An Investigation into the Effect of Different Plasticizer Systems on the Release Profile of Theophylline Beads Coated Utilizing a Method of Applying Micronized RS PO Polymer in Dry Form with a Conical Rotor Processor

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PURPOSE

To investigate the effect of different plasticizer systems on the release profile of Theophylline multi-particulate beads coated with micronized RSPO polymer in dry form.

METHODS

3kg of 30/35 mesh sugar spheres were loaded into a Vector GXR-35 Rotor. 409g 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 2 KG batches. 400g of Eudragit RSPO was loaded into the powder feeder and dry coated onto the drug loaded spheres using two binding/plasticizing solutions: 30% Triethyl Citrate (TEC) and 30% Dibutyl Sebacate (DBS) in water. Tween 80 was added to both solutions at a 0.5% level as an emulsifying agent. Samples were taken at 200g and 400g of RSPO 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)
30% DBS in water	250	8-10	50	17-20
30% TEC in water	250	8-10	50	17-20

EQUIPMENT

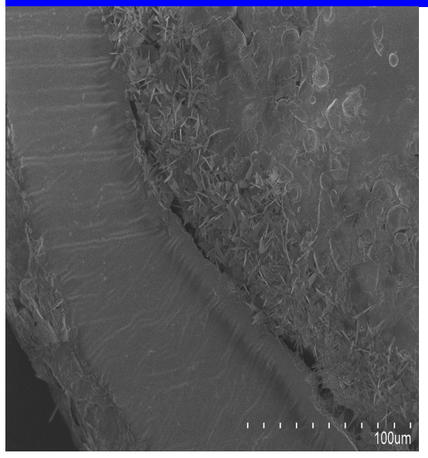
Vector Corporation Granurex GXR-35

RESULTS

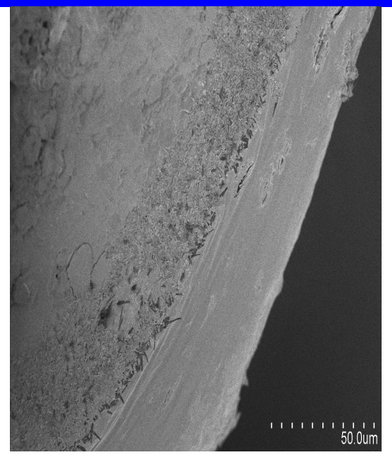
PROCESS DATA

Plasticizer System	RS PO Applied (g)	Total Plasticizer Applied (g)	Dry RS PO Addition Rate (g/min)	Plasticizer system Spray Rate (g/min)	Process efficiency (%)	Process Time (min)	Coating Applied (%)
30% TEC in Water	400g	120g	**10.0**	10.00	98.2	40	20
30% DBS in Water	400g	120g	**10.0**	10.00	96.1	40	20

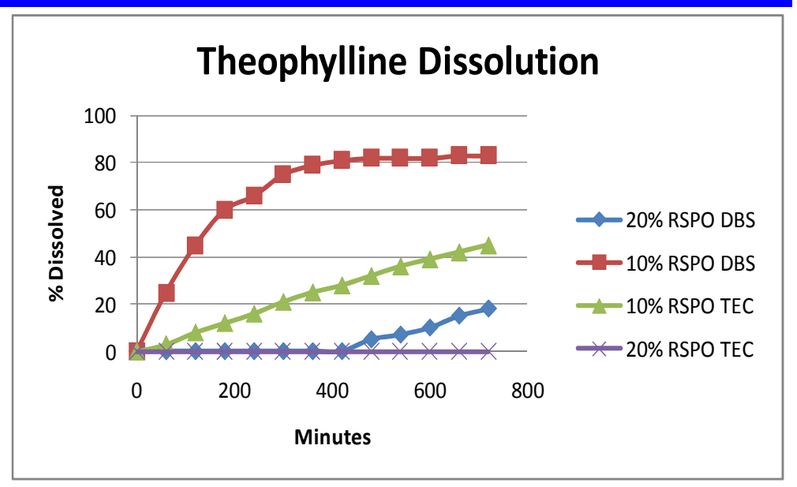
SEM IMAGES AND DISSOLUTION DATA



RSPO/DBS Cross Section



RSPO/TEC Cross Section



Both the DBS and TEC coating systems resulted in smooth, shiny coatings on the surface of the beads. The DBS beads were not tacky and were easily handled following processing. Dissolution showed that a sustained release profile was achieved at both 10% and 20% coating levels, with the 10% level releasing 85% of the Theophylline over 12 hours and the 20% coating level releasing only 15% after 12 hours. The TEC beads produced a nearly zero-order release after 12 hours at the 10% coating level and released no drug at the 20% coating level after 12 hours. The TEC beads remained very tacky following processing and were susceptible to blocking and agglomerating in storage

CONCLUSIONS

The results of the dissolution testing clearly showed that changes in the plasticizer system caused significant differences in release rates at the same coating levels. The coating using the DBS based plasticizer solution provided a superior post processing handling to the coating using the TEC based plasticizer solution, but had a faster release rate than the TEC plasticized beads. Modifications to the concentrations of the TEC or the additions of glidants to the coated beads in future testing could alleviate the blocking issues seen in this testing.

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