An Investigation into the Effect of Different Plasticizer Systems on the Enteric Protection of Theophylline Beads Coated Utilizing a Method of Applying Eudragit® L-100 and Eudragit® S-100 Polymers in Dry Form with a Conical Rotor Processor

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PURPOSE

To investigate the effect of different plasticizer systems on the enteric protection of Theophylline multi-particulate beads coated with Eudragit® L-100 and Eudragit® S-100 polymers in dry form.

METHODS

3kg of 20/25 mesh sugar spheres were loaded into a Vector Granurex® GXR-35 Rotor. 529g of micronized Theopylline was loaded into a K-Tron KT-20 Powder Feeder and dry layered onto the spheres, using a 5% PVP K-30 binding solution in water. Following the drug layering, the spheres were separated into 1 KG batches. Eudragit® L-100 was loaded into the powder feeder and dry coated onto the drug loaded spheres using two binding/ plasticizing suspensions: 50% Triethyl Citrate (TEC) and 50% Dibutyl Sebacate (DBS) in water. Tween 80 was added to both suspensions at a 0.5% level as an emulsifying agent. The process was repeated for the S-100 polymer system. Samples were taken at 25%, 30% and 35% of polymer applied for each plasticizer system. Dissolution testing was completed to study the change in release.

PROCESS CONDITIONS

Plasticizer system	Rotor Speed (RPM)	Airflow (CFM)	Process Air Temperature (ºC)	Product Temperature (ºC)
50% DBS in water	250	8-10	50	17-20
50% TEC in water	250	8-10	50	17-20

EQUIPMENT

Vector Corporation Granurex GXR-35

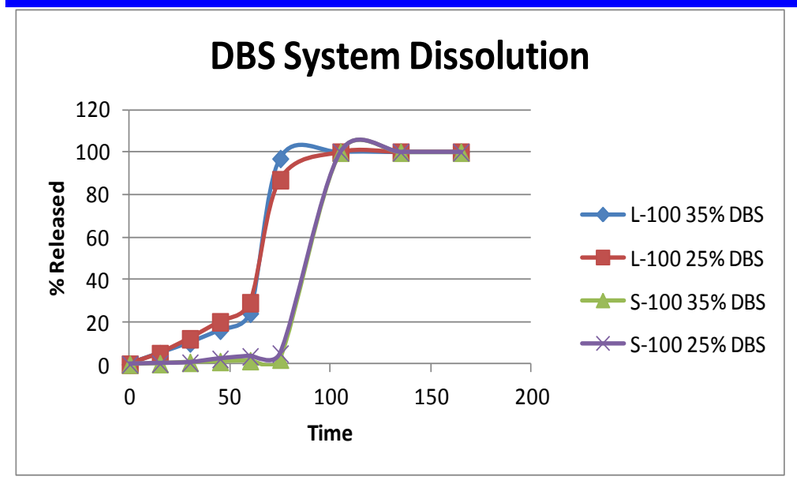
RESULTS

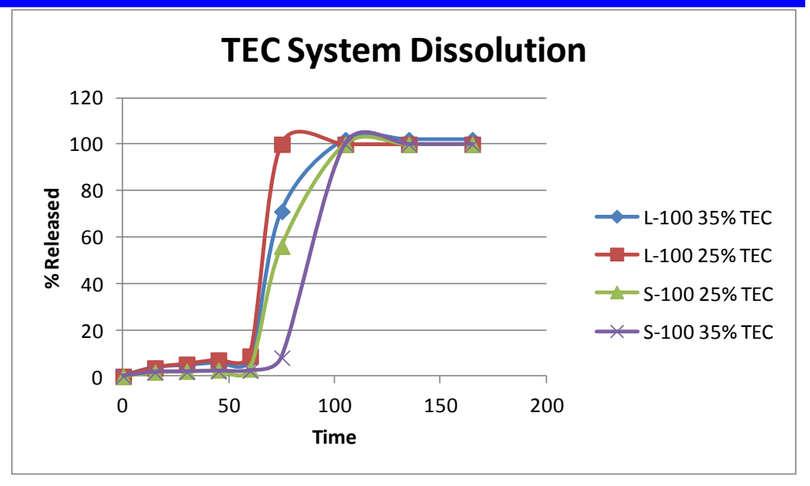
PROCESS DATA*

Plasticizer System	Polymer Applied (g)	Total Plasticizer Applied (g)	Dry Polymer Addition Rate (g/min)	Plasticizer system Spray Rate (g/min)	Process efficiency (%)	Process Time (min)	Coating Applied (%)
50% TEC in Water	350g	120g	**12.0**	12.00	98.6	28	35
50% DBS in Water	350g	120g	**12.0**	12.00	98.1	28	35

*Process data applies to both S-100 and L-100 polymer systems

DISCUSSION AND DISSOLUTION DATA





Both the DBS and TEC coating systems resulted in smooth, shiny coatings on the surface of the beads for both polymer systems. Neither plasticizing system displayed tackiness during the coating process. Dissolution showed that both plasticizer systems performed well with the S-100 polymer, providing enteric protection at coating levels of 25% and higher with minimal leakage in the acid phase. In the case of the L-100 polymer, the TEC system significantly outperformed the DBS system. The TEC/L-100 coated beads had good enteric protection at levels of 25% coating and higher, with minimal leakage in the acid phase. The DBS/L-100 beads showed significantly less enteric protection, with over 20% drug leakage in the acid phase.

CONCLUSIONS

The dissolution data showed very little difference in the enteric protection for the S-100 polymer regardless of the plasticizer system used. Both the TEC and DBS systems allowed the S-100 to fully form a film and provide enteric protection with minimal drug loss. For the L-100 polymer, TEC proved to be a more effective plasticizer than the DBS. The L-100 coated beads leaked a significant amount of drug when the DBS plasticizer system was used. At the same coating levels, the L-100 coated beads with the TEC system showed minimal drug leakage. SEM imaging also showed that the L-100 coating was not fully coalesced and had several cracks and holes in the coating with the DBS system. For the L-100 polymer system, TEC is a more effective plasticizer for dry powder coating applications.