Rotor-granulator powder layering process for pellets using fully formulated enteric and reverse enteric polymers: Acryl-EZE® and EUDRAGIT®E PO ReadyMix

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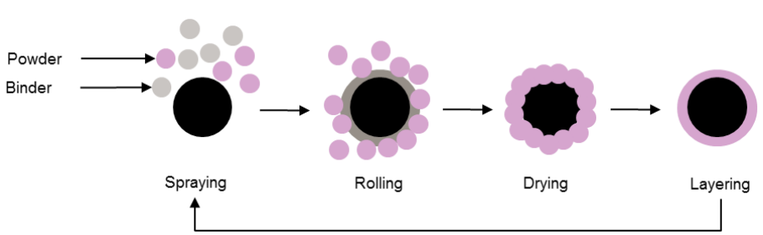
Introduction

Conventional functional coating systems require the use of aqueous coating dispersions with limitation for highly moisture sensitive actives or solvent systems requiring additional safety measures. As there is no drying for the solvent needed, powder layering processes are quicker and it do not require the use of any solvents and uses only minimal amount of water emulsified with liquid plasticizer as a binder to facilitate film formation. The purpose of this study was to investigate a rotor-granulator powder layering process for two commercially available ready-to-use coating systems: EUDRAGIT® E PO ReadyMix and Acryl-EZE®. EUDRAGIT® E PO ReadyMix is soluble below pH 5.0 and swellable and permeable above pH 5.0 making it an ideal choice for taste masking (reverse enteric) applications whereas Acryl-EZE® is an enteric coating system that resists acidic pH in the stomach and is completely soluble above pH 5.5.

Experimental methods

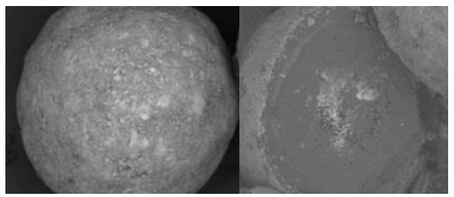
Sugar spheres (707-841 µm) were dry-drug layered with 28% acetaminophen (APAP) using a 5% polyvinyl pyrrolidone (PVP K 30) binder solution in a Freund-Vector Rotary Granulator/ Coater. The drug layered pellets were powder coated with EUDRAGIT® E PO ReadyMix and Acryl-EZE® 93A separately. For EUDRAGIT® E PO ReadyMix coating, 7% dibutyl sebacate was used as a binder and plasticizer. The powder was applied at 12 g/min, while the plasticizer solution was sprayed at 10 g/min. For the Acryl-EZE® coating, 30% triethyl citrate was added as a plasticizer. The powder and plasticizer solution were applied at 12 g/min. Both processes utilized rotor speed of 250 rpm and airflow of ~21 m^3/h with a product temperature range from 17-19°C during the process, warming to 30°C during drying and a total process time of 50 minutes. The drug pellets were coated to achieve a 10, 20, 30, 40 and 50% total weight gain. To investigate effect of curing, pellets were cured for 24 hours at 45°C. Additionally, EUDRAGIT® E PO ReadyMix coated pellets were put on storage stability testing at 40°C/75% r.h. for a period of 1 month in sealed HDPE bottles and moisture content was measured using a loss on drying apparatus. Dissolution testing was conducted using USP apparatus 1 in 0.1N HCl and buffer pH 6.8 at 70 rpm. Samples were analyzed using fiber optic dissolution system. Scanning electron microscopy (SEM) was used to observe the coating characteristics. Additionally, the pellets powder coated with EUDRAGIT ® E PO ReadyMix were exposed to a range of pH media to investigate the effect of different physiological pH on the drug release profile.

Figure 1: **Process scheme for the rotor-granulator powder layering**



Results and discussion

Figure 2: **SEM images of a pellet dry coated with EUDRAGIT® E PO ReadyMix; surface (left) and cross section (right)**



Pellets powder coated with EUDRAGIT® E PO ReadyMix showed a lag time of up to 35 minutes in phosphate buffer pH 6.8, dependent on the total weight gain (Figure 3, right). This indicates the taste masking potential of powder coated EUDRAGIT® E PO ReadyMix. For the dry coating application, the plasticizer also served as an efficient binder resulted in dense coated film as can be seen in the SEM images (Figure 2). Moreover, the moisture content of the pellets was measured by loss on drying apparatus before and after 1 month storage at 40°C/75% r.h which keep unchanged at 2%. This confirms the efficacy of powder coated EUDRAGIT® E PO ReadyMix for moisture protection. APAP released immediately in acidic media thus exhibiting immediate release profile (Figure 3, left). Additionally, effect of various physiological pH on the dissolution properties was evaluated for the 50% w/w EUDRAGIT® E PO ReadyMix formulation (Figure 4). At phosphate buffer pH 6.2 a 3.5 minute lag time was observed while all the lower pH media showed immediate release profile. For the powder coated pellets with 50% w/w Acryl-EZE® 93A less than 10% APAP was released in the initial 120 minutes in pH 1.2 media (Figure 5, right) followed by complete release when the media was switched to phosphate buffer pH 6.8 (Figure 5, left). Curing did not appear to have a significant impact on the dissolution characteristics of the powder coated pellets. With the dry powder coating technique, 30% weight gain was needed for achieving minimum and 50% for achieving optimum functionalities of both polymers. Additional formulation optimization is to recommend to adjust the lag time depending on the desired application as well as the used drug.

Figure 3: **Powder coating with EUDRAGIT® E PO ReadyMix - dissolution profiles of APAP in pH 1.2 media (left) and phosphate buffer, pH 6.8 (right)**

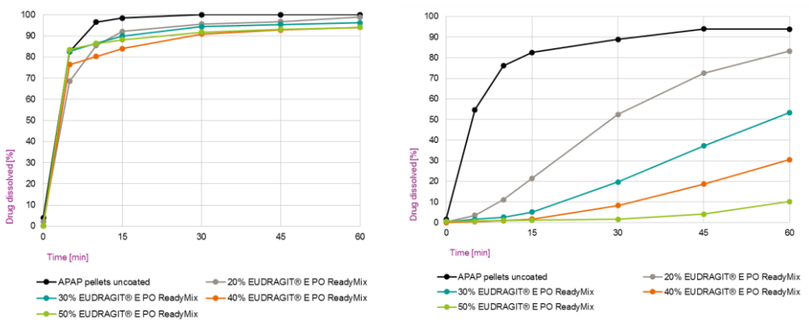


Figure 4: **Effect of dissolution test media on APAP pellets powder coated with 50% EUDRAGIT® E PO ReadyMix**

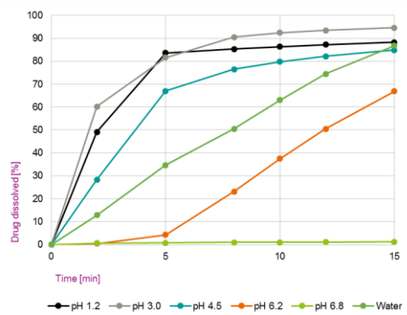
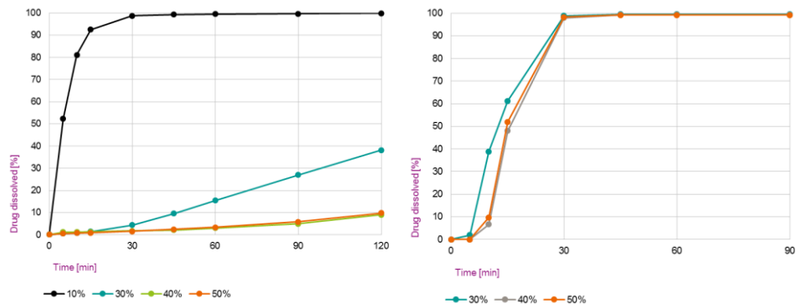


Figure 5: **Powder coating with Acryl-EZE® 93A: Dissolution of APAP pellets in pH 1.2 media (left) and phosphate buffer, pH 6.8 (right)**



Conclusion

This study demonstrates feasibility of dry powder coating technique with fully formulated coating systems to achieve uniform coatings. EUDRAGIT® E PO ReadyMix has been successfully demonstrated to achieve taste masking functionality by using the dry powder layering process. Enteric protection has also been accomplished by powder layering with Acryl-EZE® 93A. Compared to aqueous or solvent coating, the dry coating process is much less time consuming and has advantages in applications to moisture and heat sensitive actives. For APAP pellets used in this study, minimum 30% total weight gain was needed while total weight gain of 50% yielded optimum results for both ready to use coating systems.

References

1. Evonik Industries AG (2012): EUDRAGIT® Application Guidelines, Ed. 12th

Evonik. Power to create.