High Shear Wet Granulation: DFF Sensor vs. Granulator Shaft Amperage

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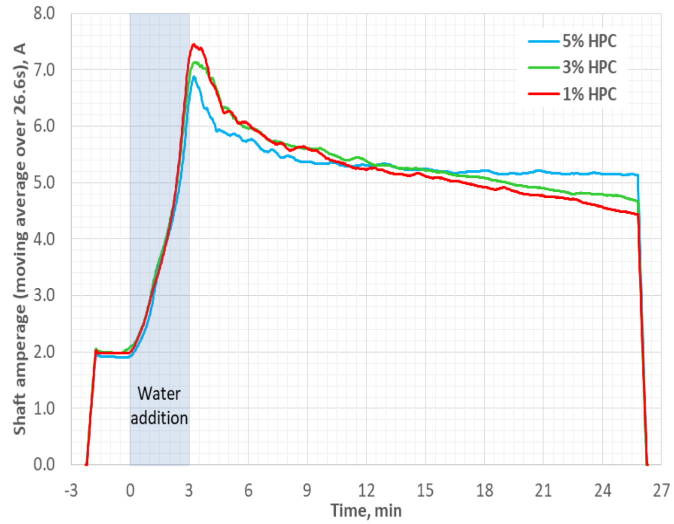
In-line characterization of wet mass during high shear wet granulation (HSWG) forms the basis of process analytical technology (PAT) tools that assist robust and reproducible manufacture by enabling process monitoring, trending, and control. In addition, PATs can be used to guide development, scale-up, and equipment interchangeability. We have recently shown the application of drag force flow (DFF) sensor for monitoring wet mass consistency, which correlates with granule density during HSWG and its application to process scale-up (Narang et.al., 2015, 2016, see also White Papers 8 and 9). In the present study, we compared the sensitivity of the DFF force pulse magnitude (FPM) signal to the simultaneous measurement of the motor current (amperage) during processing of a placebo formulations in a Bohle 4L

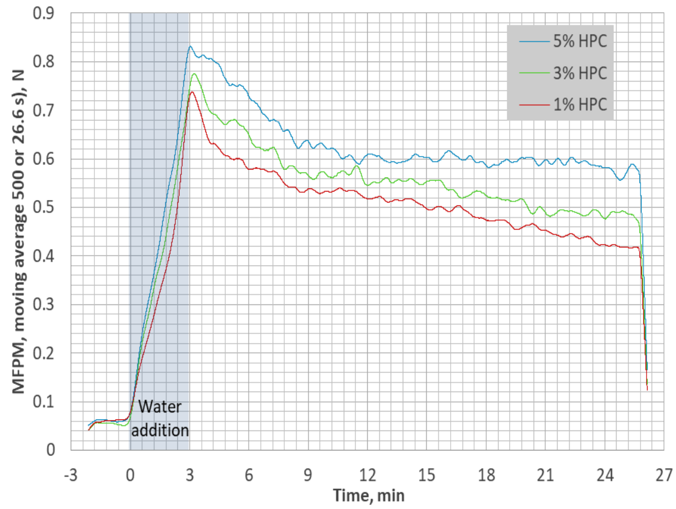
granulator at 375 RPM (18.8 blades/s, tip speed 3.5 m/s).

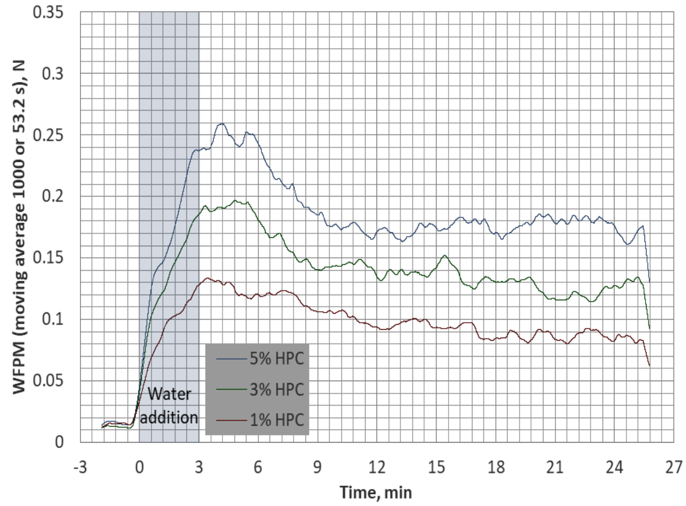
Experiment

The DFF probe was installed vertically inside the granulator bowl with the probe tip positioned at 0.7 cm above the blade as shown on the photograph.

The three formulations consisted of 37% anhydrous lactose, 1% croscarmellose sodium, and 1%, 3%, or 5% HPC with 61%, 59%, or 57% microcrystalline cellulose in







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respective batches. Granulation was carried out with 40% water (320 g for batch size of 800 g) added over 3 minutes. Force was measured every 0.002 s (500 Hz). Granulator current was recorded once every 1.4 s.

Results and Discussion

The time course of mean FPM (MFPM) and the width of "instantaneous" FPM distribution (WFPM) are compared in the above plots with time evolution of the amperage. See details on MFPM and WFPM calculations in White Paper 3.

Both FPM and current measurements feature steep rise of the signal following water addition and consistent decline afterwards. The maxima of both amperage and MFPM coincide with the end of water addition while WFPMs reach maxima 30-60 seconds after the water addition stops.

For amperage measurements, the largest magnitude of response at the end of water addition was observed for a smallest concentration of the binder in the formulation (1% HPC). In contrast, the MFPM and WFPM peak values are consistently proportional to the binder concentration, with 5% HPC having highest values throughout the granulation cycle, following the formulation with 3% HPC and then with 1% HPC. In addition, the FPM distributions are consistently broader (well separated out) for higher HPC content, as demonstrated by comparing WFPM signals.

The evolution of the granulation process is expected to be more rapid with increasing amount of binder. Granulation starts as soon as water adds to the powder. The number, size, and density of granules increases with added amount of water. When granulation is efficient, rapid formation of granules of various sizes is followed by granule destruction processes (Iveson et.al., 2001). Higher binder content leads to greater granule sizes and densities, which is reflected in the consistently wider distribution widths and higher mean FPM for higher HPC concentration formulations.

These data show that impeller current measured in a 4L Bohle granulator is unable to differentiate between formulations with different binder concentration, while FPM offers distinction that is expected between these formulations. In addition, the widths of FPM distributions reach a peak some time after the water addition process ends, which may be indicative of granulation end point.

Bibliography

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