COMPARISON OF DIFFERENT METHODS OF BINDER ADDITION ON PARTICLE SIZE AND SHAPE FOR HIGH-SHEAR GRANULATION PROCESSES

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PURPOSE

To study the effects on particle size and shape for high-shear granulations using differing means of binder activation.

METHODS

Immediate release (IR) and controlled release (CR) formulations were granulated in a 25 liter high-shear mixer (GMX-25, Vector Corporation). Mixer blade speeds used standard manufacturer settings. Both formulations utilized dry binder which was activated by water addition. Water was added by pouring, pumping, and atomized spray. Granulations were split into two portions; one was wet-milled in a mill (COMIL 194S, Quadro) and dried in a fluid bed (FL-M-15, Vector Corporation); the other portion was only fluid bed dried. Resulting granulations were analyzed via sieve analysis and particle size imaging (QICPIC, Sympatec).

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

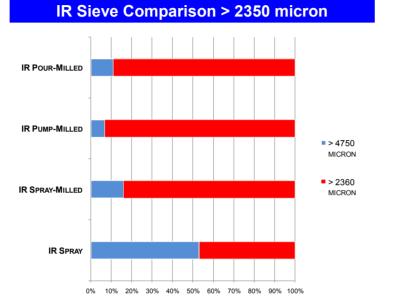
Table	Table 1 – Formulations					
Ingredients	IR Granulations	CR Granulations				
Lactose	55%	70%				
Starch 1500	15%	-				
MCC, Avicel PH-101	30%	-				
HPMC, Methocel K4M	-	30%				
Dry Weight (Kg)	6.1	5.6				
Water Added (Kg)	1.8	22				

Table 2 – Processing Parameters

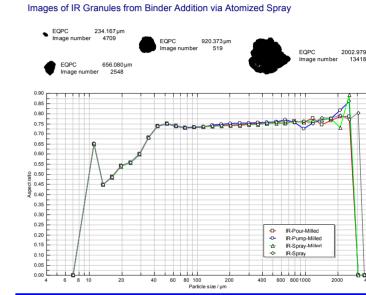
Wet Granulation		
Pre-Mix (Time/Tip Speed)	2.5 minutes / 5.4 mps	
Infusion (Time/Tip Speed)	IR = 7 minutes / 5.4 mps	
	CR = 9 minutes / 5.4 mps	
Wet Mass (Time/Tip Speed)	3 minutes / 8.4 mps	
Infusion Types		
Pour	All added in 30-60 seconds	
Pump	IR = 210 g/min	
	CR= 260 g/min	
Spray	Same pump rates @ 70 kPa air pressure	
Milling	Rounded Edge Blade; 900 rpm;	
	0.375 inch (9.5 mm) square hole screen	
Drying	52-57°C final product temperature	

RESULTS

IR Particle Size Analysis < 2350 micron

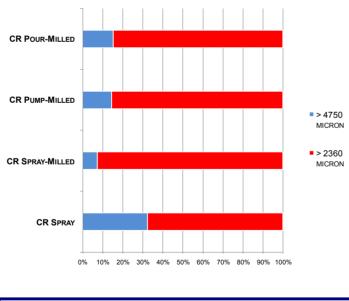


X_{10} VMD X_{50} X_{90} 210 526 1977 804 369 1989 728 IR PUMP-MILLED 143 IR SPRAY-MILLED 188 558 1811 795 IR SPRAY 234 656 2074 920 IR-Pour-Milled IR-Pump-Mille -∆- IR-Spray-Milled ->- IR-Spray



IR Particle Image Analysis < 2350 micron

CR Sieve Comparison > 2350 micron



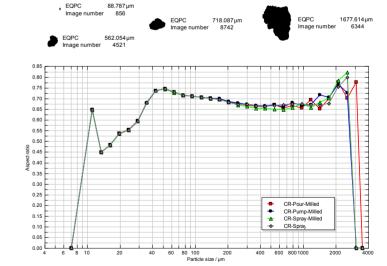
CR Particle Size Analysis < 2350 micron

VMD

	CR Pour-Milled	97	514	2083	790
	CR PUMP-MILLED	99	636	1965	829
	CR SPRAY-MILLED	97	608	1566	735
	CR SPRAY	88	562	1664	717
1.1					
1.0	CR-Pour-Milled CR-Pump-Milled]			<u> </u>
0.9	★ CR-Spray-Milled ◆ CR-Spray-			• · · · · · · · · · · · · · · · · · · ·	
0.8 -			/		(A)
office 0.7			-		
Density distribution q3*				/	
0.4					-\/\
0.3		2//			* A +
0.2					- /
0.1					₩
0.0	8 10 20 4	0 60 80	100 200 Particle size / um	400 600 800 1000	2000

CR Particle Image Analysis < 2350 micron

Images of CR Granules from Binder Addition via Atomized Spray



CONCLUSIONS

The means of adding binder will have differing degrees of effects on particle size and shape depending on the type of formulation used for high-shear granulations. Imaging techniques do offer an excellent means of understanding how granulations are impacted by differing processing methods/steps.



