TOP-DRIVE VS. BOTTOM-DRIVE HIGH-SHEAR GRANULATION: EFFECT ON GRANULE PROPERTIES OF AN IMMEDIATE RELEASE FORMULATION

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PURPOSE

To compare top-drive (TD) high shear granulation versus bottom-drive (BD) high-shear granulation.

METHODS

Blends of pre-gelatinized starch, microcrystalline cellulose, and impalpable lactose were granulated with increasing amount of water using a 25-liter top-drive (TD) high-shear granulator (Vector GMX-25) and a same sized bottom-drive (BD) high-shear granulator (Powrex FM-VG-25). Mixer blade speeds used were standard manufacturer settings.

Granulates were fluid-bed dried and milled with a FitzMill Comminutor. The particle size profile, bulk and tap density, flow index, and Carr index of milled granules were measured.

A quantity of 591g of milled granules from each batch were blended with 6g of dye and 3g (0.5%) of magnesium stearate (MgSt) in a PK Blend Master V-blender (0.946 liter; 1 quart).

Blended granules were pressed into tablets on a four station instrumented Stokes model 512 press operating at 40 rpm. Compaction profiles were determined at 5, 10, 15, 20, and 23 kN.

Note: Formulation and process parameters are listed in Tables 1 and 2.

Table 1 – Immediate Release Formulation

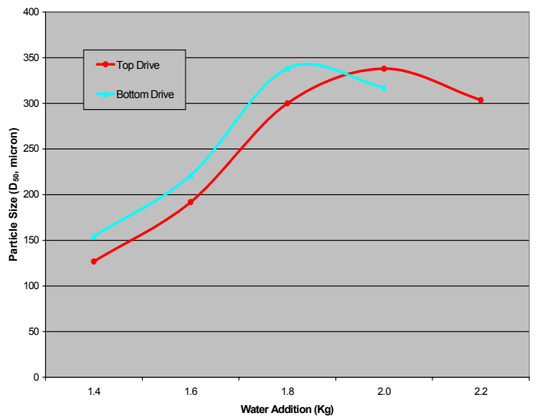
Ingredients	TD Granulations	BD Granulations
Starch 1500	15%	15%
MCC, Avicel PH-101	30%	30%
Lactose	55%	55%
Dry Weight (Kg)	6.1	6.1
Water Added (Kg)	1.4 / 1.6 / 1.8 / 2.0 / 2.2	1.4 / 1.6 / 1.8 / 2.0

Table 2 – Processing Parameters

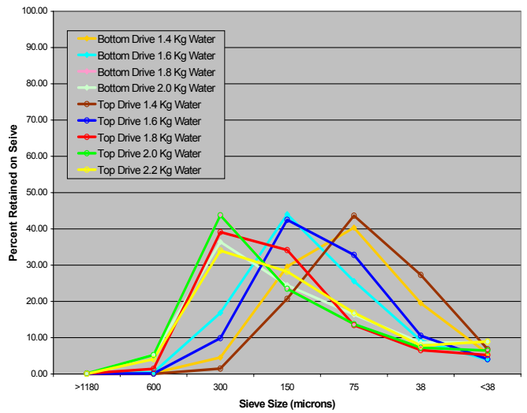
Wet Granulation	
Pre-Mix (Time/Tip Speed)	3 minutes / 5.4 mps for TD; 4.2 mps for BD
Infusion (Rate/Tip Speed)	266 g/min / 5.4 mps for TD; 4.2 mps for BD
Wet Mass (Time/Tip Speed)	3 minutes / 8.4 mps for TD; 8.1 mps for BD
Drying	65-70°C
Milling	6 Blades; Knives forward; Fast speed; 0.050 inch (1.3 mm) hole screen
Blending	10 min for dye; 5 min for MgSt; @ 24 rpm
Compaction	300 mg; 3/8 inch (9.5 mm) std. cup tablets @ 5, 10, 15, 20, and 23 kN

RESULTS

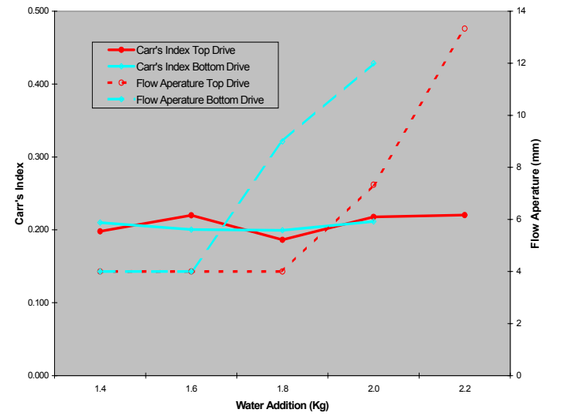
Particle Size (D_{50}) Comparison



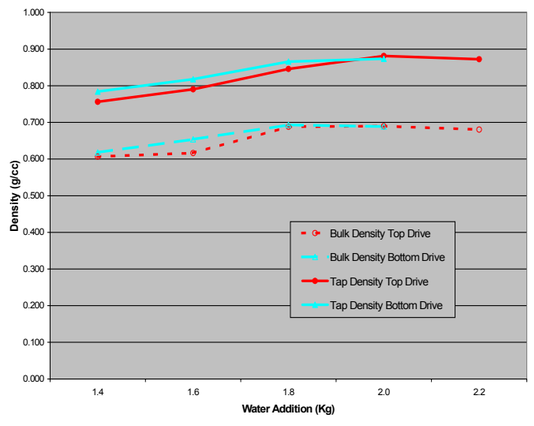
Particle Size Distribution



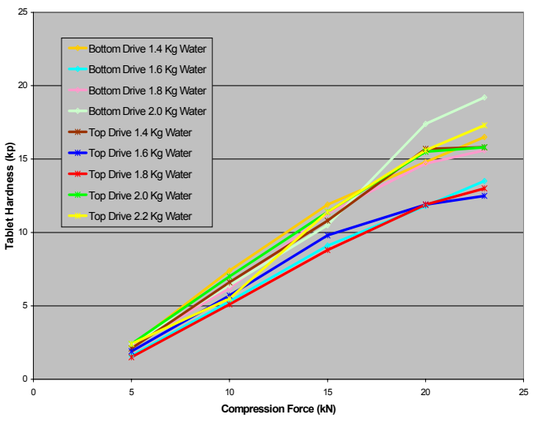
Flow Indices



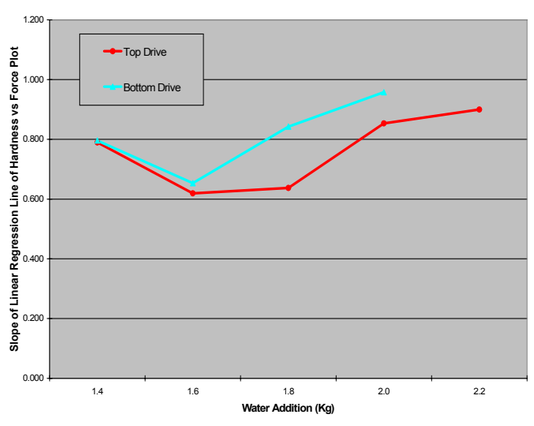
Density Comparisons



Compaction Comparison



Hardness vs Compaction Force Slope



CONCLUSIONS

Top-drive and bottom-drive granulators produced granulations with no significant differences except that flow of dried granulate through a narrow aperture became more difficult at higher water levels. Granulation coarseness and tap density increased with increasing water addition to a point and then began to level off. Compaction profiles were not dependent on equipment design for the same level of water addition.

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