

THE CHANGE IN PARTICLE SIZE OF IMMEDIATE RELEASE AND CONTROLLED RELEASE FORMULATIONS DURING HIGH-SHEAR WET-GRANULATION PROCESSES

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PURPOSE

To study the particle size changes that occur during the water infusion and high shear (or wet-mass) phases of a wet-granulation process.

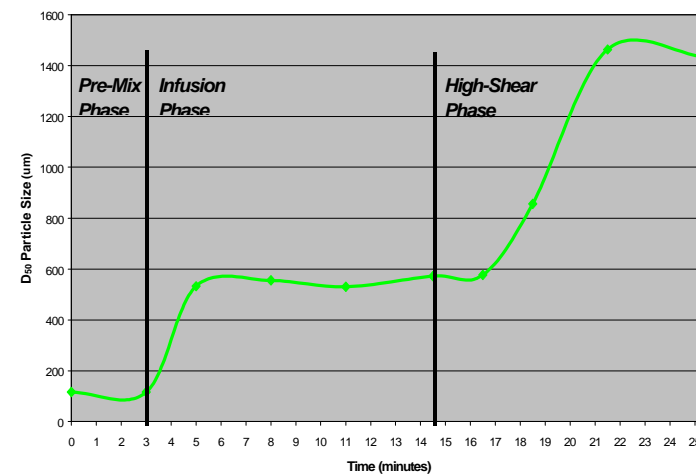
METHODS

One immediate release (IR) and one controlled release (CR) formulation were used in this study. Formulations and process parameters are shown in Tables 1 and 2. The granulations were made in a 600-liter high shear unit (Vector GMX-600). Mixer blade speed was 98 rpm for pre-mix and water infusion steps and 155 rpm for high-shear step. The chopper was run on high speed for the high-shear step. Samples were withdrawn after pre-mix, during water infusion, and during the high-shear phase. Each sample was dried with 65°C air using a fluid-bed dryer until the product was less than 2.5% moisture content. Sieve analyses were performed to determine the arithmetic mean diameters (D₅₀) of the dried granules.

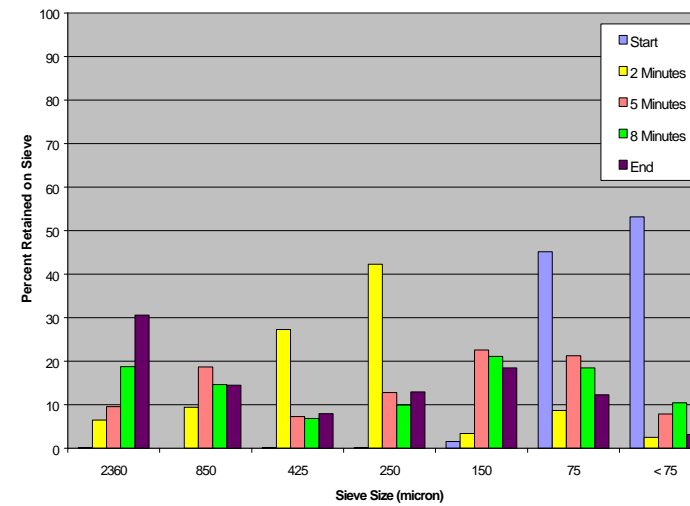
RESULTS

Immediate Release Formulation Summary

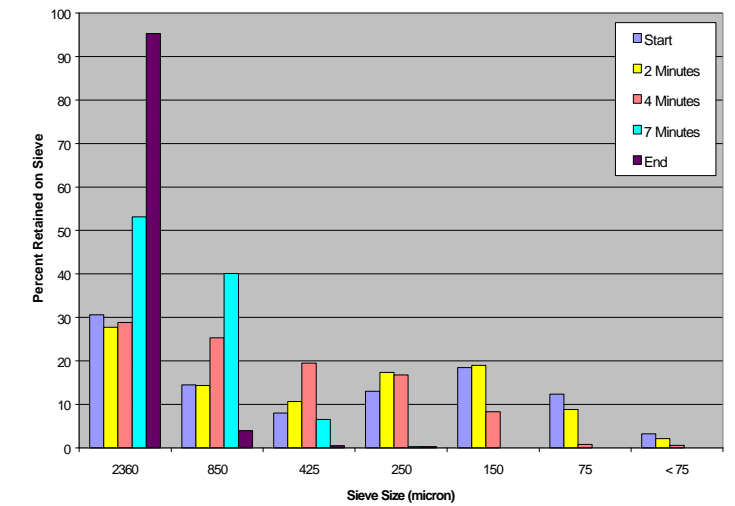
Immediate Release Formulation Particle Size Change Over Time



Particle Size Distribution - IR Formulation - Water Infusion Phase

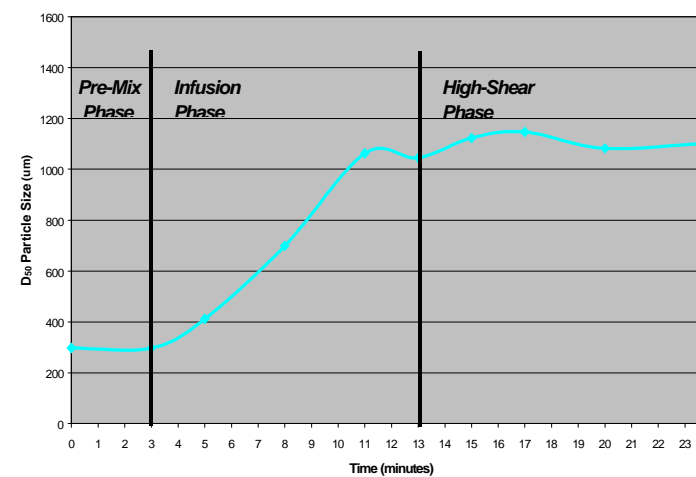


Particle Size Distribution - IR Formulation - High-Shear Phase

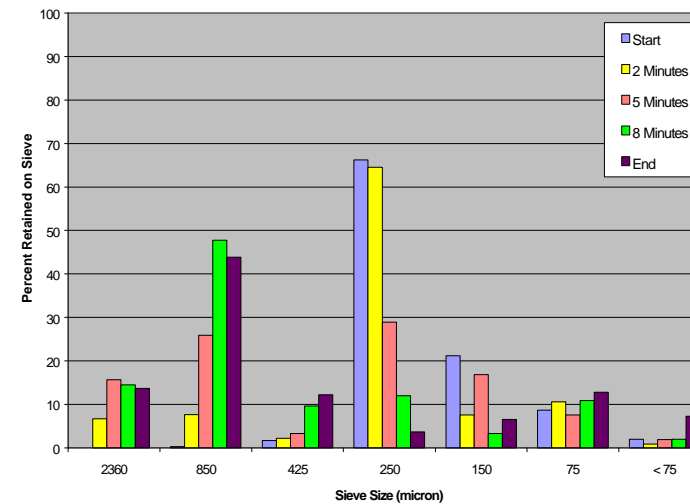


Controlled Release Formulation Summary

Controlled Release Formulation Particle Size Change Over Time



Particle Size Distribution - CR Formulation - Water Infusion Phase



Particle Size Distribution - CR Formulation - High Shear Phase

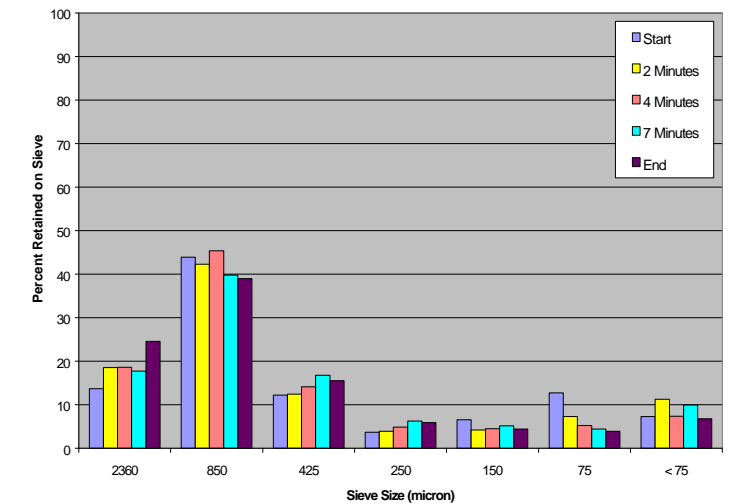


Table 1 – Formulations

Dry Ingredients	Immediate Release	Controlled Release
HPMC, K 4 M	--	30%
Starch 1500	15%	--
MCC, 50M	30%	--
Lactose	55%	70%
Batch Volume (L)	300	300
Batch Weight (Kg)	146.7	134.1
Bulk Density (g/cc)	0.489	0.447

Table 2 – Processing Parameters

Process Parameters	Immediate Release	Controlled Release
Pre-Mix Time	3 minutes	3 minutes
Water Infusion Time	11.5 minutes	10 minutes
Water Added	48.0 Kg (24.7 %)	52.5 Kg (28.1%)
Wet Mass Time	11 minutes	11 minutes

CONCLUSIONS

In the wet-granulation processes studied, the particle size of the material increased as binding solution and energy were applied to the dry ingredients. The phase where the majority of the particle size growth occurred depended on the design of the formulation and process. In the case of the IR formulation, the greatest particle growth occurred during the high-shear phase; whereas the water infusion phase provided the greatest particle growth for the CR formulation.