Novel Rotor-Granulator Powder Layering Process to Obtain Sustained Release Pellets with EUDRAGIT® RS PO

Abhishek Kathuria[1], Shawn Kucera[1], Jian-Xin Li[1], Shawn Engels[2], Brian Jensen[2]
1 Evonik Degussa Corp., Pharma Polymers, Piscataway, NJ, USA
2 Vector Corporation, Marion, IA, USA

Introduction

EUDRAGIT® polymers have been widely known for their sustained release properties when used in coating and matrix applications.
This study explores the use of EUDRAGIT® RS PO in a novel dry powder layering process to achieve sustained release pellets. Further a need of reducing the particle size of commercially marketed EUDRAGIT® RS PO is investigated.

Experimental Methods

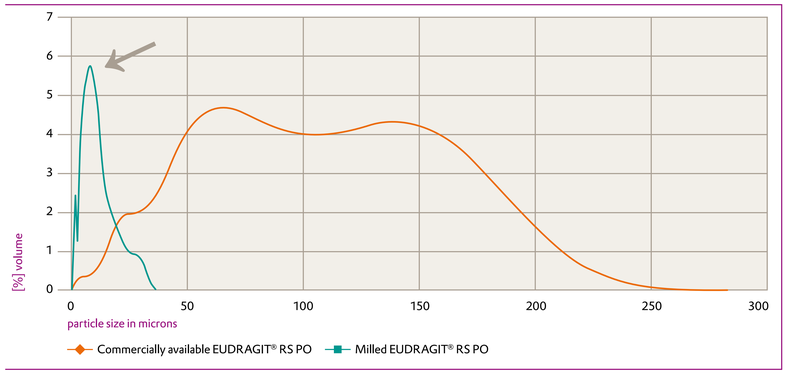
Materials:
30/35 mesh sugar spheres (Paular Corporation, NJ, USA), theophylline, PVP K-30, acetone, polysorbate 80 (Soectrum Chemical, CA, USA), dibutyl sebacate (DBS) and triethyl citrate (TEC) (Vertellus, NC, USA)

Equipment:
Vector GXR-35 Rotary Granulator/Coater (Vector Corporation, IA, USA), Fluid Energy Mill (Sturtevant Inc., MA, USA), Enhanced Laser Diffraction Particle Size Analyzer - Beckman Coulter LS230 (Beckman Coulter, CA, USA).

Method:
Neutral pellets (30/35 mesh) were dry-drug layered with theophylline using 5% PVP K-30 binding solution in water in Vector GXR-35 Rotary Granulator/Coater.

Separately EUDRAGIT® RS PO powder was micronized by jet-milling (Beckman Coulter L230) to a d50 of about 8 microns. The particle size distribution of polymer powder before and after milling is represented below:

Particle size distribution



The drug layered pellets were divided into eight sub-groups and coated with the formulations described in table below:

Description of formulations investigated

Formulation	1	2	3	4	5	6	7	8
Solvent	Water	Water	Water	Water	Acetone	Water	Acetone	Water
Plasticizer	DBS	DBS	TEC	TEC	TEC	DBS	DBS	TEC
Polymer State (Micronized/Unmicronized)	M	M	M	M	M	M	M	UM
Percent polymer coating	10%	20%	10%	20%	10%	15%	10%	10%
Legend:	M: Micronized, UM Unmicronized							

400 g of EUDRAGIT® RS PO was loaded into the powder feeder and dry coated onto the drug loaded spheres using binding/plasticizing dispersion as described in the matrix above.

The plasticizer dispersion/solution was prepared in solvent at a 30% solids level. Polysorbate 80 was added to aqueous dispersions at a 0.5% level as an emulsifying agent.

Solid polymer powder and the plasticizer dispersion/solution was sprayed at a proportion of 1:1 in the Vector GXR-35. Spray rate was approximately in 10-12 gm/min for each.

Samples were taken as described in the matrix above. Furthermore, selected samples were cured to identify if there is any effect of curing on the release profile from samples.

Analytics:
The surface and cross-sectional morphology of the polymer-coated pellets was observed via scanning electron microscopy.

Dissolution testing was conducted per USP specifications using USP apparatus 2 (basket method) in 900 ml of 37.2°C DI Water at 100 rpm to test for drug release profile of the beads.

Results and Discussion

Unmicronized EUDRAGIT® RS PO was not effective in producing any sustained release effect.

The particles produced using DBS (30%) as plasticizer were free flowing and non-lumping. The particles manufactured using TEC (30%) as plasticizer clumped up and could not be manufactured as a viable product. TEC at 30% level was obviously too high and will need to be lowered to achieve better results.

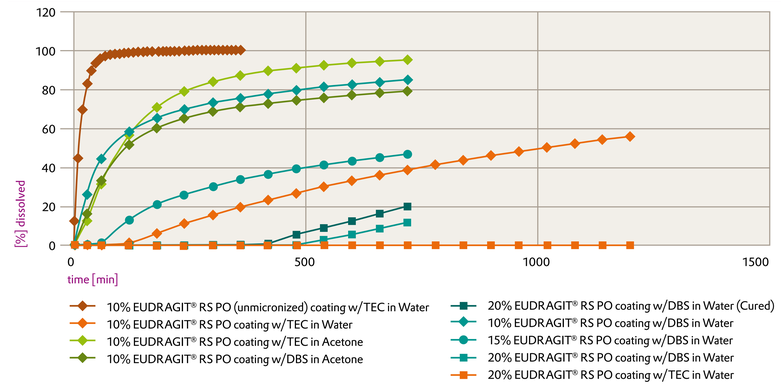
The release rates from both the particles were largely independent from the plasticizer or the solvent used for plasticizer dispersion. The most significant variable for the release rate was the amount of EUDRAGIT® RS PO coating applied. The release rate slowed down as the coat applied increased from 10% to 15%, and significantly more when the coating applied increased to 20%.

Curing at 40°C for 24 hours had no significant impact on the release curves for which it was studied. It appeared that the coating process was very effective in getting the plasticizer equilibrated across the film.

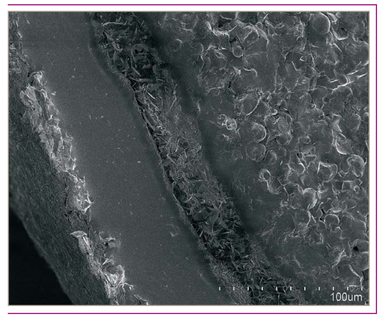
Comparison of processing methods

	Polymer Spray Rate	Coating Time to achieve 10% coat
Conventional Process (2000 g batch – GPCG 1.1)	8 g/min (~ 2.4 g/min actual polymer)	250 min
Rotor Granulator Powder layering	10 – 12 g/min	40 min

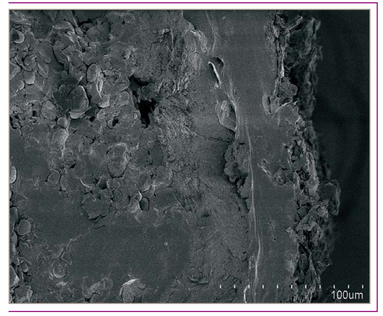
Dissolution profiles SR Pellets



10% EUDRAGIT® RS PO Coating with DBS



10% EUDRAGIT® RS PO Coating with TEC



Conclusion

The effectiveness of the application for achieving sustained release profiles using micronized EUDRAGIT® RS PO was demonstrated. The results indicate that no curing is needed if micronized EUDRAGIT® RS PO is used.
The advantages of using this technology are:

- Need of minimal solvent.
- Faster application rate (up to 6 times faster than conventional coating applications).
- Uniform cohesive, dense film with free flowing particles.
- Possibility of a continuous coating process.

References

EUDRAGIT® Application Guidelines, 11th Edition (09/2009), Evonik Röhm GmbH

Evonik. Power to create.

FREUND VECTOR

EVONIK INDUSTRIES