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Comparing the Performance of Wet and Dry Polymer Binders in High Shear Wet Granulation and Twin-Screw Granulation Processes

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PURPOSE

The purpose of this study was to identify the critical process attributes needed to switch from a high shear wet granulation batch process to a twin-screw wet granulation continuous process.

METHODS

A full factorial design of experiments (DoE) was constructed to study the effect of binder choice, liquid to solid (L/S) ratio, binder addition method, and granulator type. The formulations used for all trials on the high shear wet granulator (HSWG) and twin screw (TS) granulator are listed in table 1. For the HSWG the L/S ratio ranged from 0.3 to 0.5 g/g. For the TS granulation the L/S ratio ranged from 0.4 to 0.6 g/g. For both granulators, some of the trials used dry binder addition and some used pre-dissolved binder addition. The HSWG trials were conducted in a GMXB-Pilot with the 10 L bowl attachment. The granulated material was wet milled using a Quadro® Comil® U10 and then dried using a VFC-LAB 3 FLO-COATER® fluid bed dryer. The dried material was then milled to final particle size using a Quadro® Comil® 194S. The TS granulation trials were conducted in a GF-215 twin screw continuous wet granulation unit. The dry material blend was fed into the twin screw barrel using a Coperion K-Tron powder feeder. The granulated material was discharged into a conical mill before entering the spiral dryer. The material collected from the dryer did not require any further milling. A Sartorius Mark 3 Moisture Analyzer was used to measure sample %LOD and particle size distribution was determined by laser diffraction particle size (Mastersizer 3000, Malvern Panalytical, Worcestershire, United Kingdom). For all granulation samples, flat-faced tablets of approximately 100 mg and a diameter of 6 mm were prepared using a single-punch tablet press (FlexiTab, Syntegon Technology GmbH, Hüttlin, Germany). Tablets were produced using compression forces across the range 2–12 kN (n=10 tablets per force). Individual tablet weight, thickness and breaking strength were determined at each compression force using a Sotax ST50 semi-automated tablet hardness tester (SOTAX AG, Aesch, Switzerland).

Table 1. Formulation for HSW and TS granulations

Formulation Component	Quantity (% w/w)
Micronized Acetaminophen	52.1 %
Microcrystalline Cellulose	39.6 %
Croscarmellose Sodium	2.6 %
Silicon Dioxide	0.5 %
Binder (HPMC / HPC / PVP)	5.2 %
Total	100.0 %

RESULTS

The first quality attribute investigated was granulation particle size distribution (PSD). This attribute is only important until the granules reach the required flowability to produce acceptable tablets. All granulation samples produced flowable granules.

Tablet hardness is the next important quality attribute. Tablet hardness depends on the compression force applied to the tablet. Tablet tensile strength was measured over a range of compression forces to determine the slope of the compression profile, k. The higher the k value, the greater the increase in tensile strength when compression force increases.

Figure 2 below was used to determine which formulation choices generated granules that produced tablets with the highest k value. Binder type, binder addition method, and L/S ratio were evaluated to determine optimization for HSWG and TS granulation.

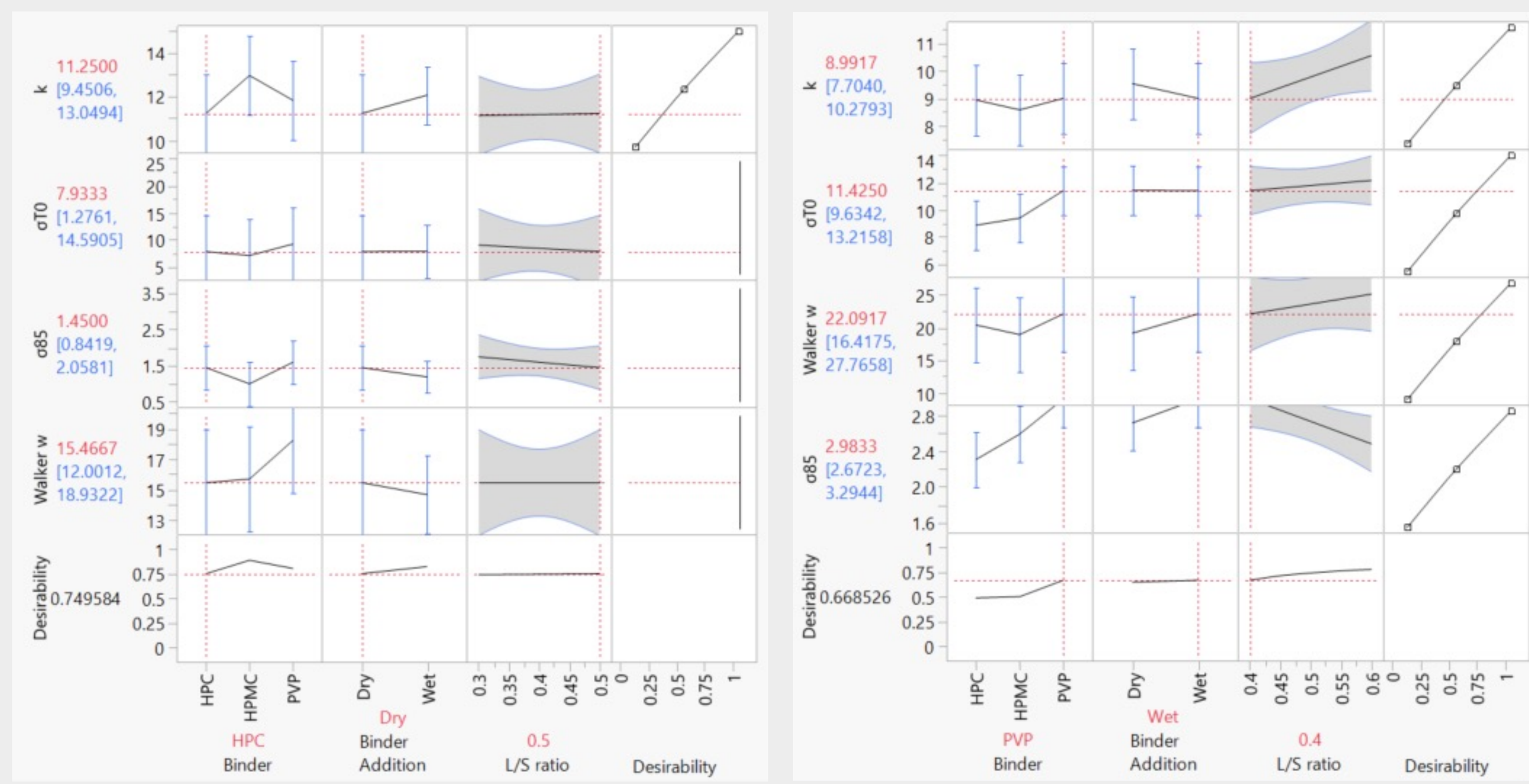

Figure 2. Profiler optimization for HSW granulation (left) and TS granulation (right).

Figure 1. F-V GMXB-Pilot HSWG (10L)

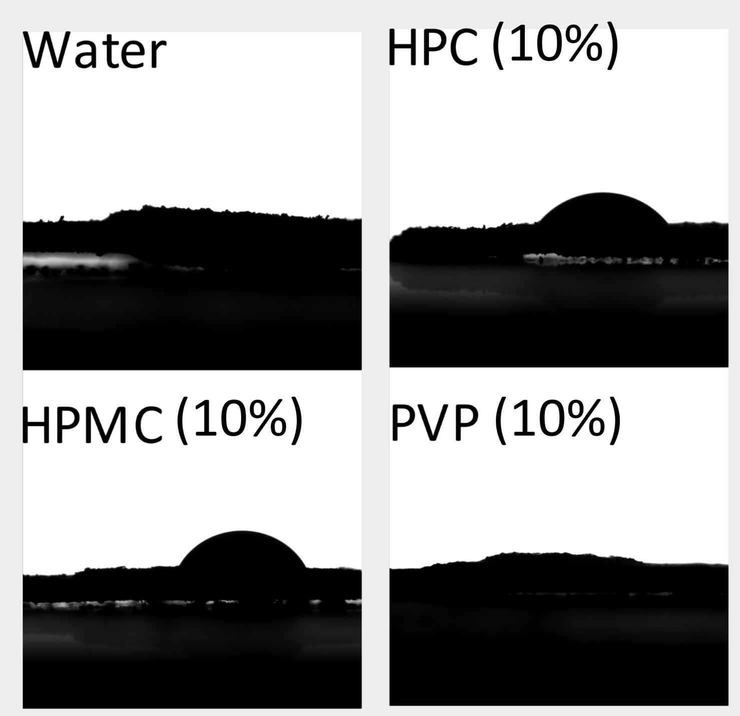

Figure 4. Binder droplet photos 3 seconds after initial contact

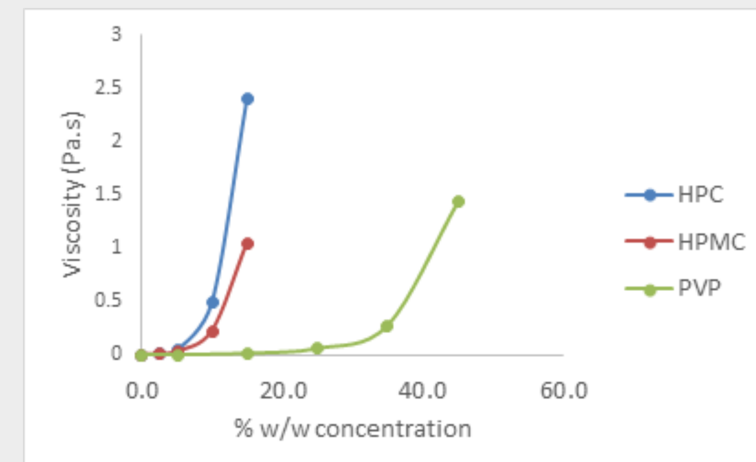

Figure 3. Viscosity of PVP, HPMC, HPC at 20 °C

A series of rheological analysis of the binders was conducted to understand the behaviour of the binders in each granulator system. For some of the experiments involving higher concentrations of dissolved HPC and HPMC in solution, some of the binder had to go in the dry blend because of the increase in viscosity. Figure 3 above explains this. PVP has a low viscosity throughout the entire range of solution concentrations used (5-20%).

A drop penetration experiment was also performed to compare the different binders. Four solutions (water, HPC, HPMC, and PVP) were dropped onto a powder bed and monitored to determine penetration time. Figure 4 shows these results, which could explain why PVP works better for TS granulation, where the entire granulation process is completed within seconds and HPMC works better in HSWG, where the granulation process is completed in approximately 5 minutes.

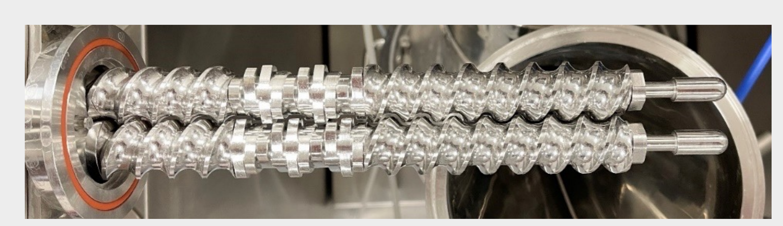

Figure 5. Photo of TS extruder

CONCLUSIONS

Although both granulators can produce granulations suitable for tableting, they require different process parameters and formulations for optimization. The high shear wet granulation process is optimized with HPC as the binder and dry binder addition. When transferring an established HSWG process to a TS granulator, reduce the L/S ratio, and dissolve a low viscosity binder into the spray solution.

Figure 6. F-V GF-215 TS Granulator

ACKNOWLEDGEMENT

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