Rapid Polymeric Coating Technique Using Powder Layering in Rotor-Equipped Fluid Bed

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ABSTRACT

The development of a powder coating methodology including the utilization of a new type of fluidized bed apparatus is reported. Several different polymer systems were tried and compared to solvent-based techniques using acetaminophen as a model drug. Process parameters are described and the performance of the polymer coating system relative to solvent-based coating system is compared.

INTRODUCTION

Powder coating of active ingredients has been reported by a number of groups.[i] Advantages include the absence or great reduction in the use of organic solvents and a relatively large reduction in coating times. Aqueous coatings can require extended coating times and possible migration of aqueous soluble drugs into the coating polymer layer. Current powder coating techniques have been recently reviewed providing an excellent summary of the various coating polymer / plasticizer combinations and application methods that have been employed.[ii] A number of the techniques utilize extruded polymers that have been plasticized and cryogenically ground or higher levels of plasticization than is normally used in solvent coatings to achieve proper film formation. Often relatively higher polymer weights have to be used to achieve performance equivalent to solvent-based techniques.

Freund International has recently introduced a coating apparatus that utilizes a rotating bowl providing a torroidal motion to the particulates that produces increased shear in the particle bed. Air flows used for rapid coating solution evaporation are introduced from above and around the edge of the spinning bowl. The combination of shear forces in the product bed and improved air contact with the particles aids to reduce agglomeration during curing at elevated temperatures. The controlled air flow provides rapid distribution of coating polymer particulates without excessive losses to filters in the expansion chamber.

Processing times of approximately 1/5th or shorter as compared to solvent-based systems

Goals for the for the Development of Dry Fluid Bed Coating System

- Shift from organic solvent-based coating to aqueous systems (environment, safety, cost)
- Aqueous coating systems for enteric protection
- What if active sensitive to water?
- Problem of high coating times, especially with aqueous systems or high molecular weights requiring dilute feed solids
- Development of novel approach for enteric coating using high solids methods in order to drastically cut fluid bed batch times

EXPERIMENTAL

Initial studies were done in a conventional fluid bed coating apparatus without internal Wurster insert. It became clear that careful control of airflows, temperatures and improved mixing in the fluid bed would be very important. It was decided to do further studies with the new Freund Granurex equipment.

Acetaminophen was chosen as a model drug for layering on sugar spheres. One of the side ports of the Freund Granurex was equipped with an air/solids eductor. Solids were supplied using an Acc-u-Rate® screw powder feeder. Control of air flow to the eductor port allowed the powders to be dispersed effectively into the bed. A small amount of silica flow aid was added to improve reproducible powder flow rates. A 5% solution of hydroxypropyl methyl cellulose (HPMC, Shin-Etsu E-5) solution was prepared to act as a binding agent for the drug layering process. The ratio of binder addition to active ingredient was fixed but conditions of airflow and temperature had to be adjusted to ensure that a very high fraction of active ingredient ended up applied to the sugar sphere surface rather than forming agglomerates. After process optimization, the active ingredient coating of the sugar spheres was at very high efficiency.

Sugar spheres (2 Kg), 0.5 to 0.7 mm, were coated with 0.953 Kg of acetaminophen containing 0.016 Kg of fumed silica. After complete addition of the active ingredient, a seal layer of the same HPMC solution was applied to prevent any interaction of the active with the coating and to reduce any possible attrition of active from the bead surfaces.

Four polymer / plasticizer combinations were tested in these initial trials:

1. Hydroxypropyl methyl cellulose acetate succinate (HPMCAS, Shin-Etsu Aqoat AS-LG), triethyl citrate (TEC), acetylated monoglyceride (AMG); 1.5:1 ratio of plasticizers; 2:1 polymer to plasticizer
2. HPMCAS, Shin-Etsu Aqoat AS-LG , 5:3 ratio of TEC/AMG ; 2:1 polymer to plasticizer
3. 1:1 Eudragit L100 / S100, talc, sodium lauryl sulfate, acetyl tributyl citrate (ATBC), AMG
4. Ethyl Cellulose, talc, dibutyl sebacoate, AMG

A number of plasticizer systems have been reported for the HPMCAS polymer. In this study, two ratios of plasticizer were used. Polymers were mixed with talc to provide uniform feed rates to the coating chamber. Plasticizers were blended with a mixture of ethanol and water to provide sufficient dilution to assure consistent wetting of the bead surface. An essential parameter to maintain during the process was the proper plasticizer to polymer ratio. A 30% coating (as calculated from total bead weight) was applied to two (2) kilos of active ingredient layered cores in less than one hour. A 40% coating weight was achieved in less than 90 minutes. Coating application efficiency was consistently at about 94% for the HPMCAS and 98% for the ethyl cellulose. A water/EtOH mixture was atomized into the bed for another hour to begin to fuse the polymer beads. The bed was then heated to a bed temperature of 50 degrees C for 15 minutes. Inlet temperatures, rotor speeds, top and slit air flows were all carefully controlled during each step in the process. Pressure drop across filter socks was carefully observed. After the polymer fusion step, the bed was cooled to ambient and the product discharged.

RESULTS

Dissolution results for the dry-coated beads from the HPMCAS, Eudragit, and Ethyl Cellulose polymers are shown in Figure 1. The Eudragit mixtures did not provide enteric protection while the Ethyl Cellulose system did achieve slow release.

Figures 2 and 3 are expanded scale results for comparison between the dry coating-based system and the same polymer applied from solvent. The solvent-based system does provide better protection at somewhat lower polymer loadings even if one considers that only 93% of the powder was layered onto the beads. However, there only needs to be approximately 20% greater polymer loading with the current system to achieve equivalent performance. Further studies of other plasticizer systems may produce improved polymer particulate fusion.

CONCLUSIONS

Further refinements of plasticizer and fusing conditions are needed yet to provide equivalent powder layering to solvent-based coating methods. One distinct advantage achieved with the powder polymer layering technique is processing times of approximately 1/5th or shorter as compared to solvent-based systems.

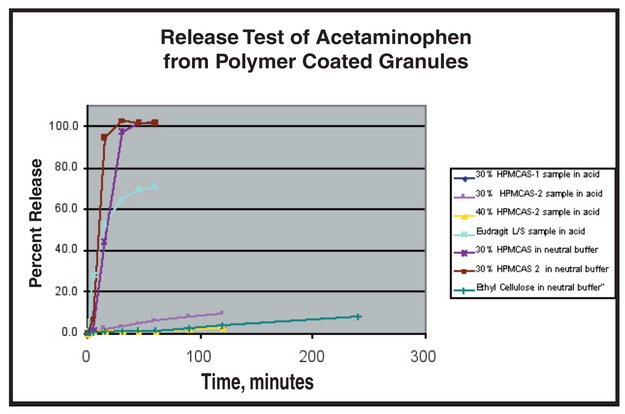

Figure 1

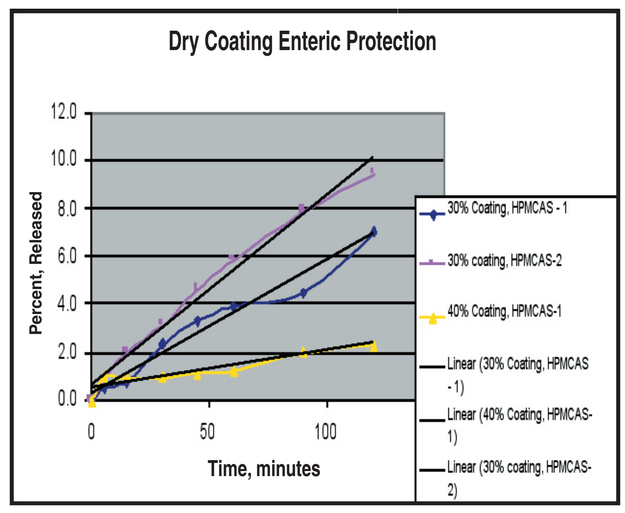

Figure 2

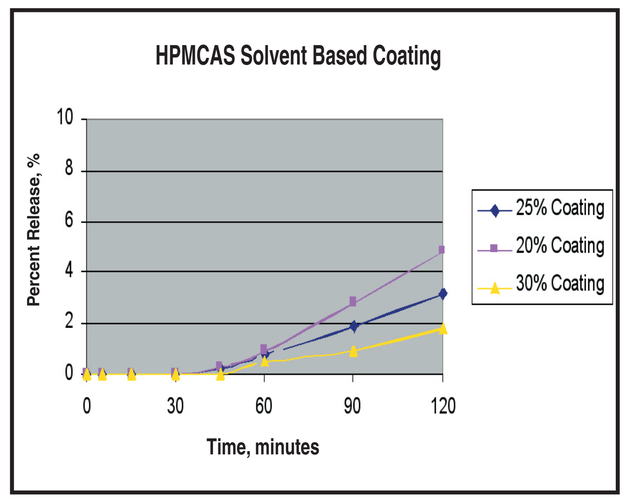

Figure 3

[i]Obara S. Maruyama N, Nishiyama Y, Kokubo H. Dry Coating : an Innovative enteric coating method usinga a cellulose derivative. Eur. J. Parmaceut biopharmaceutic 1993; 47:51-59
[ii]R. Bodmeier, J. McGinity Powder coating Systems, Dry Coating of Solid Substrates with Polymeric Powders, Drug Delivery Technology, October 2005, Vol 5, 70-73

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