Controlled Release Coatings of Ethylcellulose on Drug Loaded Multiparticulates: A Comparison of a Novel Rotor Dry Powder Layering Process to a Traditional Wurster BottomSpray Coating Process.

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ABSTRACT SUMMARY

Controlled release coatings of ethylcellulose were applied to drug loaded sugar spheres with three different processes: dry powder layering, aqueous Wurster coating and organic solvent based Wurster coating. Comparative analysis of the three processes showed that the dry powder layering process was able to apply the ethylcellulose coatings in a faster, more efficient process than the traditional spray coating systems and still achieve controlled release.

INTRODUCTION

Spray coatings of ethylcellulose for controlled release on multi-particulate dosage forms are common in the pharmaceutical industry, but can be disadvantageous because of long process times, need for organic solvent capabilities, and particulate agglomeration. This study highlights the advantages of a rotor dry powder layering process in overcoming these deficiencies by comparing performance, productivity, and cost to solvent-based Wurster coating and aqueous-based Wurster coating.

EXPERIMENTAL METHODS

Sugar Spheres (#20-25 mesh; Suglets® Colorcon Inc., USA) coated with acetaminophen (APAP) at a 28% w/w level were used as core materials for each of the coating processes. Using a conical rotor, (Granurex® GXR-35, Freund-Vector Corporation, USA) the drug layered beads were powder layered with micronized ethylcellulose (ETHOCEL™ EXP-1, The Dow Chemical Company, USA) using a 40% dibutyl sebacate (DBS) emulsion as a binder/plasticizer. For comparison, APAP drug layered beads were also coated in a bottom spray fluid bed (VFC-3 8" Wurster, Freund-Vector Corporation, USA) using an organic solvent based ethylcellulose (ETHOCEL™ STD 10 Premium, Dow) solution in ethanol and an aqueous ethylcellulose DBS based dispersion. Dissolution was evaluated for the various weight gains of dry powder, organic and aqueous coatings. A cost model analysis was also completed for each coating method utilizing Venlafaxine HCl, taking into account processing, raw material, capital equipment and utility costs.

EQUIPMENT

Freund-Vector Corporation
Granurex® GXR-35

Freund-Vector Corporation
VFC-3, 8" Wurster

RESULTS AND DISCUSSION

Coatings achieved through the dry layering process were consistent, reproducible, and demonstrated controlled release at 10-25% weight gain and took 25-50 minutes of coating time. Wurster spray coatings took 110-240 minutes to achieve the same coating levels. Figure 1 (below) shows the dry powder layered coatings had the same dissolution performance as the aqueous wurster coatings, but needed more weight gain to achieve the same performance as the organic wurster coatings.

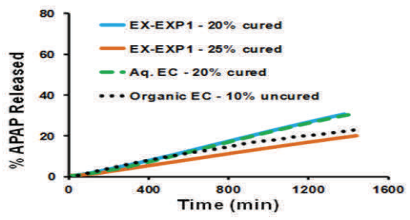

Figure 1: Dissolution chart showing identical release profiles from the aqueous Wurster coated beads and the dry powder layered beads at the same coating levels.

A complete production and cost comparison of the three processes based on the annual production of Venlafaxine HCl revealed that the dry powder layering process far outperformed the aqueous wurster process and was nearly identical to organic solvent wurster coating in total cost to manufacture. (Figure 2)

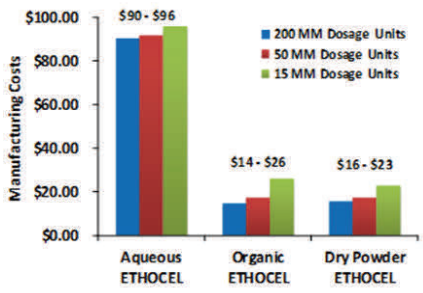

Figure 2: Manufacturing Cost Comparison chart showing the manufacturing cost difference between aqueous Wurster manufacturing, organic Wurster manufacturing and dry powder manufacturing.

In terms of the days required to manufacture Venlafaxine HCl (Figure 3) and the total manufacturing capacity for a year (Figure 4), the dry powder layering process significantly outperformed both the organic wurster coating and the aqueous wurster coating processes.

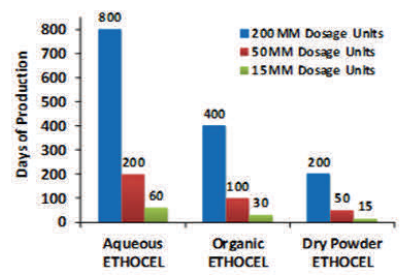

Figure 3: Manufacturing time comparison chart showing the difference in days required to manufacture Venlafaxine HCl utilizing aqueous Wurster, organic Wurster and dry powder layering manufacturing based on use of one 32" Wurster and one 125 cm rotor.

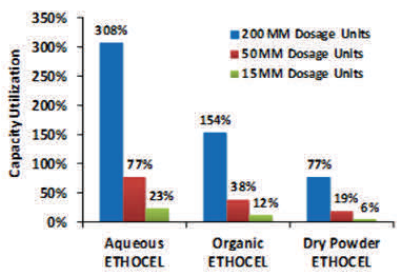

Figure 4: Manufacturing capacity chart showing the % capacity utilization to manufacture Venlafaxine HCl using aqueous wurster, organic Wurster and dry powder manufacturing based on use of one 32" Wurster and one 125 cm rotor.

CONCLUSIONS

The rotor dry powder layering process demonstrated controlled release coatings and was applied at rates 2-4 times faster than traditional spray coating systems, although it did require more polymer weight gain to achieve the same performance as the solvent based solution. The rotor dry powder layering process also A) eliminates organic solvent based formulations which help alleviate concerns around environmental health and safety considerations and B) eliminates aqueous based formulations which enable coatings to be applied to water sensitive ingredients.
Further testing with experimental ethylcellulose samples, various curing times and conditions as well as different polymer/plasticizer combinations is needed to optimize performance for the dry layering process. These optimizations have the potential to further improve the performance of the dry powder layering process, and may further reduce the processing time and polymer amount required to achieve desired release profiles.