorphs can complicate the crystallization, especially if the solubility curves cross at some temperature. Solvent evaporation often makes more sense than cooling when considering options such as fines destruction. Addition of anti-solvents also may outperform other means of generating supersaturation.

You should evaluate, at least on paper, all these routes before selecting a process design or type of crystallizer.

Many process designs run into problems when the meta-stable-zone width isn’t well defined or understood. Indeed, I’ve seen numerous difficulties occur because of this oversight. You should generate solubility curves both from solution and dissolution of the product to determine this no-man’s land of solubility. Such curves will help any manufacturer of crystallizers make the best suggestion for a device. Also, this information will ease grappling
The alternatives suggested don’t address one of the most critical choices made in the process design: whether to opt for batch or continuous crystallization.

The most overlooked physical properties in a crystallization process are growth and nucleation rate. Growth often is expressed as time to reach an average size and never has been studied as a function of supersaturation and particle size. I realize that both nucleation and growth aren’t easy to understand, but an analysis of the particle size distribution gives a starting point to estimate growth and evaluate other routes that might provide a better and cheaper product.

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Corral Compliance with Dry Vacuum Technology

Controlled vacuum helps meet environmental regulations in the pharmaceutical and fine chemical industries

By Raj Bhatnagar, Gardner Denver Nash

Stable and reliable vacuum is key to a variety of processes, ranging from distillation to vapor recovery. With a number of available technologies to choose from, many industries are looking to dry vacuum technology to meet tightening environmental regulations and overcome existing systems’ technical limitations.

Controlled vacuum can be applied to a range of processes for a number of different reasons:

- **Increasing efficiency.** Vacuum can be applied to the main condenser of a power plant to minimize the amount of steam required while maintaining efficient turbine operation.

- **Boosting output.** Refineries apply vacuum to crude towers to enable the proper distillation and recovery of hydrocarbons at much lower temperatures without cracking valuable, high-molecular-weight hydrocarbon chains.

- **Maintaining quality.** In pharmaceutical processes, vacuum is used not only to illicit a reaction, but also to help to maintain the color and quality of the final product.

Applying vacuum to any process is an important and often delicate operation. The lack of a stable and reliable vacuum can have a detrimental effect on not only the process, but also the end product. As a result, a number of different technologies can be used to create vacuum, depending...
VACUUM TECHNOLOGY PERFORMANCE RANGE
Figure 1: This chart compares various vacuum technologies.

on the equipment and application. Types of vacuum pumps include:

- Liquid ring vacuum pump
- Steam jet
- Water jet
- Oil jet booster
- Diffusion pump
- Piston pump
- Blowers
- OTO pump
- Vane pump
- Dry pump

- Northey claw
- Dry screw pump

Vacuum technology, including pumps, liquid rings and hybrids, offers varying performance (Figure 1).

PROS AND CONS OF VACUUM TECHNOLOGY
All of these technologies have advantages and disadvantages. The following table provides examples.
These technologies also share a common limitation. With the exception of dry screw pumps, which have a compression ratio of 7,600:1 or higher based on a suction pressure of 0.1 torr in a single stage, the others have limited compression ratios.

To select the right technology for the application, engineers need to be aware of and understand the technology, as well as have a deep knowledge of the application and processes in place. As with any complex system, it is crucial that each element is selected and combined to not only realize, but also maximize, the anticipated reliability, efficiency and total cost of ownership (TCO).

When the right pump has been selected, engineers then can begin to select the remaining elements, such as heat transfer equipment, vessels, piping diameters and orientation, VFDs, and instrumentation and control equipment. Each element must be designed and selected to work in concert with the main vacuum producer to achieve the best result.

It therefore is important to consider an OEM vacuum vendor with the engineering expertise and capability to not only design and supply the complete system, but also provide a complete system warranty and support package.

**DRY TECHNOLOGY GAINING PROMINENCE**

Driven by increasingly stringent environmental regulations, chemical, pharmaceutical and research facilities are turning to dry technology for applications such as:

<table>
<thead>
<tr>
<th>Technology</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Industries and Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steam Ejectors</td>
<td>Reliable; efficiency can be improved when combined with other technologies such as liquid ring</td>
<td>Inefficient; not environmentally friendly</td>
<td>Ideal for refinery crude tower distillation, other oil and gas applications and chemical refining applications</td>
</tr>
<tr>
<td>Liquid Ring Vacuum Pumps</td>
<td>Handle slugs of liquids and near isothermal compressor; good scrubber; extremely durable</td>
<td>Low efficiency; high water usage; performance based on vapor pressure of the seal liquid and composition of gas handled</td>
<td>Ideal solution for paper mills, vapor recovery systems and other general industrial, chemical, oil and gas, mining and power generation applications</td>
</tr>
<tr>
<td>Blowers or Boosters</td>
<td>Large capacity capable of pulling deep vacuum; efficient when combined with other technologies such as liquid ring; increase capacity when combined with dry screw pumps</td>
<td>Limited by temperature rise and differential pressures; compression is limited to a ratio of 2:10 based on operating pressure</td>
<td>Rapid evacuation; applications in which this compression ratio is desired combined with other technologies such as liquid ring or dry vacuum to improve system efficiency</td>
</tr>
</tbody>
</table>
• Distillation
• Reactors
• Evaporators
• Extruder vent gas
• Drying
• Filtration
• Mixing
• Stripping
• Freeze drying
• Sterilization
• Lab R&D applications in which gas compositions and conditions can change from product to product

In addition to compliance with regulations, dry screw pumps provide several functional features:

• Ultimate blank-off pressure of less than 0.1 torr
• Operation across the entire pressure range (using single-stage compression)
• High efficiency (CFM/BHP)
• Wetted parts that are coated
• Process that runs cleaner without the use of any liquid
• No product contamination
• No waste produced, so no contaminants to dispose of
• Solvent or vapors that can be condensed in an after-condenser without contamination
• Machine capacity that can be increased by adding a vacuum booster ahead of the dry screw pump

**DRY SCREW VACUUM PUMPS**

One such product, the Dry-Pro range of dry screw vacuum pumps (Figure 2), is designed to boost process capacity while maintaining a completely dry system and provides the above-mentioned dry technology features.

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