Enteric Coating of Multi-Particulates with Dry Powder Application of Glidant Utliizing a Modified Wurster Spray Gun System

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INTRODUCTION

Bottom Spray Wurster technology is commonly used in the pharmaceutical industry as a method for applying active and functional coatings, including sustained release and enteric polymer coatings, to multi-particulate substrates. Typically aqueous dispersions of polymers are diluted and are mixed with appropriate glidant, such as talc, to reduce blocking and agglomeration during the drying of the polymer solution on the surface of the multi-particulate. These solutions and suspensions are applied via air atomizing spray guns. The need to dilute the solution can increase the application time needed for proper drug release or enteric protection.

The need to add glidant to the solution can create sedimentation and plugging in the solution lines. This study focuses on whether a modified Wurster gun, which allows dry powder to be injected separately into the spray zone could be utilized to efficiently coat multi-particulate cores in an existing Wurster system utilizing an enteric polymer and dry powder layering technology.

EXPERIMENTAL METHODS

5 kg of 18/20 mesh Suglets (Colorcon) containing 10% Acetaminophen were loaded in to a Freund-Vector VFC Lab-3 fluid bed equipped with an 8" tapered Wurster insert. An enteric polymer, Eudragit L 30 D 55 (Evonik) was applied as a 30% w/w suspension via the spray system. Micronized talc (Spectrum) was put into a KTron KT-20 loss-in-weight powder feeder and was simultaneously applied through a modified accelerator air sleeve on the spray gun. As a control, Eudragit L 30 D 55 was also applied per the manufacturer's recommendation (15% polymer solids) in a conventional manner with the glidant (talc) added to the suspension. Batches of beads were coated to a 15% and a 20% coating level.

These trials were then scaled up to a 50 kg batch size in a Freund-Vector VFC-60M Fluid bed equipped with an 18" straight sided Wurster Insert. The same powder addition system and polymer weight gains were applied in the production scale batches as the R&D scale batches.

Agglomeration rates were measured utilizing a QICPIC (Sympatec) Particle Image analyzer, and were reported as a percentage of each batch. Dissolution testing was completed on all batches to ensure proper acid resistance and subsequent release of the acetaminophen. All of the batches were repeated in triplicate to confirm results.

EQUIPMENT

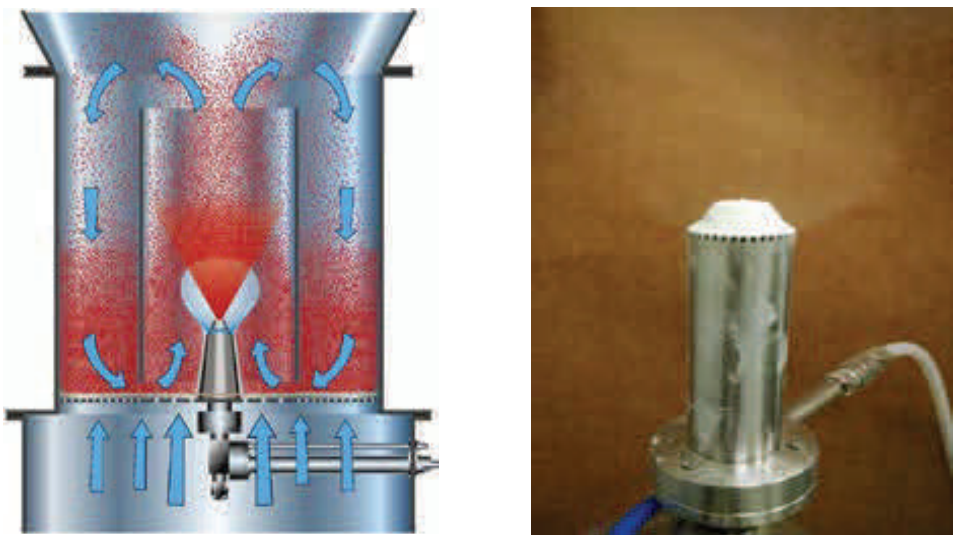

Diagram of a Freund-Vector Wurster coating system (Left) and a modified Wurster Accelerator spray gun with powder delivery capabilities (Right)

RESULTS AND DISCUSSION

For the trials in the VFC-3 with the 8" Wurster using the powder application, the coating was applied in 43 minutes at an 86% efficiency. There was 0.9% agglomeration on average for these batches. The standard suspension application was applied in 119 minutes at an 84% efficiency. These trials had an average of 0.6% agglomeration. In the scaled up trials which were run in the VFC-60 with the 18" Wurster using the powder application, the coating was applied in 42 minutes at 96% efficiency. Again, the agglomeration rate was very low at 0.2%. In the repeated trials using the suspension system, the coating was applied in 117 minutes at an 83% efficiency. These trials had an agglomeration rate of 0.4%.

The dissolution testing showed that all of the trials completed in the VFC-3 with the 8" Wurster system sufficiently provided enteric protection, regardless of whether the talc was added in the suspension or with the dry powder application system. The beads were held in the acidic solution for two hours before being moved into 6.8 pH buffer. (see Chart 1).

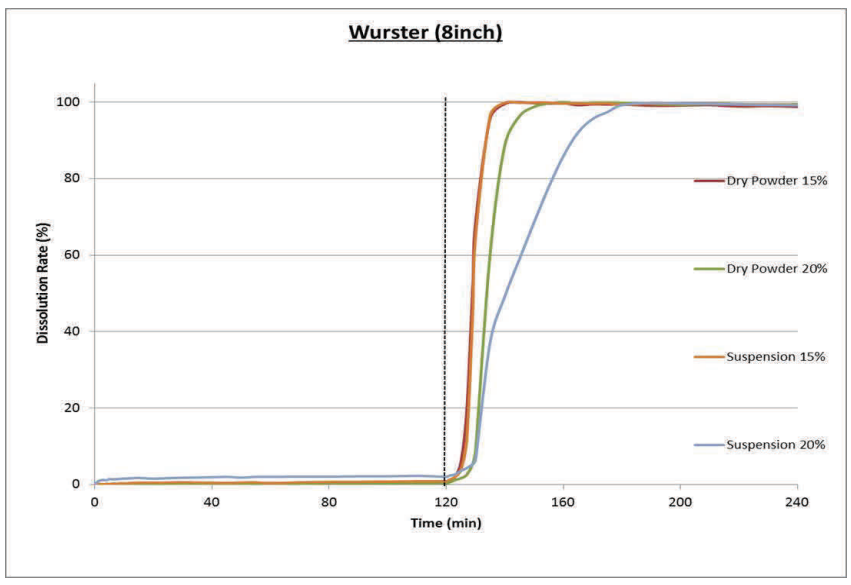

Chart 1: Dissolution graph showing the release rate of the 8" Wurster trials using the suspension and dry powder application methods.

The testing also showed that for the trials conducted in the VFC-60 with the 18" Wurster insert, the batches that were run with the dry powder addition of the talc sufficiently provided enteric protection, while the standard application resulted in some leakage of the acetaminophen into the acidic media. (see Chart 2).

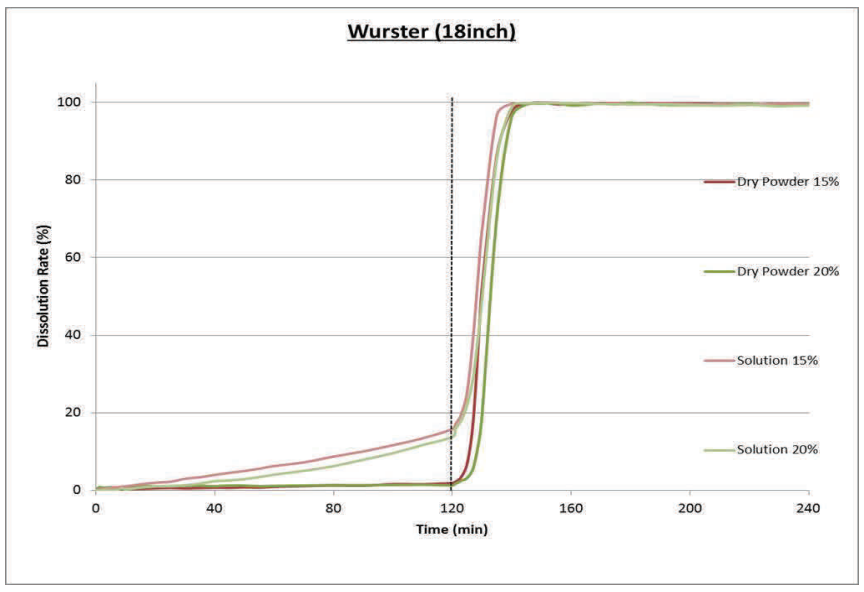

Chart 2: Dissolution graph showing the release rate of the 18" Wurster trials using the suspension and dry powder application methods.

In all of the trials, there was no significant difference seen between the 15% and 20% coating weight gains for either the dry powder application of talc or the standard suspension application. All of the acetaminophen was released within 20 minutes in the 6.8 pH buffer solution for all of the trials, indicating proper enteric performance for all of the trials.

CONCLUSIONS

Using the modified Wurster Accelerator system to apply the glidant (talc) as a dry powder, the 20% polymer application was accomplished almost three times faster than conventional methods. The ability of the modified system to deliver the talc directly into the spray zone and distribute the talc over the surface of the multiparticulates allowed for accelerated spray rates, reduced agglomeration percentages and also allowed for the application of the aqueous dispersions at twice the concentration of the standard recommended application.

The efficiency of polymer application with the dry powder application was as good or better than the conventional suspension application. Leakage of the acetaminophen in the acidic medium was less than conventional application in the production scale batches. Agglomeration was acceptable at far less than 1% for all application methods. Using the Wurster Accelerator Dry Powder Application System will increase productivity and produce coated multi-particulates that are equal or superior to conventional suspension coating methods. Adapting this dry powder technology to conventional Wurster systems has the potential to improve productivity and reduce processing issues associated with spraying polymer systems with glidant suspended in them.

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