MONITORING FLUIDIZED-BED DRYING OF PHARMACEUTICAL GRANULES USING ACOUSTIC SENSORS

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1. INTRODUCTION

In the manufacturing of pharmaceutical tablets, one of the steps is the granulation of the excipient, binder and active drug. Often, a two-step process is required to accomplish this. First, agglomeration is performed in a high-shear mixer. Second, the wet granules are dried. The result is a dry mixture with a larger size distribution and better flowability than the starting materials. Fluidized-bed drying is often the drying method of choice due to its rapid mixing and uniform temperature distribution. The particles are suspended in warm up-flowing air, maximizing the exposed solid surface area. Care must be taken to avoid over-drying, which may cause the granules to become brittle, and cause product loss due to attrition.

Typically, fluidized-bed drying is monitored by removing samples from the bed at certain time intervals and measuring the moisture content of the samples. Sampling is often inaccurate due to the difficulties in collecting representative samples. Also, the moisture analysis is performed off-line, and takes several minutes to complete. Another technique is to monitor the temperature of the bed or of the air at the outlet. While the surfaces of the granules remain moist, the temperature of the granules will not exceed the wet bulb temperature of the drying gas. When the surface of the granule becomes dry, the granule temperature will approach the dry bulb temperature of the gas. This increase in bed temperature is commonly used to detect the drying end-point. Monitoring temperature only provides information about the moisture content of the granules. Often, attrition becomes a problem well before the desired moisture content is reached. This cannot be detected by monitoring temperature alone.

Acoustic monitoring has been shown to be a useful monitoring tool in high-shear wet granulation (Daniher et al, 2005), pneumatic transport (Albion et al., 2005) and rotary drying (Smith, 2004). The application to fluidized-bed drying monitoring is based on the fact that the sound produced by the collisions of dry granules is different from sound produced by the collisions of moist granules. These collisions are dependant on the quality of the fluidization hydrodynamics. The sounds from a well fluidized bed will differ from that of a non-fluidized bed. If these sounds can be recorded and transformed into a useful voltage signal, it may provide a non-intrusive, passive method of monitoring the drying process. This objective of this research is to show the potential of acoustics for monitoring the drying of pharmaceutical granules.

2. METHOD

The fluidized-bed drying apparatus was a conical column with the dimensions given in Fig. 1. The distributor was stainless steel 100 μm mesh. Four air outlets were located on the top of the column. These outlets were fitted with filter cloth to prevent dust from escaping. A port fitted with a sampling thief was located at the base of the stainless steel column. Sound data was obtained using two PCB Piezotronics model 130D10 electret microphones and 130P10 preamplifiers. The positions of the sensors on the granulator equipment are indicated in Fig. 1. Microphone 1 was attached flush to the exterior of column. Microphone 2 was centered in one of the air outlets, on the exterior of the filter cloth. The data from both sensors was acquired using a 16-bit National Instruments DAQCard-6036E. The samples were recorded at a sampling rate of 40,000 Hz.

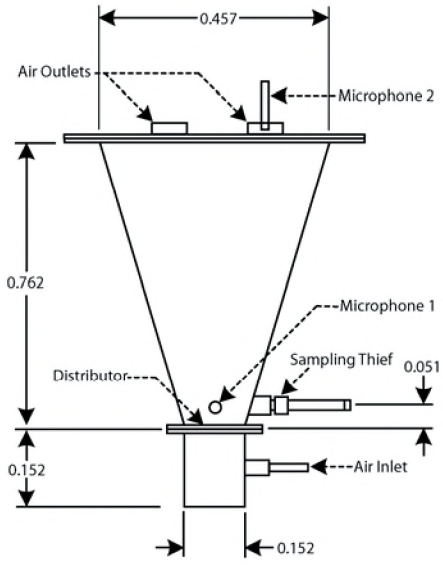

Fig. 1. The fluidized-bed dryer dimensions in meters.

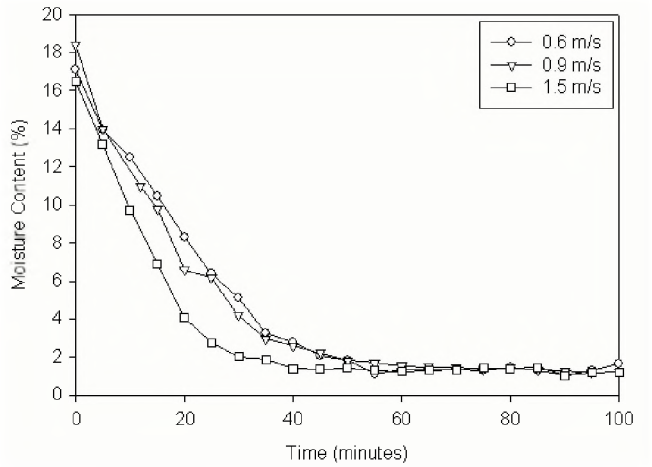

Fig. 2. Moisture content of granule samples taken during the drying process.

Placebo granules consisting of lactose monohydrate (87wt% dry basis), corn starch (10wt%) and polyvinylpyrrolidone (3wt%) were granulated with 18wt% de-ionized water. 2.1 kg of wet granules were dried in the fluidized bed dryer over 100 minutes. The inlet air temperature was 21 °C and the superficial air velocities at the distributor were 0.6, 0.9 and 1.5 m/s. Samples were taken every 5 minutes and analyzed for moisture content using a Mettler Toledo HG63 halogen moisture analyzer. The microphone signals were recorded for the entire drying process and analyzed offline in 10 second segments.

3. RESULTS

Fig. 2 is a plot of granule moisture content as a function of time during the drying process. The change in superficial air velocity between 0.6 and 0.9 m/s did not affect the drying profile. There was an increase in the drying rate at 1.5 m/s. The profile of the mean frequency of the microphone 1 signal (Fig. 3) showed a peak occuring at about 40 minutes for air velocities from 0.6 to 0.9 m/s and 20 minutes for 1.5 m/s. These times approximately corresponded to a bed moisture content of 3 to 4% . The mean frequency of the microphone 2 signal (Fig. 4) showed a sharp decrease occuring at approximately the same times.

4. CONCLUSIONS

The mean frequency profiles detect the 3 to 4% moisture range rather than the equilibrium moisture content of 1.5%. This indicates that rather than moisture content, the signal may be monitoring a range of other factors such as granule hardness or size distribution. As the granules approach 3 to 4% moisture, attrition may become significant. The resulting increase in fines would build up on the surface of the filter cloth and could cause the sudden drop in mean frequency. Since the detection of the onset of attrition cannot be detected by monitoring temperature, having a method to do this is advantageous. Acoustic monitoring is non-intrusive, in-expensive, and requires no modification to existing fluidized-bed drying equipment if a microphone is located externally.

REFERENCES

Albion, K., Briens, L., Briens, C. & Berruti, F. (2005). Flow regime determination in horizontal pneumatic transport of fine powders using non-intrusive acoustic probes. Powder Technology, (submitted).

Daniher, D., Briens, L. & Tallevi, A. (2005). End-point detection in high-shear granulation using sound and vibration signal analysis. Powder Technology, (submitted).

Smith, R.J. (2004). Monitoring of a rotary dryer using acoustic emissions, Master's Thesis. The University of Western Ontario.

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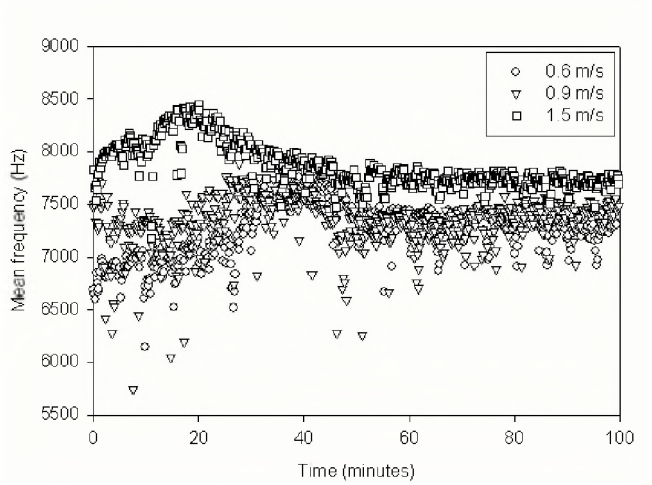

Fig. 3. Mean frequency of the microphone 1 signal (base of cone).

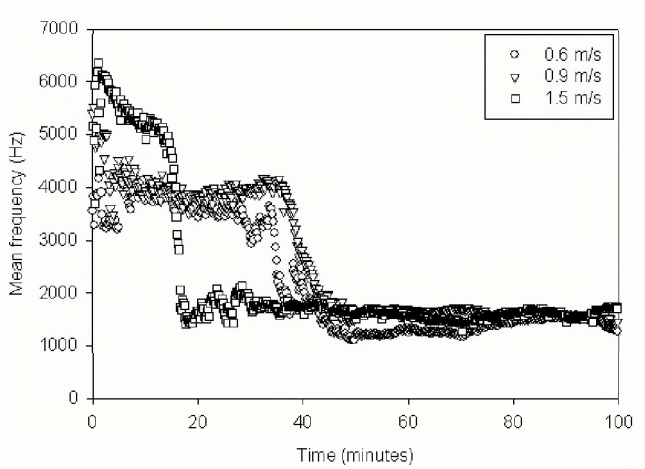

Fig. 4. Mean frequency of the microphone 2 signal (air outlet).