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Importance of Inlet Air Velocity in Fluid Bed Drying of a Granulation Prepared in a High Shear Granulator

Julia ZH Gao*, David B. Gray, Rajeshwar Motheram, and Munir A. Hussain

Pharmaceutical Research and Development, DuPont Parmaceuticals Company, Experimental Station, P.O. Box 80400, Wilmington, DE, 19880-0400

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INTRODUCTION

Fluidized bed technology has been widely used in the pharmaceutical industry for drying, granulating, and coating. A fluid bed dryer significantly reduces drying time compared with a tray dryer or vacuum dryer. A fluid bed dryer exposes the entire product surface area to the high-volume air stream and heat is transferred to the product surface by convection. However, if the inlet air velocity is not properly selected, consistent and uniform drying will not be obtained. This report describes the importance of inlet air velocity in obtaining fluid bed drying uniformity.

MATERIALS

The granules consisted of 47.5 to 59.4 kg of dry solids, of which 63% (wt/wt) was active bulk drug. Purified water (USP) was used to granulate the dry solids. The aforementioned drug can be characterized as a crystalline, non-hygroscopic, and cohesive powder. It is poorly water soluble and has very low bulk density.

KEYWORDS: Inlet Air Velocity; Fluid Bed Drying; Drying Uniformity; Sample Locations

***)Corresponding Author:** Julia ZH Gao, Pharmaceutical Research and Development DuPont Pharmaceuticals Company, Experimental Station; P.O. Box 80400 Wilmington, DE 19880-0400; Telephone: 302-695-8395; E-mail: zhihui.gao@dupontpharma.com

METHOD

The manufacturing process involved granulating the dry components containing 63% water-insoluble, low-density drug in a high shear granulator (Gral 600L, GEI Processing, Towaco, NJ), wet milling in a Granumill (Model 6-372544-40 BP03, Magnetek Louis Allis, St Louis, MO), and vacuum transfer to a preheated fluid bed dryer (Aeromatic model S6, Niro Inc, Columbia, MD) equipped with a distribution plate of 6% opening. The granules were dried at an inlet temperature of 60^{o}C. Two different inlet air velocities were examined for their effect on drying uniformity in the manufacture of the granule batches (Table 1). For comparison purposes, all batches were manufactured using the identical process parameters in the Gral 600L high shear granulator.

Table 1. Fluid Bed Drying Processing Parameters

Processing Parameters	Process 1	Process 2
Material Conveyance		
Air Velocity	3000 cfm	2800-3000 cfm
Shaker Duration	None	10 seconds
Shaker Frequency	None	1 minute
Drying		
Air Velocity	3000-3300 cfm	0-10 minutes: 2800 cfm 10-20 minutes: 2400 cfm 20-30 minutes: 1800 cfm 30-46 minutes: 1400 cfm
Shaker Duration	30 seconds	30 seconds
Shaker Frequency	3 minutes	3 minutes
Drying Time	19 minutes	46 minutes

Drying of the granules was stopped when the sample taken from the fluid bed sampling port reached a Loss on Drying (LOD) value of 1% to 3% as measured by a moisture balance at 105°C. To confirm that the drying was complete, samples were taken for LOD measurement using a sampling thief from various locations (top, middle, and bottom) in the fluid bed dryer.

RESULTS AND DISCUSSION

LOD values of samples collected from various locations for the 2 batches of granules dried at the high air velocity (process 1) are provided in Table 1.

Table 2. LOD Values of Samples Collected from Different Locations at the End of Drying Using Process 1

	Sampling Location	% LOD, Mean (± SD)
Batch 1	Sample port on the fluid bed dryer[1] Top of the fluid bed dryer[2] Middle of the fluid bed dryer[2] Bottom of the fluid bed dryer[3]	1.2 3.1 (0.2) 2.6 (0.1) 2.2 (0.4)
Batch 2	Sample port on the fluid bed dryer[1] Top of the fluid bed dryer[2] Middle of the fluid bed dryer[2] Bottom of the fluid bed dryer[3]	1.2 3.2 (0.1) 2.7 (0.2) 1.9 (0.3)

[1]Single measurement.
[2]Mean of 4 determinations.
[3]Mean of 3 determinations.

The drying process was stopped based on the LOD value from the sample port, and the granules were discharged to a fiber drum. As seen in Table 2, nonuniform drying in the fluid bed dryer occurred for those 2 batches. The sample collected from the sampling port of the fluid bed dryer did not represent the entire batch. Additional testing of the samples collected from various locations in the fiber drum revealed higher LOD values that were outside the specification (1%-3%).

The general phenomena involved in fluid bed drying are well described in various texts 1-3. Because fluid bed drying is a process in which a drying air is forced through a solids bed at velocity sufficient to partially suspend the granules, it should be conducted at air velocities well below the entrainment (conveyance) velocity but high enough to lift the granules. Examination of the drying process (ie, flow of the granules at the sight glass of the drying bowl and the exhaust air temperature) suggested that the air velocity used for process 1 (3000-3300 cubic foot per minute (cfm)) was excessive for the amount of material in the fluid bed dryer. The rapid rise in the exhaust air temperature (19 minutes, Figure1) is an indication of extremely high air velocity and poor fluidization in the fluid bed. As a result, the material swayed from side to side within the dryer, instead of fluidizing. The excess air was not used for heat transfer.

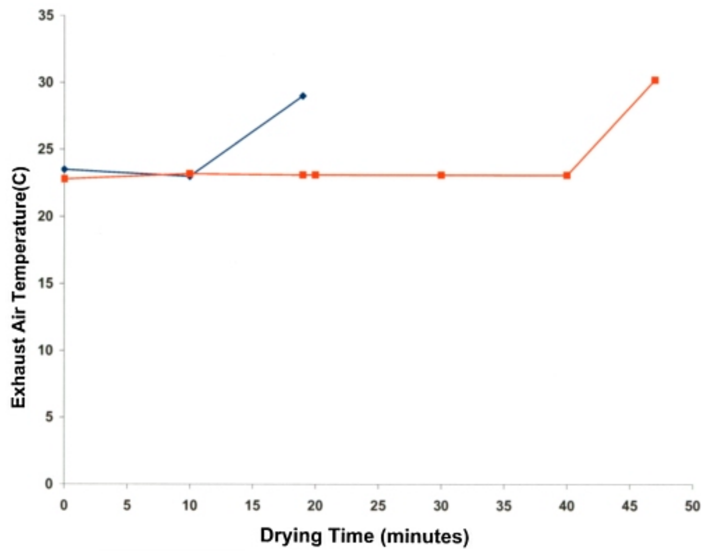

Figure 1. The effect of drying process on the exhaust air temperature vs drying time profile (blue line with diamonds: Process 1; red line with squares: Process 2).

To overcome the undesired bed swing, reduced air velocity was used in process 2. An air velocity of 2800 cfm was used for the first 10 minutes and was gradually lowered to 1400 cfm by the end of the drying (Table 1). In addition, filter shaking during product transfer from the high shear granulator into the fluid bed dryer was included to minimize the formation of crusts in the filter bags, thus improving drying efficiency. LOD values of samples collected from various locations within the fluid bed dryer for granule batches dried using process 2 are given in Table 3. Drying process 2 provided uniform and consistent LOD readings between sampling port and various locations within the dryer. Although at reduced air velocity drying time was increased, as seen in Figure 1, this drying process allowed proper fluidization of granules and provided enough time to allow diffusion of the moisture from the granulation core to the surface. Chemical stability, dissolution, and processing characteristics of the finished product were not affected by changing the drying process (data not shown).

Table 3. LOD Values of Samples Collected from Different Locations at the End of Drying Using Process 2

	Sampling Location	% LOD, Mean (± SD)
Batch 1	Sample port on the fluid bed dryer[1]	1.4
	Top of the fluid bed dryer[2]	1.6 (0.2)
	Middle of the fluid bed dryer[2]	1.5 (0.1)
	Bottom of the fluid bed dryer[3]	1.5 (0.1)
	Sample port on the fluid bed dryer[1]	1.4
	Top of the fluid bed dryer[2]	1.9 (0.3)
	Middle of the fluid bed dryer[2]	1.7 (0.1)
Batch 2	Bottom of the fluid bed dryer[3]	1.7 (0)

[1]Single measurement.
[2]Mean of 4 determinations.
[3]Mean of 3 determinations.

CONCLUSIONS

This report shows that inlet air velocity can play a critical role in maintaining proper fluidization and, ultimately, uniform drying. The mechanism by which air velocity affects fluidization has been discussed by various researchers [4-5]. An indication of good fluidization is a free downward flow of the granules at the sight glass of the drying bowl, but such limited observation could be misleading. In such cases, the exhaust air temperature can be used to detect poor fluidization. If the exhaust air temperature rises more rapidly than anticipated, as seen with process 1 (Figure 1), it is an indication that fluidization is incomplete.

In conclusion, a fundamental understanding of the mechanism of fluidization by inlet air will help in the development of a fluid bed drying process that produces uniformly dried granules and minimizes the number of process problems encountered.

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