

# TOP-DRIVE VS. BOTTOM-DRIVE HIGH-SHEAR GRANULATION: DISSOLUTION PROFILES OF IMMEDIATE RELEASE TABLETS

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## PURPOSE

To compare tablet dissolution profiles from granulations made with both top-drive (TD) and bottom-drive (BD) high shear granulators.

## METHODS

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

Granulates were fluid-bed dried and milled with a FitzMill Comminutor. Particle size (D<sub>50</sub>) was determined via sieve analysis.

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 tableted on a Stokes model 512 press using compaction pressures of 5, 10, 15, 20, and 23 kN.

Tablets were then subjected to dissolution testing using an USP apparatus type 2 equipped with in-situ fiber optic based UV.

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

Table 1 – Immediate Release Granule Formulation

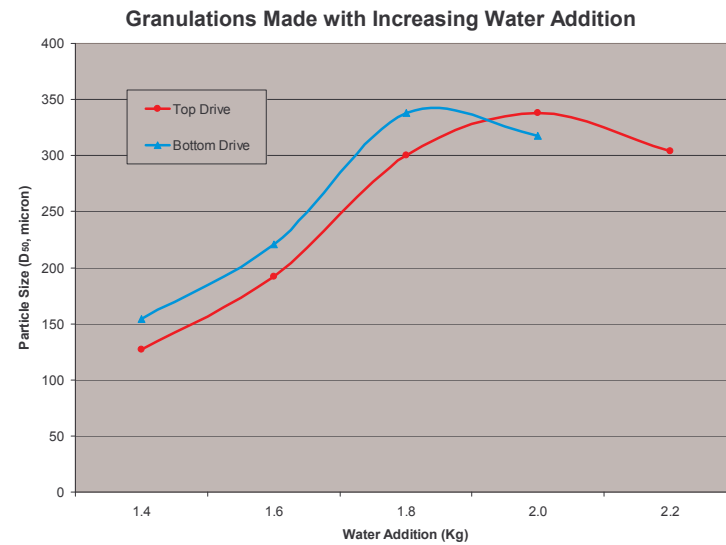
Ingredients	TD Granulations	BD Granulations
Starch 1500	15%	15%
MCC, Avicel PH-101	30%	30%
Lactose	55%	55%
Dry Weight (Kg)	6.1	6.1
Water Added (Kg)	1.4 / 1.6 / 1.8 / 2.0 / 2.2	1.4 / 1.6 / 1.8 / 2.0

Table 2 – Processing Parameters

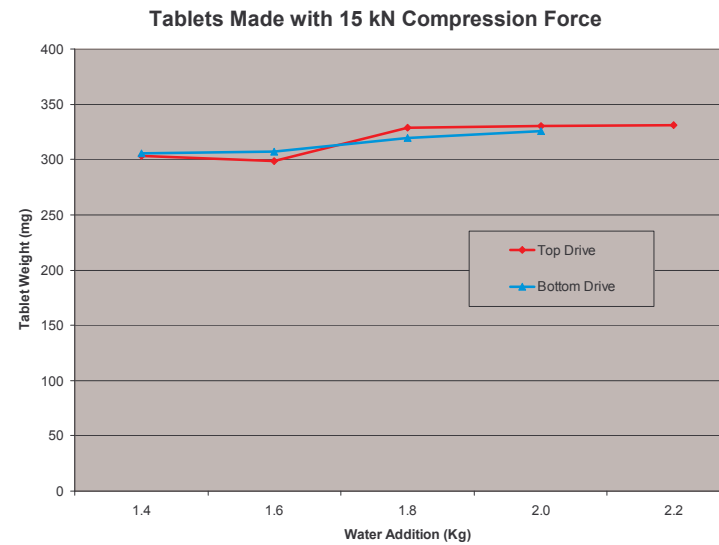
Wet Granulation	
Pre-Mix (Time/Tip Speed)	3 minutes / 5.4 mps for TD; 4.2 mps for BD
Infusion (Rate/Tip Speed)	266 g/min / 5.4 mps for TD; 4.2 mps for BD
Wet Mass (Time/Tip Speed)	3 minutes / 8.4 mps for TD; 8.1 mps for BD
Drying	65-70°C
Milling	6 Blades; Knives forward; Fast speed; 0.050 inch (1.3 mm) 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

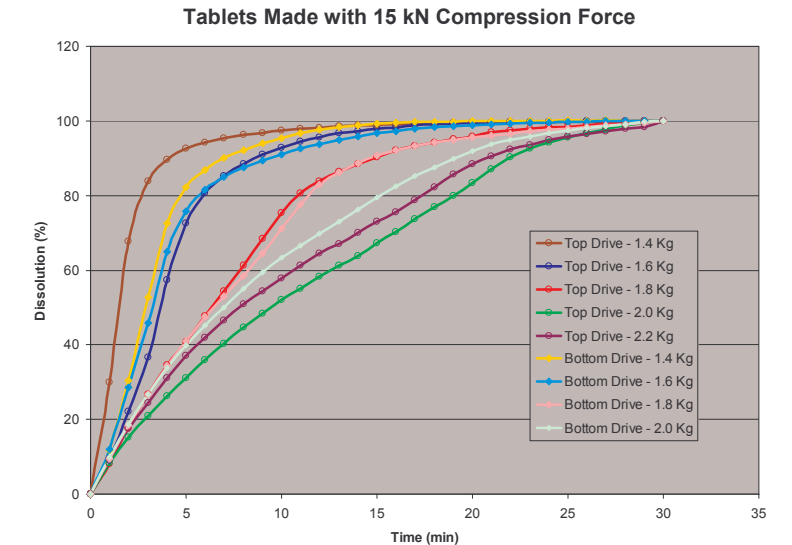
### Particle Size (D<sub>50</sub>) Comparison



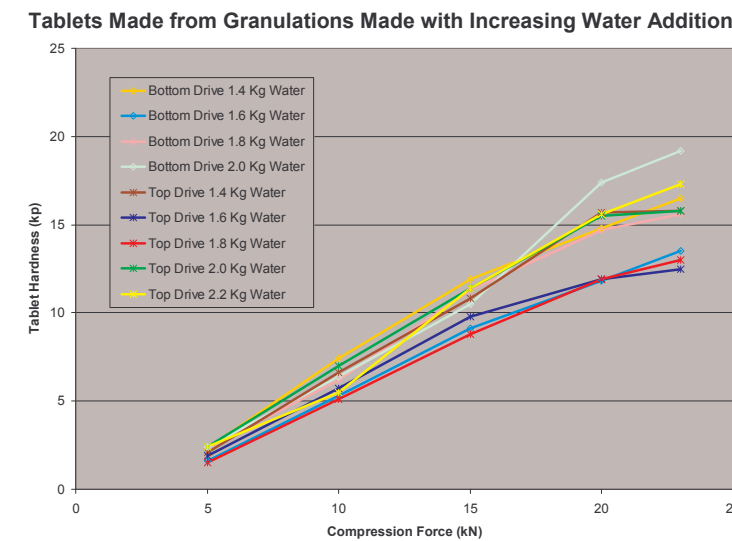
### Tablet Weight Comparison — Water Amount



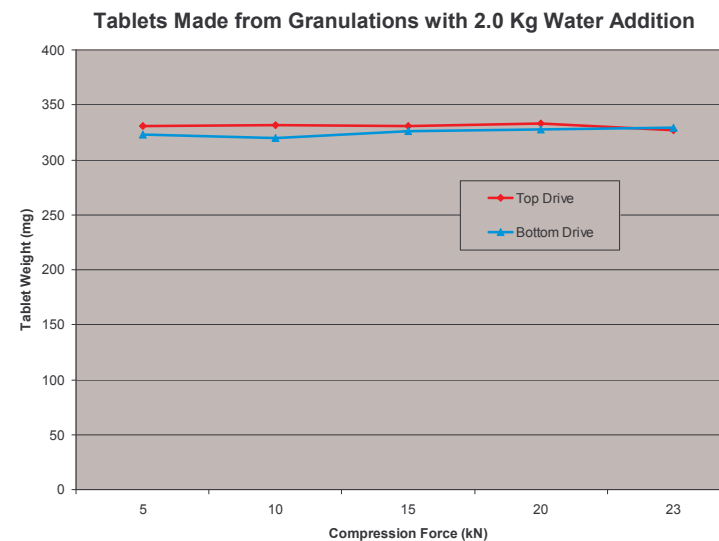
### Dissolution Comparison— Water Amount



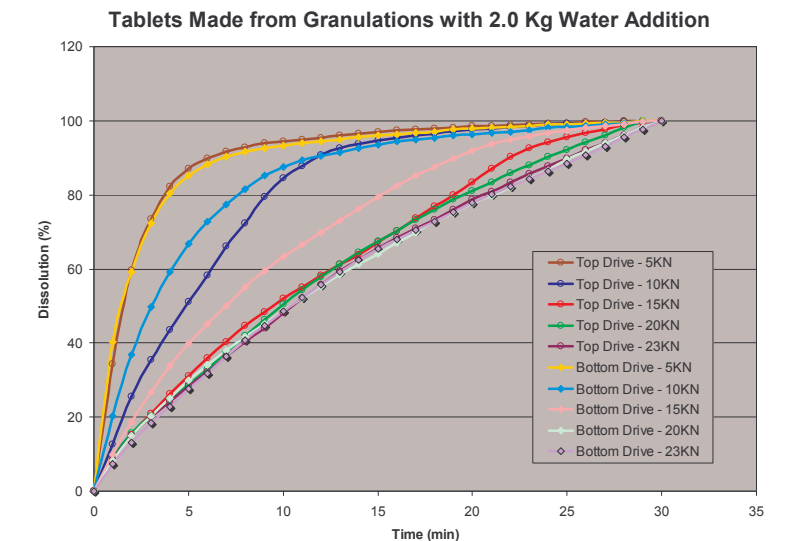
### Compaction Comparison



### Tablet Weight Comparison — Compression



### Dissolution Comparison— Compression



## CONCLUSIONS

Dissolution profiles were similar (f2 values ranged from 50-96) after the first five minutes for a given water addition and compression force; and were not dependent on equipment design for all tablets studied. For a given level of water addition, increasing compression force resulted in decreased tablet dissolution rates for both top drive and bottom drive granulators. Generally, increasing the amount of water used to make the granulations caused a slower dissolution rate.

## ACKNOWLEDGEMENTS

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