# GMS as Effective Anti-Agglomeration Agent in Drug Layering of MCC Spheres

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## INTRODUCTION

Glyceryl monostearate has been successfully used as an anti-agglomeration agent in Wurster fluid bed coating and as a slip aid in tablet coating with acrylic polymers, such as Eudragit L30D55. Drug layering is typically performed through the use of cellulosic polymers, and has the added challenge of accounting for API characteristics (e.g., solubility, dose). These experiments compare the use of GMS and talc as anti-agglomeration agents in drug layering with cellulosic polymers.

## EXPERIMENTAL METHODS

Microcrystalline cellulose spheres with a particle size distribution of 700-1000 µm (Cellets 700, Glatt) were drug layered using five different aqueous coating suspension formulations. Hydroxypropyl methylcellulose (HPMC, Walocel HM5, Dow) was used as the film former, with triethyl citrate (TEC, Vertellus) as the plasticizer. Acetaminophen (APAP, Spectrum, solubility: 12.78 mg/mL at 20°C) was used as a model drug. The ratio of API to HPMC was 3:1 for all experiments. Two formulations used talc (Brenntag) and two used Plasacryl T20, a commercially available GMS emulsion distributed by Evonik Industries. As Plasacryl T20 contains GMS, TEC, and Polysorbate 80, no additional TEC was required for those formulations. One formulation was used as a control, containing no anti-agglomeration agent. Coating suspensions were prepared at 25% solids.

Coating Formulation (% polymer weight)

| Sample ID | APAP | HPMC | Talc | Plasacryl T20 | TEC |
|---|---|---|---|---|---|
| A | 300 | 100 | — | — | 10 |
| B | 300 | 100 | 50 | — | 10 |
| C | 300 | 100 | 100 | — | 10 |
| D | 300 | 100 | — | 20 | — |
| E | 300 | 100 | — | 40 | — |

Coating Formulation (% of coating solids)

| Sample ID | APAP | HPMC | Talc | Plasacryl T20 | TEC |
|---|---|---|---|---|---|
| A | 73.17 | 24.39 | — | — | 2.44 |
| B | 65.22 | 21.74 | 10.87 | — | 2.17 |
| C | 58.82 | 19.61 | 19.61 | — | 1.96 |
| D | 71.43 | 23.81 | — | 4.76 | — |
| E | 68.18 | 22.73 | — | 9.10 | — |

The coating suspensions were applied to the MCC spheres using a Vector FLM-1 fluidized bed coater equipped with a Wurster column, a 1.2 mm liquid nozzle, and a 3 mm air cap. The coating process conditions were held constant between the experiments. All formulations were coated to a 39% theoretical API weight gain, and therefore varied in overall coating weight gain. Critical coating parameters were selected in order to differentiate the effectiveness of the level and type of anti-agglomeration agent. The coating parameters used are found in the table to the right. The spray rate was stepped up from 10 to 35 g/min at identical timepoints during each coating run. The length of each coating run varied, due to the change in overall weight gain required to apply 39% theoretical API weight gain.

The effectiveness of each anti-agglomeration agent was evaluated by passing drug layered beads through a US18 mesh sieve (1000 micron). Single beads passed through the sieve, and agglomerated beads were retained on the sieve. Agglomeration results are reported as percent retained on the sieve.

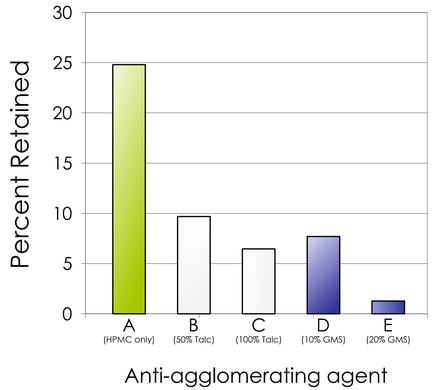
Coating Conditions

| | |
|---|---|
| Product Temperature | 40-50 °C |
| Air Volume | 64-66 CFM |
| Nozzle Air | 36 PSI |
| Spray Rate | 10-35 g/min |
| Batch Size | 500 g |
| Coating Time | A: 44 minutes<br>B: 49 minutes<br>C: 52 minutes<br>D: 48 minutes<br>E: 48 minutes |

## RESULTS AND DISCUSSION

Both talc and GMS demonstrated reduction in agglomeration compared to the control experiment with no anti-agglomeration agent. When GMS was used at a level 10 times less than the level of talc used in comparative experiments, a similar level of detackification was achieved (Experiment C verses D). When GMS was used at a level 5 times less than the level of talc used in comparative experiments, in both instances GMS outperformed talc as an anti-agglomeration agent (Experiment B verses D, and Experiment C verses E).

Agglomeration Results




## CONCLUSION

GMS can be effectively used as an anti-agglomeration agent at levels between 10 and 20% of typical talc levels with similar or improved reduction in agglomeration in drug layering formulations. In this study, coating parameters were selected to facilitate agglomeration, though coating process parameters could be optimized to reduce agglomeration further with either level of GMS or talc. The reduced level of detackifier required when using GMS also reduces the overall coating suspension required to apply a specific dosage in drug layering applications. This results in lower process times and additional cost savings. GMS also increases the ease of processing due to elimination of the settling of talc and reduction in gun clogging concerns.

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