Utilization of a Novel Rotor-Granulator Powder Layering Technique to Tasted Mask Acetaminophen Pellets with EUDRAGIT® E PO

Shawn Kucera[1], Jian-Xin Li[1], Shawn Engels[2], Brian Jensen[2]
[1]Evonik Degussa Corp., Piscataway, NJ, USA; shawn.kucera@evonik.com; [2]Vector Corporation, Marion, IA, USA

Introduction

EUDRAGIT® E PO is a polymer commonly used for the taste masking of bitter drugs. The polymer can be applied from an organic system using a volatile solvent or formulated as a colloidal solution as an aqueous-based system. A new technology, recently developed by Vector Corporation, has used film-forming polymers to coat dosage forms via a powder layering technique.

The purpose of this study was to investigate the taste masking of acetaminophen beads with EUDRAGIT® E PO powder utilizing a novel, low temperature rotor-granulator process.

Experimental Methods

Materials:
EUDRAGIT® E PO (Evonik Röhm GmbH, Darmstadt, Germany), PVP K-30, polysorbate 80, and micronized acetaminophen (Spectrum Chemical, Gardena, CA, USA), dibutyl sebacate (DBS) and triethyl citrate (TEC) (Vertellus, Greensboro, NC, USA).

Table 1: Coating formulation and process conditions for 40% weight gain EUDRAGIT® E PO on a 3 kg batch of acetaminophen-layered sugar spheres

	Plasticizer system	
	10% TEC in water	10% DBS in water
EUDRAGIT® E PO applied [g]	400.0	400.0
Total plasticizer applied [g]	33.0	33.0
Dry EUDRAGIT® E PO addition rate [g/min]	10.0	10.0
Plasticizer system spray rate [g/min]	8.0	8.0
Process efficiency [%]	96.1	98.2
Process time [min]	40	40
Coating applied [% weight gain EUDRAGIT® E PO]	40.0	40.0

Methods:
Sugar spheres (3 kg, 30 – 35 mesh) were loaded into a Vector GXR-35 Rotary Granulator/Coater (Vector Corporation, Marion, IA, USA). Micronized acetaminophen was dry layered onto the spheres using a 5% PVP K-30 binding solution in water. Following the drug layering, EUDRAGIT® E PO was dry coated onto the spheres using a 10% solution of either DBS or TEC in water.

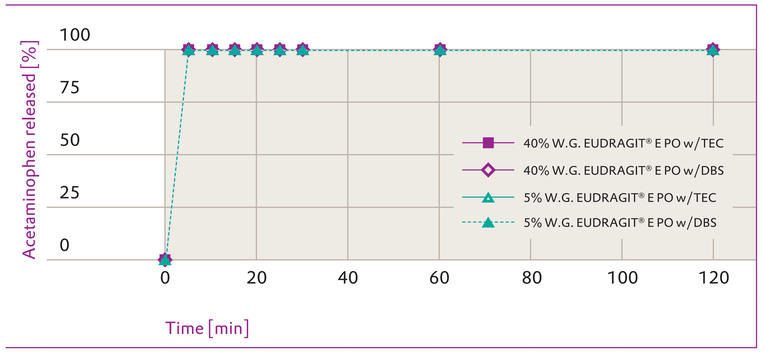
Polysorbate 80 was added to both solutions at a 0.5% level as an emulsifying agent. Samples were taken at various weight gains for each plasticizer system and cured at 0, 2, 3, and 24 hours at 40°C in an oven. Dissolution was performed according to USP Method 1 (basket method) at 75 rpm in 900 ml of 37.2°C, 0.1 N HCl (USP pH 1.2). Taste masking was determined by having 7 volunteers place ~300 mg of the coated pellets on the tongue for a period of 1 minute. The surface and cross-sectional morphology of the coated pellets was observed via scanning electron microscopy.

Results and Discussion

Product Yield:
For the 40% EUDRAGIT® E PO weight gain batches, the layering process produced yields of 98.2% for the DBS plasticized system and 96.1% for the TEC plasticized system. The GXR-35 and powder feeder were free of powder for the DBS formulation, while the TEC formulation showed a small buildup on the rotor, which led to lower overall process yield.

Dissolution:
All formulations released 100% of the active ingredient within 5 minutes of testing in the pH 1.2 media regardless of weight gain, curing conditions, or plasticizer system utilized.

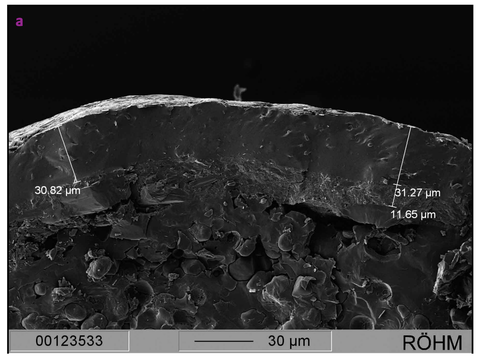
Figure 1: Drug release rate of EUDRAGIT® E PO coated acetaminophen pellets with either a 5% or 40% polymer weight gain in 900 ml of 0.1 N HCl media

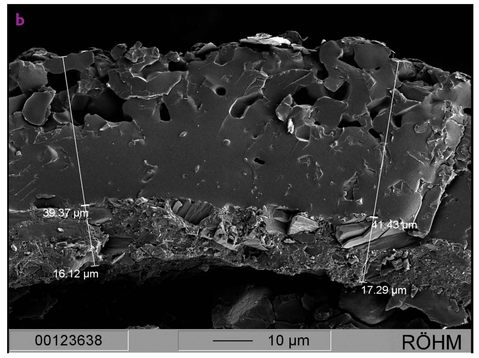


Taste Masking:
A minimum of 5% EUDRAGIT® E PO polymer weight gain was required to achieve total taste masking of the beads for a period of 1 minute, with the formulation containing TEC described as having a slightly sweeter taste than the formulation containing DBS.

Morphology:
Scanning electron microscopy revealed that complete film formation was achieved directly after processing and that no curing step was required. Formulations containing TEC exhibited a more porous film structure than those containing DBS, indicating that for powder layered systems, DBS should be the plasticizer of choice.

Figure 2 a and b: Cross-sectional SEM of acetaminophen layered pellets coated with 20% EUDRAGIT® E PO and a plasticizing system utilizing (a) DBS, (b) TEC





Conclusion

Powder layering via a rotor-granulator was shown to be a fast and effective method to taste mask acetaminophen pellets with EUDRAGIT® E PO. The amount of EUDRAGIT® E PO needed for successful taste masking was comparable to that required for a more traditional fluidized bed coating process.

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