Evaluation of Static or Dynamic Curing Process for Improved Controlled Release, Dry Powder Coatings of Ethylcellulose using a Rotor Coater

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PURPOSE

ETHOCEL HP is a micronized ethylcellulose dry powder specifically designed to achieve controlled release barrier membranes using a rotor system. This dry powder coating shows 40 – 60% reduction in coating times versus spray coating alternatives such as aqueous ethylcellulose dispersions or solvent based spray coatings and is solvent free. The coating process feeds ETHOCEL HP from the dry powder state along with a combination of water and plasticizer to allow proper particle-particle and particle-substrate adhesion and drives down the Tg of ethylcellulose to temperature relevant to film formation. Due to the nature of this coating process, curing is a required process parameter for improved film formation and stability. This study highlights the influence of static and dynamic curing steps on dissolution performance and stability at accelerated conditions.

METHODS

Sugar spheres (#20-25 mesh; Suglets® Colorcon Inc., USA) coated acetaminophen (APAP) at 28% w/w level were used as core materials for the dry powder coating process. Using a conical rotor, (Granurex® GXR-35, Freund-Vector Corporation, USA) the drug layered beads were powder layered with ETHOCEL HP (The Dow Chemical Company, USA) using a 30% Triethyl citrate emulsion as a binder/plasticizer to a 20% weight gain level. The ETHOCEL HP was applied at 15 g/min and the wetting solution at 13 g/min. After the coating was applied samples were either statically or dynamically cured at different times and lengths. Static curing is where sample were removed from the coater and placed on a tray and in an oven whereas dynamically curing uses the combination of the rotational movement of the coated samples plus hot air blown from above to help induce proper film formation. Dissolution and SEMS images were used to determine which curing conditions provided the best performance. Stability was also assessed at 1, 3, and 6M time points for samples stored at 30˚C/65% RH.

EQUIPMENT

Freund-Vector Corporation
Granurex® GXR-35

RESULTS

APAP sugar spheres were successfully coated to 20% w/g of ETHOCEL HP at a coating efficiency between 94 – 98% for all coating trials. After the samples were coated, they were statically cured in the oven at 60˚C for 2 hours or dynamically cured at 40 or 60˚C for 60 min.

Figure 1 shows the drug release of APAP for the uncured vs various curing conditions and illustrates dynamic curing reduces drug release much more when compared to static curing. Furthermore, dynamic curing at 40°C versus 60°C showed no major difference which might indicate lower temperatures are still sufficient for proper film formation. Drug release profiles were also determine for samples dynamically cured at 40° C or 60° C for 15 min, compared to the 1 hr. dynamic cure profile, and determined to be nearly identical in drug release. (Figure 2) This indicates that samples might only require a 15 minute cure step and can further increase the fast coatings times associated with the dry powder coating method. Uncured, statically cured at 60°C for 2 hours, and dynamically cured for 60°C for 1 hour were placed on stability at 30° C/65%RH for 1M, 3M, and 6M time points (Figure 3 – 5). All samples showed a drop in drug release from 0 to 1M assessment and was most dramatic for the uncured sample. Regardless of static cure or dynamic curing, drug release profiles remained stable after the first month. Due to the accelerated conditions of 30°C/65%RH at 6M it is concluded that samples either dynamically or statically cured demonstrate excellent stability.

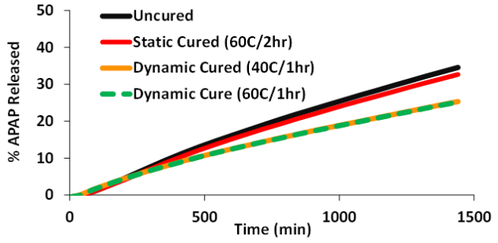

Figure 1. APAP drug release for uncured vs various curing conditions

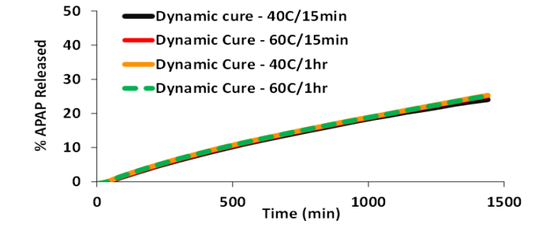

Figure 2. Dynamic curing at 40 or 60°C for 15 or 60 min

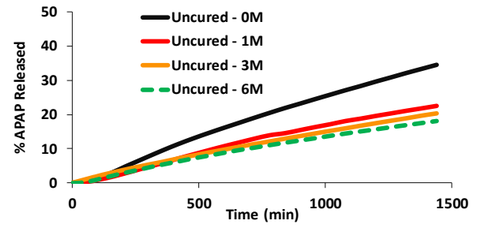

Figure 3. APAP drug release for uncured samples placed on 30°C/65%RH

SEM IMAGES

Figures 6 – 8 show SEM images for uncured, statically cured (60°C/2hr), and dynamically cured (60°C/1hr). Cross sectional images show that the uncured samples were more porous and less complete than the statically or dynamically cured. The surface morphology also shows that uncured and statically cured samples appear to have less film coherence compared to the very smooth surface of the dynamically cured samples.

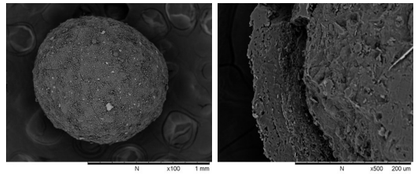

Figure 6. Uncured surface (left) and cross-section (right) SEM images of barrier ETHOCEL HP membrane at 20% wg

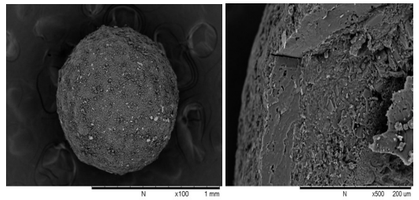

Figure 7. Statically cured at 60°C for 2hr surface (left) and cross-section (right) SEM images of barrier ETHOCEL HP membrane at 20% wg

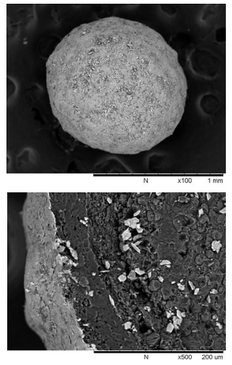

Figure 8. Dynamically cured at 60°C for 1hr surface (top) and cross-section (bottom) SEM images of barrier ETHOCEL HP membrane at 20% wg

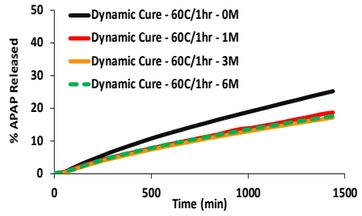

Figure 4. APAP drug release for dynamically cured samples at 60C/1hr that were placed on 30°C/65%RH stability

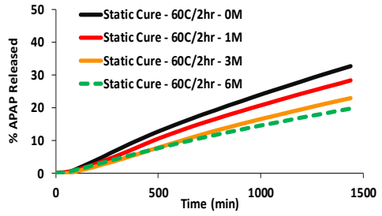

Figure 5. APAP drug release for statically cured samples at 60C/2hr that were placed on 30°C/65%RH stability

CONCLUSIONS

- ETHOCEL HP and the rotor coater are able to achieve controlled release barrier membranes very quickly compared to existing spray coating alternatives
- A cure step is required for ETHOCEL HP coatings to be stable and coatings show to be stable up to 6M at 30°C/65% RH accelerated conditions
- Dynamic curing is a combination of rotational movement and force hot air to help induce film formation and 1 hr of dynamic curing shows to provide similar to improved performance compared to traditional static curing for 2 hours at the same temperature
- Overall dynamic curing could further increase productivity by reducing required curing time as well as offer true one pot processing where multiparticulates could be drug layered, followed by functional layering (ETHOCEL HP), and curing all in the same unit.