

**A CASE STUDY ON THE PREVENTION OF SEGREGATION CAUSED
BY UNCONTROLLED AGGLOMERATION DURING THE DRYING OF A
PHARMACEUTICAL POWDER IN A BOLZ-SUMMIX® CONICAL SCREW DRYER**

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During start-up of a new Bolz-Summix® conical screw dryer, the bulk product agglomerated due to its sticky nature during a critical phase of the drying cycle. Down stream from the dryer, in the feed chute to the tableting machine, segregation of the coarse product from the fine gave validation problems. This case study shows, that by slightly differing the process conditions during the drying stages, granulating could be eliminated, minimizing segregation.

1. Introduction

In many branches of industry, drying and mixing of particulate solids is an essential and critical process step to obtain the desired product specification. Various types of mixers and dryers are available in the process industry to meet the specific needs of each process. These mixers and dryers are basically divided between continuous operation and batch. The latter method of operation is often dictated by the process and product parameters, such as, multi purpose plants or where total batch integrity is required for quality and validation control as in the pharmaceutical and specialized food industry, enabling them to verify the product before it can be released on the market.

2. Scope of new process line for drying and homogenizing product

One of our pharmaceutical customers recently decided to build a new plant to increase production of one of their medical products. Currently it is dried in tray dryers then granulated, mixed and stored in a small silo, before tableting. A schematic flow sheet of the process is presented in Figure 1. Whilst this method meets their specification, there are disadvantages; the main ones are listed below:

- **The process is rather labor intensive, i.e. operating the tray dryer.**
- **Cleaning in place (CIP) is impossible.**
- **Problems on validating the equipment.**
- **Crusher gave wide particle range.**
- **Problems with air quality and environment**

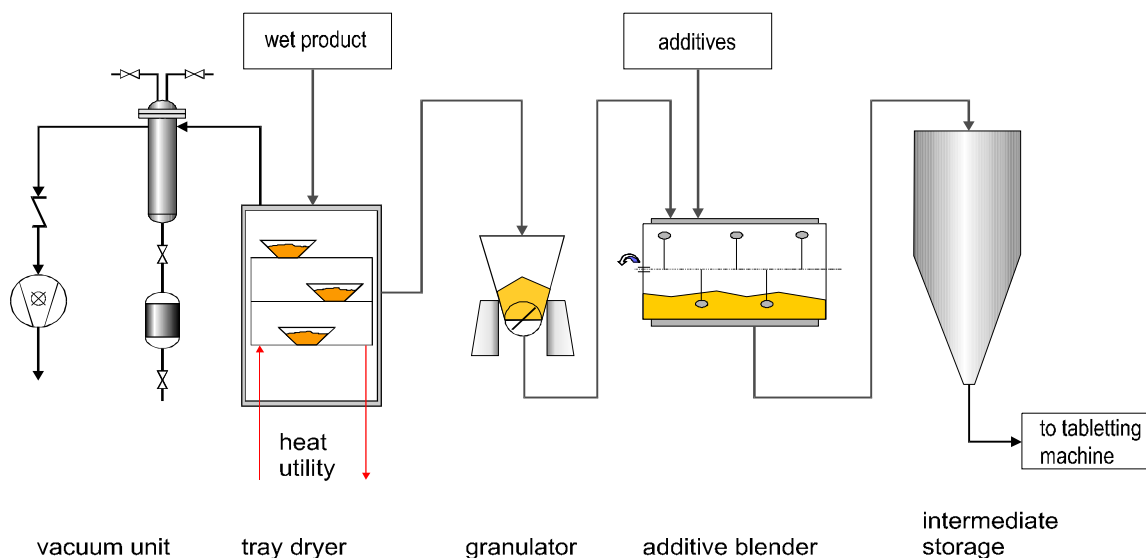


Figure 1, *Simplified flow sheet of drying and homogenization process, showing the basic steps*

To eliminate most of the problems, our customer produced the following specifications for drying and homogenizing a pharmaceutical product, to meet the validation requirements of the pharmaceutical industry.

- **Process has to be a closed system.**
- **Flexibility in product and batch size for multi purpose plant.**
- **Process equipment must comply with FDA requirements.**
- **Process equipment has to be fully CIP cleanable**
- **Reduce the number of pieces of equipment**

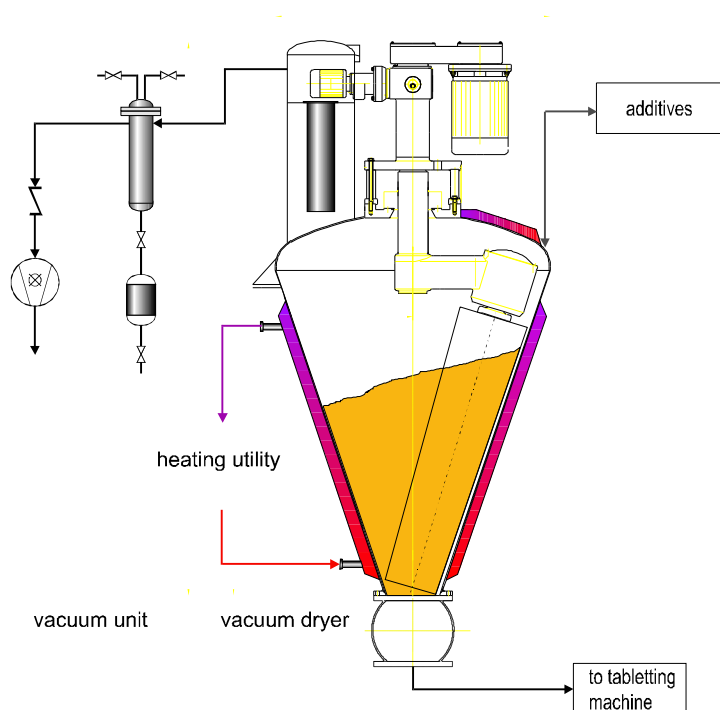


Figure 2, *Simplified flow sheet of drying and homogenization process in one process step*

Our solution was to combine the drying and homogenization steps in one vessel, eliminating the risks of contamination while unloading the tray dryer, and transporting it to intermediate storage. A conical screw mixer adapted for vacuum drying was an ideal answer. In this case it met all the process parameters, providing a closed system, indirect heating at low temperatures under vacuum, suitable for toxic products or solvents.

3. The Bolz-Summix® conical screw mixer and dryer

The conical screw mixer manufactured by Bolz-Summix®, relies on gravity, combined with a mechanical action of the screw. One or more worm screws are suspended from an orbital arm, circumventing the periphery of a cone. The screw rotates within their own axis, and secondly adjacent to the conical vessel wall, by the movement of the arm. The screw conveys the material upwards against the cone wall, and at the same time, moves the product around the vessel. The material outside the influence of the screw flows downwards by gravity and re-circulates. The result is a three dimensional convective material flow.

The Bolz-Summix® conical screw mixer has been adapted for vacuum drying by providing heating jackets or coils to the external cone, cover and filter housing. Dry running mechanical seals, or lip seals, have been developed for both orbit arm and mixing screw to meet the severest process conditions under vacuum, when drying toxic products and solvents. As the drive system is provided with an oil-free arm, there is no possibility of oil contaminating the product.

Pilot scale tests in a 30 liter portable Bolz vacuum dryer, confirmed that the drying process could be carried out to the clients specification. Moreover, because of the gentle homogenizing action of the mixing screw during the drying stage, no product agglomeration occurred. This eliminated the need for a lump breaker in the dryer. After the primary product was dried to their specification of 1 wt% moisture, it was then cooled down; additives were mixed, producing a homogeneous end product, ready for tableting.

4. Start-up of the production unit

After the first test runs, with dummy products, the conical vacuum dryer appeared to function correctly. However, during start-up with the actual product, two problems occurred:

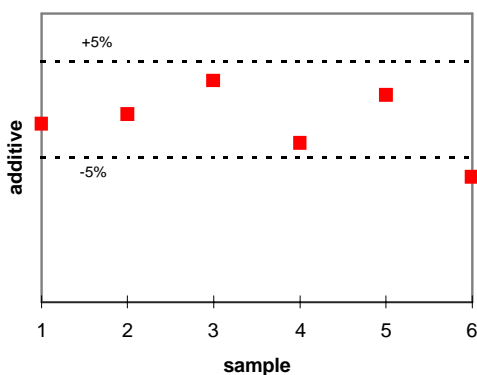
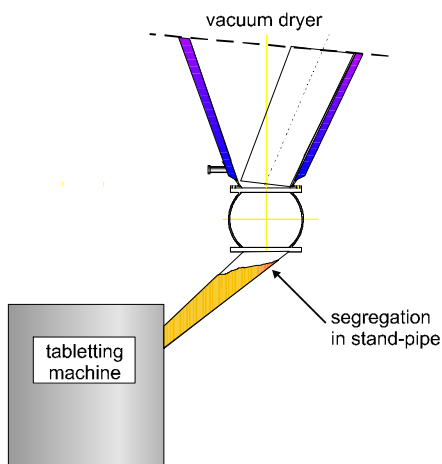


Figure 3, *Samples show segregation in last sample*

1. The concentration of the active additive component was not within the specified range, over the last few kilograms being discharged from the dryer, see Figure 3;
2. During a stage of the drying cycle the product became rather sticky and agglomeration occurred.

The first problem was located in the off loading chute between the dryer and tableting machine, Figure 4. The segregation phenomenon occurred because the particle diameter of the bulk product differed widely from the fine additives. The result of this being, the high concentration fines in the last few kilograms did not meet the specification.

The second problem emanated from the 'sticky drying phase' when coarse bulk particles were produced in the form of small granules. This 'sticky' phase had to be avoided, since the resulting coarse particles increased the drying time, due to lower heat transfer coefficients caused by product sticking to the wall. It also increased power consumption, as the product would not flow within the screw. The question raised as to this did not occur during the trials, because it caused severe problems on the production unit.



In the drying cycle, a sticky phase can occur when the evaporation resistance is too high. These problems generally occur when the filter, condenser or vacuum pump are undersized, overloading the evacuation of the vapors. As this is normally a capacity problem of the vacuum unit, they generally occur at the beginning of the cycle. The evaporation resistance may also be too high, due to internal particle resistance, when the solvent has to be removed from within the pores of the particles. At this point, any undue mechanical forces imparted in a mechanical drying step before the contact drying phase may result in drying problems later in the process to achieve the final moisture content, in a reasonable time.

Figure 4, Segregation in outlet chute

The 'sticky drying phase' is graphically represented in Figure 5. The intersection between drying curve A and stickiness curve C of the product, produces a sticky product. During these process conditions the moisture content was between 4 to 1.5-wt%.

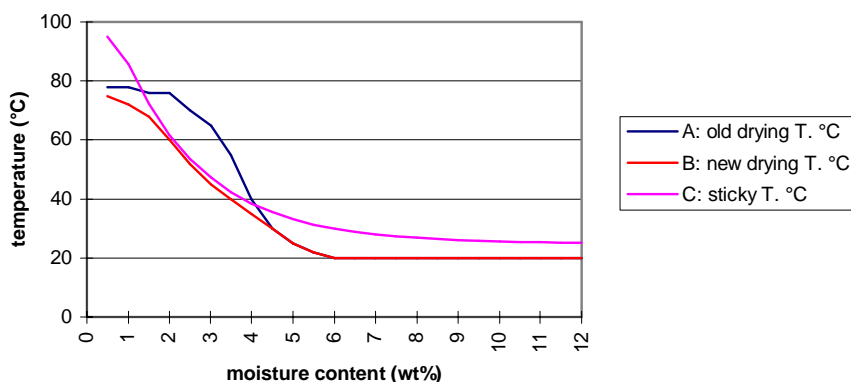


Figure 5, Drying curves and stickiness curve for pharmaceutical product

The stickiness curve was obtained by heating wet product, in our test unit until it became sticky. This was repeated over several times at various moisture contents on material from their new centrifuge. By reducing the jacket temperature profile at the end of the drying cycle based on product temperature, it was possible to avoid the 'sticky drying phase'. From this it was possible to optimize the process as follows:

- **Finer bulk product, without granulates being formed.**
- **Shorter drying time due to higher heat transfer coefficient, all at lower jacket temperatures**
- **Lower power consumption on the drive**

Moreover, the finer particulates cause less segregation in the outlet chute, enabling the process to be fully validated as the final few kilograms of a batch are still within specification.