Evaluation of Hot Melt Extruded Caffeine Pellets Containing POLYOX™
Water Soluble Resins
Nasrin Mahmoudi, Kevin O’Donnell, Brandon Rowe, Harold Bernthal, Amina Faham

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PURPOSE
Hot Melt Extrusion (HME) is a continuous manufacturing method for controlled and fast preparation of many solid dosage forms including pellets, tablets and films. It requires minimum processing steps which makes it highly efficient. POLYOX™ poly(ethylene oxide) (PEO) melts to form a thermoplastic water-soluble polymer with a low melting point of 65 °C. These polymers are excellent choices for HME among other applications and used in many pharmaceutical dosage forms. The purpose of this study was to understand the impact of vitamin E succinate (VES) on the HME process of high molecular weight POLYOX™ as well as the performance of the resulting extrudates using caffeine as model drug.

RESULTS
All six drug-free polymeric powders were extruded into white slightly opaque strands under the processing conditions. As the level of VES increased, the melt pressure decreased. The influence of VES on melt pressure was similar for both POLYOX™ grades. The melt pressure significantly dropped from approximately 1200 psi to 800 psi during extrusion of neat polymer vs polymer with 10% VES, respectively (Figure 1). Melt pressure for caffeine blends with either hydroxypropyl cellulose (HPC) or VES were the lowest among the tested formulations. As the level of HPC increased the melt pressure decreased (Figure 2). Extruder torque was 12.7-13% vs 22% for the formulation without HPC. Average amount of caffeine was 16.6, 19.8, 20.0 and 20.2% in each of four extruded formulation. SEM and IR analysis (not shown here) confirmed the crystalline state of caffeine in the pellets. Table 6 compares properties of Caffeine 20 mg dose tablets tested for dissolution. Tablets containing HME-2 formulation showed lower TS as compared to that of tablets containing HME-1. Both tablets released all of drug within 0.5 h. There was no significant difference in drug release of the tested formulations in three dissolution media as expected considering the nonionic nature of the POLYOX™. Accelerated stability studies for 12 weeks indicated no significant changes in the drug release of either pellets or tablets (Figure 6). However, pellet formulation without VES showed faster release and higher variability (F=55) compared to formulation with VES demonstrating the benefit of VES in making a more homogenous extrudate.

CONCLUSION(S)
The study showed that vitamin E succinate may be used as processing aid in hot melt extrusion of high molecular weight grades of POLYOX™ which is a common polymer for use in controlled release dosage forms particularly in abuse deterrent formulations. It is shown that the melt pressure significantly reduced from 1200 psi to 800 psi during extrusion of neat polymer vs polymer with 10% VES. Stability studies indicated there were no significant changes in drug release of HME pellets following extrusion. The stabilized HME pellets of POLYOX™ as multicarriers or in tablet formulations provided flexibility of tailoring drug release profile.

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