

Optimization of Binder Level in Moisture Activated Dry Granulation (MADG) Using Absorbent Starch to Distribute Moisture

PURPOSE

To determine the optimum binder as well as the most efficient binder level needed to make successful granulations using pregelatinized starch as the absorbent diluent in the Moisture Activated Dry Granulation (MADG) process.

METHOD

Varying concentrations and molecular weights of maltodextrin and povidone were tested for binder efficiency in acetaminophen granulations using the Moisture Activated Dry Granulation (MADG) process.

Binder Concentration Levels: 7.0%
5.0%

Maltodextrin Grades: MALTRIN® M040 Maltodextrin NF (GPC) high mol wt
MALTRIN® M180 Maltodextrin NF (GPC) low mol wt

PVP Grades: Plasdione® K-90 (ISP) high mol wt
Plasdione® K-30 (ISP) medium mol wt
Kollidon® 12PF (BASF) low mol wt

Absorbent diluent: Spress® B818 Pregelatinized Corn Starch NF

Granulations were run on a Vector Corporation GMX 25 granulator. The binder was added dry and 2.80% water was mixed in to activate the binder. Spress® B818 Pregelatinized Corn Starch NF was then added to absorb and distribute the moisture in the granulation. Since minimal moisture is needed in this specialty granulation process, no drying time is required.

General Granulation Formulation:

| | |
|---|--------------------|
| APAP (Mallinckrodt 0084 Semi-fine Powder) | 59.08% |
| Binder | (7% or 5%) |
| Water | 2.80% |
| Pregelatinized Corn Starch NF | (30.87% or 32.87%) |
| Magnesium Stearate | 0.25% |
| | 100.00%* |

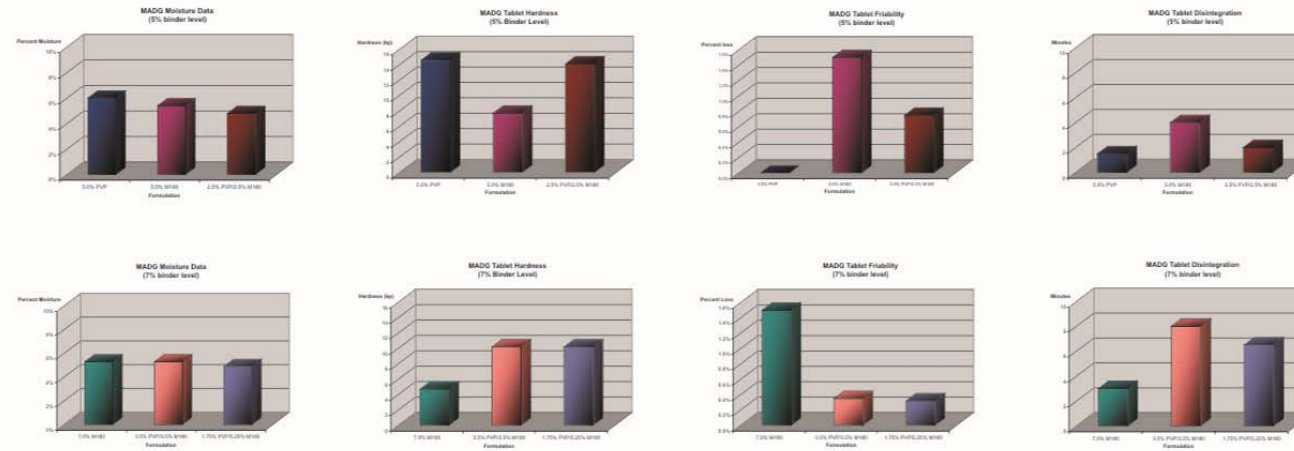
*A small amount of Blue #2 Lake was added before the Pregelatinized Corn Starch NF to help determine granulation uniformity. This amount was not included in the total granulation Percentage.

Granulation Method:

| | |
|--|---------------------|
| APAP and binder pre-mix time | 2.0 minutes |
| Water addition (impeller 300 RPM) | 4.0 minutes |
| Mix time (impeller 425 RPM, chopper low) | 3.0 minutes |
| Spress® B818 addition | |
| Mix time (impeller 300 RPM, chopper low) | 5.0 minutes |
| Magnesium stearate addition | |
| Mix time (impeller 300 RPM) | 0.5 minutes |
| Total granulating time | 14.5 minutes |

To test the quality of the granulation, 325 mg acetaminophen tablets were compressed on a Vector/Colton rotary tablet press model 2216 and analyzed for weight, thickness, friability and disintegration.

Susan Freers¹, Carrie Shipley¹, Brian Jensen², Shawn Engels², and Ismat Ullah³
¹Grain Processing Corporation, ²Vector Corporation, ³Bristol-Myers Squibb



RESULTS

Higher molecular weight maltodextrin and povidone products did not perform as well as lower molecular weight products when used as a binder in the Moisture Activated Dry Granulation (MADG) process. All formulations made with the higher molecular weight binders failed to granulate. MALTRIN® M180 Maltodextrin NF and Kollidon® 12PF povidone were determined to be the best binders in this study.

Although both can be used alone to make acetaminophen granulations, a combination of MALTRIN® M180 Maltodextrin NF and Kollidon® 12PF povidone produced the best granulations with the most robust tablets. When used alone, MALTRIN® M180 Maltodextrin NF made a uniform granulation (at both a 5% and 7% binder level) but tablet friability was high. Kollidon® 12PF, at a 5% binder level, created strong tablets with low friability, but the granulation had to be screened due to the formation of large clumps. Due to the screening process, not only was another step added, but granulation uniformity and therefore tablet dosage uniformity were in question.

Particle size of the absorbent diluent proved to be another important factor in this type of granulation. The particle size of Spress® B818 Pregelatinized Corn Starch NF had to be optimal in order to maximize granulation uniformity and flow.

CONCLUSION

Taking into consideration final granulation moisture and finished tablet data, the optimum binder for the Moisture Activated Dry Granulation (MADG) process is a combination of low molecular weight maltodextrin and povidone. Using Spress® B818 Pregelatinized Corn Starch NF as the absorbent diluent, the ideal binder level was determined to be 5.25% MALTRIN® M180 Maltodextrin NF and 1.75% Kollidon® 12PF povidone.



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