

Optimization of Cold Water Starch Granulations Using High Shear Granulating Methods and Capitalizing on the Strength of Fully Pregelatinized Starch Incorporated as a Dry Binder

B. Jensen¹, S. Freers², D. Foltz¹, C. Shipley², R. Tuohy³, M. Guokas³

¹Vector Corporation, ²Grain Processing Corporation, ³Emerson Resources, Inc.

PURPOSE

Traditional starch granulations require starch paste preparation which takes time and presents a hazard to the operator in terms of steam heating and the handling of very hot liquids. Optimization of cold water starch granulations was investigated via the dry addition of varying levels of pregelatinized starch, then granulated using varying levels of cold water addition. Dry addition of fully pregelatinized starch and granulation by the addition of cold water simplifies the granulation process which accelerates production resulting in cost reduction.

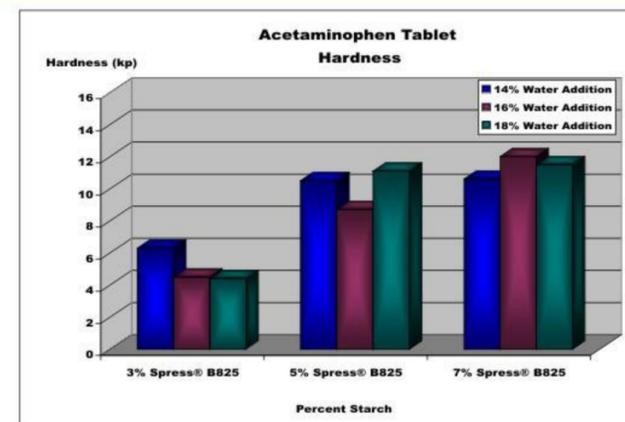
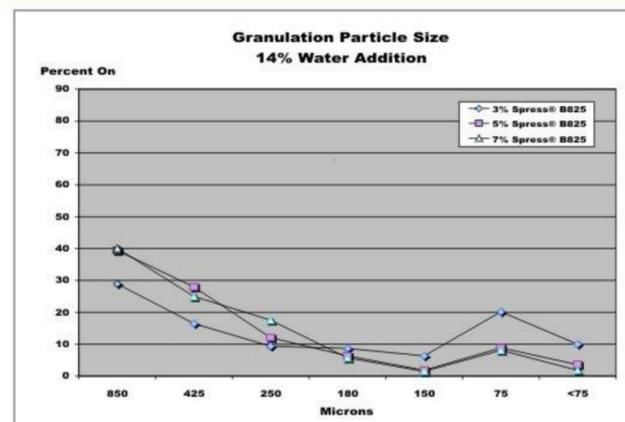
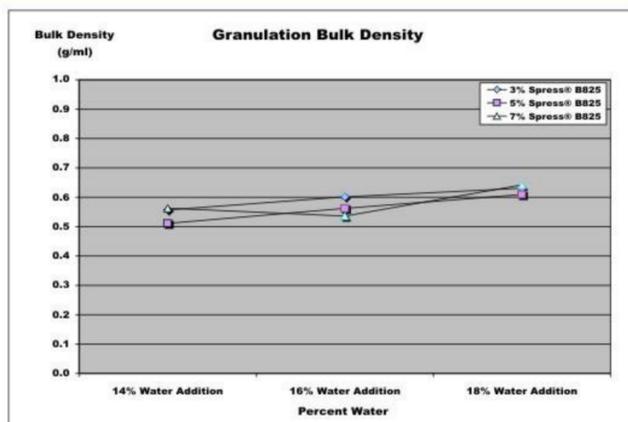
METHODS

Granulations of acetaminophen (USP semi-fine powder, Mallinckrodt) and pregelatinized starch (Spress® B825 Pregelatinized Corn Starch NF, Grain Processing Corporation) were made using three starch concentrations (3%, 5%, and 7%) and three cold water addition levels (14%, 16%, and 18%, water temperature < 27°C). An eleven minute dry mix, water addition and wet massing protocol was followed for each high shear batch using a GMX-10 top drive high shear granulator (Vector Corporation) to keep the maximum energy input to each batch the same. Each batch was dried to between 1% and 2% moisture content in a Vector fluid bed dryer, without wet milling, and then dry milled through a Quadro Comil, Model 194.

The acetaminophen/starch granulations were mixed with Avicel PH 101 microcrystalline cellulose and magnesium stearate before being compressed on a Vector/Colton rotary tablet press model 2216 equipped with 7/16 inch standard round tooling. Tablets contained 325 mg of active acetaminophen. All tablets were analyzed for weight, thickness, hardness, friability, disintegration and dissolution.

EQUIPMENT

Vector GMX 10 top drive high shear granulator
Vector FL-M-1 fluid bed dryer
Quadro Comil, Model 194
Vector/Colton rotary tablet press model 2216 equipped with 7/16 inch standard cup round tooling



GRANULATION FORMULATION

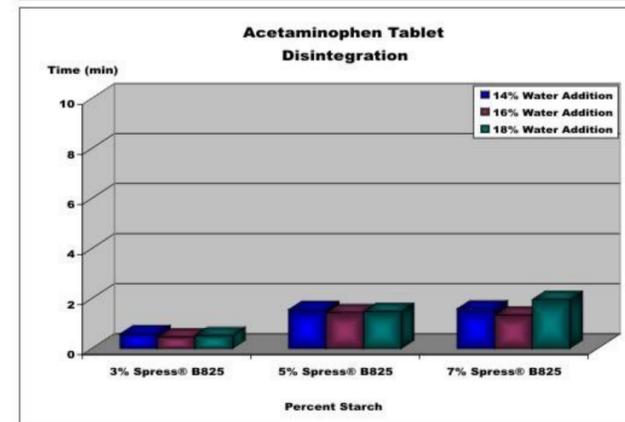
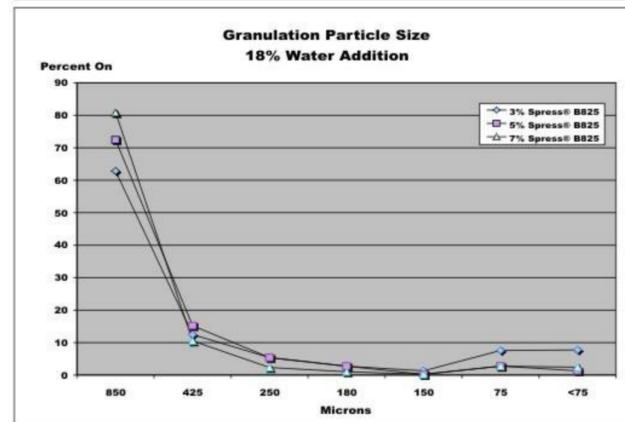
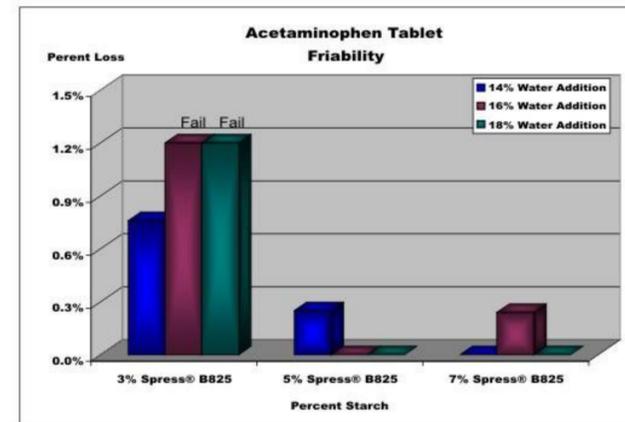
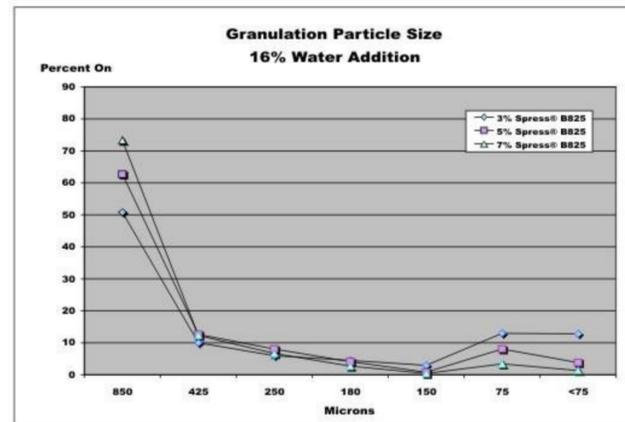
3% = 97% Acetaminophen / 3% Spress® B825
5% = 95% Acetaminophen / 5% Spress® B825
7% = 93% Acetaminophen / 7% Spress® B825

TABLET FORMULATION

Acetaminophen/Starch Granulation 85.00%
Avicel® PH 101 14.75%
Magnesium Stearate 0.25%

TABLET INFORMATION

325 mg active acetaminophen
395 mg tablet weight / 3% granulation
403 mg tablet weight / 5% granulation
412 mg tablet weight / 7% granulation



Acetaminophen Tablet Dissolution

Lot	Average*	RSD
3% Spress® B825/ 14% water addition	96.3%	7.1%
3% Spress® B825/ 16% water addition	98.8%	0.6%
3% Spress® B825/ 18% water addition	92.1%	17.7%
5% Spress® B825/ 14% water addition	97.3%	2.5%
5% Spress® B825/ 16% water addition	100.0%	1.3%
5% Spress® B825/ 18% water addition	71.7%	31.1%
7% Spress® B825/ 14% water addition	101.2%	1.2%
7% Spress® B825/ 16% water addition	102.6%	1.9%
7% Spress® B825/ 18% water addition	100.9%	2.2%

*Per USP Monograph Percent dissolved in 30 minutes

RESULTS

All tablets were consistent in weight and thickness and met USP requirements for disintegration and dissolution. Formulations with 5% and 7% starch content were superior in all respects regardless of moisture addition.

CONCLUSION

Quality granulations can be made using only cold water as a binding solution and fully pregelatinized corn starch as the binder in a high shear granulator. Using fully pregelatinized starch in the manner described eliminated solution preparation thereby reducing overall production time. For this formulation, starch content needs to be above 3% for optimum tablet characteristics.

