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Monitoring high-shear granulation using sound and vibration measurements

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Abstract

Sound and vibration measurements were investigated as monitoring methods for high-shear granulation. Five microphones and one accelerometer were placed at different locations on a 10 and a 25 l granulator and compared to find the optimum location and the effect of scale. The granulation process could be monitored using the mean frequency and root mean square sound pressure levels from acoustic emissions measured using a microphone in the filtered air exhaust of the granulators. These acoustic monitoring methods were successful for both the 10 and the 25 l granulation scales. The granulation phases, however, were more clearly defined for the larger scale granulation. The root mean square acceleration level from vibration measurements was also able to monitor the granulation, but only for the larger 25 l granulator.

Keywords: Granulation monitoring; Sound and vibration measurements; Signal analysis; Acoustic emissions; Granulator scale-up

1. Introduction

In granulation, particles are adhered together to form larger multi-particle units called granules. In the pharmaceutical industry, granulation is used to increase the drug uniformity in the product and to improve the flow rate and flow uniformity of a mixture before tabletting. It also prevents segregation, improves compaction characteristics and reduces dust.

The high-shear mixer is commonly used for producing wet granules. This machine exerts shearing and compaction forces on the particles with a large rotating impeller blade. A small side-mounted chopper blade breaks large pieces into smaller granules. Once powder components of the formulation are thoroughly mixed, a liquid solution of a binder is sprayed into the mixture. Liquid bridges are created between particles that, in combination with the shearing forces, result in agglomerate growth (Augsburger and Vuppala, 1997). Also, after liquid addition, further shearing will continue to change the granulation properties.

The high-shear granulation process must be stopped at the proper point to obtain the required granule characteristics. To determine this end-point, the granulation process must be monitored, and the measurements must be correlated to the granule properties. Improvements in this field have the potential to reduce the time required for scale-up of manufacturing new pharmaceutical products. Also, it will help to improve batch consistency to better meet product quality requirements.

Several granulation monitoring techniques for use in a process control scheme have been investigated, such as near-infrared reflectance spectroscopy (Frake et al., 1977; Han, 1998; Rantanen et al., 1998) and image analysis (Watano, 2001). These optical probe techniques require a clear line of sight into the granulator bowl; a hole must be drilled into the granulator bowl wall with a complex system to ensure the probe window is not obstructed by wet material sticking to it. Monitoring using a capacitance sensor has been able to detect increasing binder level during granulation (Corvari et al., 1992). Unfortunately, however, this technique also required a hole be drilled into the granulator lid.

During granulation, sound is produced as the particles and granules collide and impact upon the equipment and sound also comes from the working motor of the impeller and chopper. The sound can be expected to change as the particles become

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incorporated into granules and the size and number of granules change. The acoustics and the vibration of the motor will also change as the resistance of the wet-mass against the impeller increases as stronger bonds are formed and the cohesiveness of the mixture increases.

Sound monitoring during high-shear granulation has been investigated by Whitaker et al. (2000). Piezoelectric microphones were attached to the bottom of the granulator bowl of a Niro-Fielder PMA-10 high shear granulator and sound measurements recorded throughout the granulation of a 3 kg placebo formulation. The average signal level of the emissions corresponded to some changes in the granulation process, but an end-point could not be clearly determined.

Ohike et al. (1999) used a vibration probe to directly monitor the granulation of a 5 kg placebo formulation in a Niro-Fielder PMA-25 high shear granulator. A spherical probe was positioned inside the granulator bowl and attached to a strain gauge to measure particle impact on the probe. The magnitude of the peak at the impeller blade frequency obtained by fast Fourier transform (FFT) was found to increase as the median granule diameter increased. The probe was displaced more by the larger size particles than smaller ones and thus created larger vibration signal amplitudes. Also, motors powering the impeller and the chopper produced changing vibrations in the granulator. Previous work (Terashita et al., 1990a,b; Watano et al., 1992; Laicher et al., 1997; Betz et al., 2003) has also shown that the power consumption of the main impeller motor shows a characteristic profile during the granulation process. This is due to the change in resistance of the wet-mass as stronger bonds are formed and the cohesiveness of the mixture increases.

The general objective of the research presented in this article was to investigate sound and vibration monitoring to determine the end-point of granulation in a 10 l (PMA-10) and a 25 l (PMA-25) high-shear granulator. Results from the two granulators were compared to investigate scale effects. For each scale, the granulator was operated under typical processing conditions (impeller speed, water addition rates, and final moisture content); these conditions are usually not held constant during scale-up.

2. Materials and methods

2.1. Product formulation

A placebo formulation consisting of 87 wt.% (dry basis) of lactose monohydrate NF (Foremost Farms, grade 312), 10 wt.% corn starch NF (Roquette) and 3 wt.% polyvinylpyrrolidone USP (BASF) was used in the experiments. A dry mass of 2 kg was used for each batch experiment with the Niro-Fielder PMA-10 while a dry mass of 8 kg was used with the Niro-Fielder PMA-25 batches. For both scales, the main impeller was operated at 250 rpm and the chopper at 1500 rpm. USP water was injected through a nozzle into the granulator bowl using a pressure vessel and compressed dry air. A regulator was used to adjust the injection rate while an electronic balance placed beneath the pressure vessel was used to measure the amount of water added.

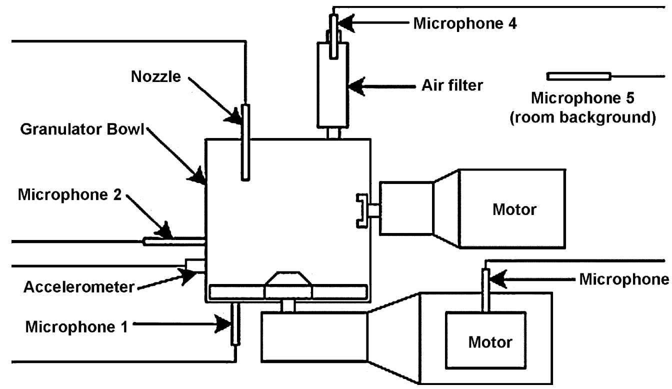

Fig. 1. The location of the microphones and the accelerometer.

2.2. Sensor measurements

Sound data was obtained using five PCB Piezotronics model 130D10 electret microphones and 130P10 preamplifiers. Vibration data was obtained using one PCB Piezotronics model 353B34 accelerometer. The sensors were temporarily but securely attached to the granulator at the locations indicated in Fig. 1. The accelerometer and microphones 1 and 2 were mounted on the granulator bowl with the microphone openings flush to the equipment surface. Microphone 3 was placed on the exterior of the motor casing and microphone 4 was centered in the air filter opening. Finally, microphone 5 was attached to the wall behind the granulator to record any significant background noise.

The data from all the sensors was acquired using a 16-bit National Instruments DAQCard-6036E. Since the granulation equipment produced sound changes detectable by human operators, the samples were recorded at a sampling rate to ensure no information is lost in the 0–20,000 Hz range. Therefore the signals were sampled at 40,000 Hz.

2.3. PMA-10 operation

The impeller and chopper were operated without water addition for the first 3 min to mix the dry powder. At 3 min, water addition was started and continued at a rate of approximately 42 g/min until 400 g of water was added. Mixing of the wet mass was continued for 2 min beyond water addition.

2.4. PMA-25 operation

The impeller and chopper were operated without water addition for the first 5 min to mix the dry powder. At 5 min, water addition was started and continued at a rate of either 180 or 140 g/min until 1480 g of water was added. Mixing of the wet mass was continued for 2 min beyond water addition.

2.5. Experimental procedure

For both granulators, the impeller and chopper were operated for the entire duration of the granulation. The amount of