Production Scale Semipermeable Coating of Push-Pull Osmotic Pump Tablets

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Abstract Summary

Opadry® CA, a fully formulated semipermeable membrane (SPM) coating system, was applied to glipizide bilayer tablets at a batch size of 70 kg using co-solvent mixtures of acetone and water at varying ratios. The SPM coating had excellent film clarity and dense film structures regardless of water concentration in the coating solutions. The push-pull osmotic pumps (PPOP) provided consistent zero order drug release. The release rates decreased with increasing coating weight gain (film thickness) of Opadry CA.

Introduction

In PPOP technology, a bilayer core is surrounded by a SPM, the permeability of which influences the rate of media influx into the core. The membrane quality is critical to the performance of the osmotic pump, as it controls the media uptake and osmotic pressure gradient, the rate of polymer hydration and, therefore, the drug release rate from the osmotic dosage form.[1] Opadry CA, a fully formulated semipermeable coating system, provides a simplified means of preparing and applying the SPM coating during osmotic tablet manufacturing. The recommended coating parameters for Opadry CA are short gun-to-bed distance, low atomizing pressure, low product temperature and relatively high spray rate.[2] Previous studies have shown that transparent and dense SPM coatings were achieved when applying those process conditions at various lab scales (1-14 kg charge).[2,3] The purpose of this study was to demonstrate the application of Opadry CA at a production scale (70 kg batch) and to evaluate the effect of co-solvent ratio on membrane quality and drug release from osmotic pumps at various weight gains.

Experimental Methods

Two coating trials were conducted using a LDCS Pro Hi-Coater System (Freund-Vector Corporation, USA) with a 36 inch, 110 liter fully-perforated pan. Opadry CA solutions were prepared at 7% w/w solids in two co-solvent ratios of acetone and water (90:10 and 94:6 w/w). Coating solutions were prepared by vigorously stirring the co-solvent mixtures, while slowly pouring Opadry CA powder into the liquid vortex, then stirring continuously for 45 minutes until fully dissolved. Opadry CA solutions were applied to glipizide bilayer 9.5 mm diameter tablets (11.2 mg dose & 330 mg tablet weight) to a theoretical weight gain (WG) of 6-10% w/w. A 3 spray gun manifold system was used with Vector AT spray guns fitted with 1.5 mm nozzles and air caps (**Figure 1**). The coating parameters are listed in **Table 1**. After coating, tablets were dried in a vacuum oven at 40°C for 24 hours. A 0.5 mm drug delivery orifice was laser-drilled (Cobalt 250, InkCupsNow, USA) through the SPM coating on the drug layer side of each osmotic tablet.

Figure 1. Three-Gun Manifold System and Spray Pattern (4.0" From Surface)

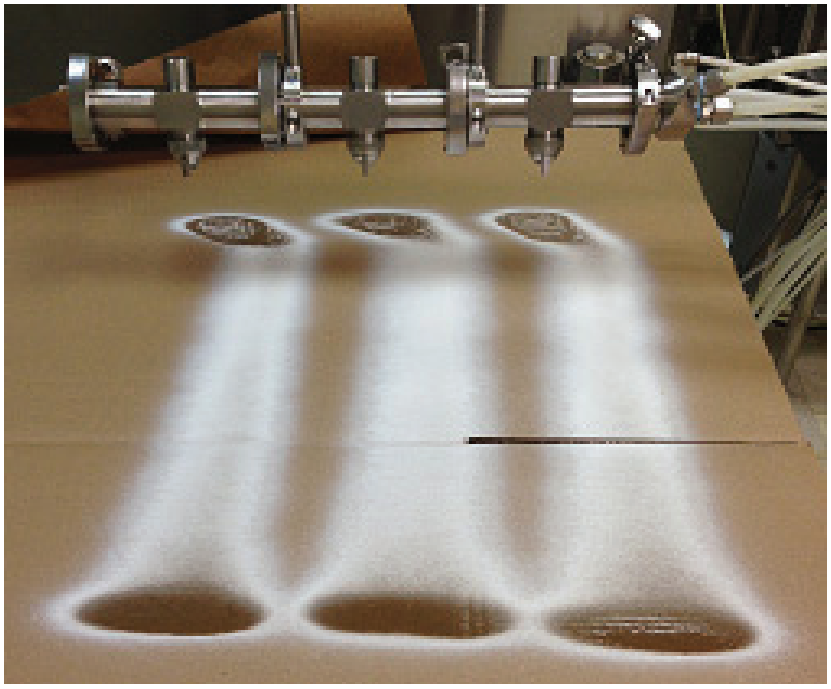


Table 1. Opadry CA Coating Parameters

Coater type	Vector LDCS Pro
Pan size	36", 110 L
Solids content (%)	7
Charge (kg)	70
Number of Vector AT guns	3
Inlet temperature (°C)	39 – 42
Exhaust temperature (°C)	27 – 29
Atomizing air pressure (Bar / psi)	1.5 / 21
Pattern air pressure (Bar / psi)	1.0 / 15
Product temperature (°C)	24 – 26
Drying air volume (CFM / m^3 / hr)	1000 / 1700
Pan speed (rpm)	10
Spray rate (g/min)	480 – 520
Gun-to-bed distance (inch / cm)	4.0 / 10.2
Coating time (min)	182 – 200

Dissolution studies were conducted in simulated intestinal fluid (SIF, pH 7.5) without enzymes using USP Apparatus II with sinkers at 50 rpm. Drug release profiles were measured using a UV-Vis spectrophotometer (Agilent Technologies, USA). The three-point dissolution performance ($t_{10\%}$, $t_{50\%}$, $t_{80\%}$, time for 10, 50 and 80% drug dissolved, respectively) was calculated. The thickness and morphology of the films were examined with a Hitachi Field Emission Scanning Electron Microscopy (FE-SEM; vs4300, Hitachi High-Tech, Japan).

Results and Discussion

Tablets were successfully coated with Opadry CA using both co-solvent ratios. Minimal spray drying was observed during both coating trials. The Opadry CA coatings had excellent clarity and gloss (**Figure 2**). The co-solvent ratio had no impact on film appearance on the tablets. The scanning electron microscopy (SEM) images showed dense and nonporous film structures (**Figure 3**) consistent with the transparent SPM coating appearance for all samples. Membrane thickness increased with increasing coating weight gain, ranging from 70-120 µm at 6-10% WG.

Figure 2. Appearance of Glipizide Osmotic Pumps: (a) Uncoated Core; (b) Coated Tablet (acetone:water, 90:10 w/w); (c) Coated Tablet (acetone:water, 94:6) at 10% WG

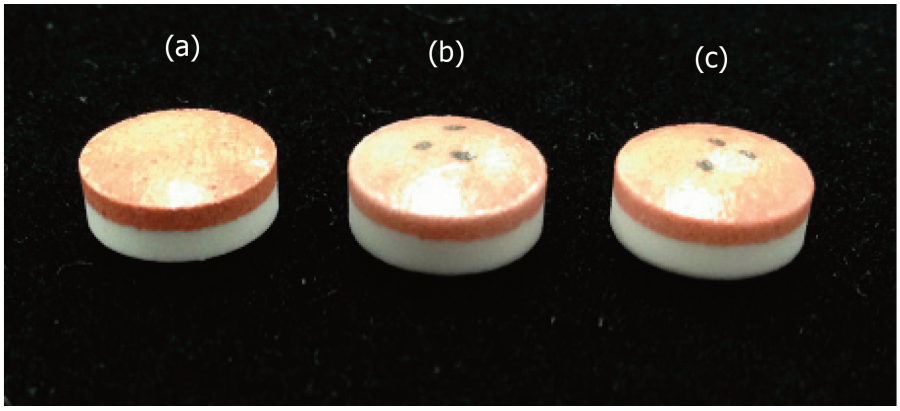
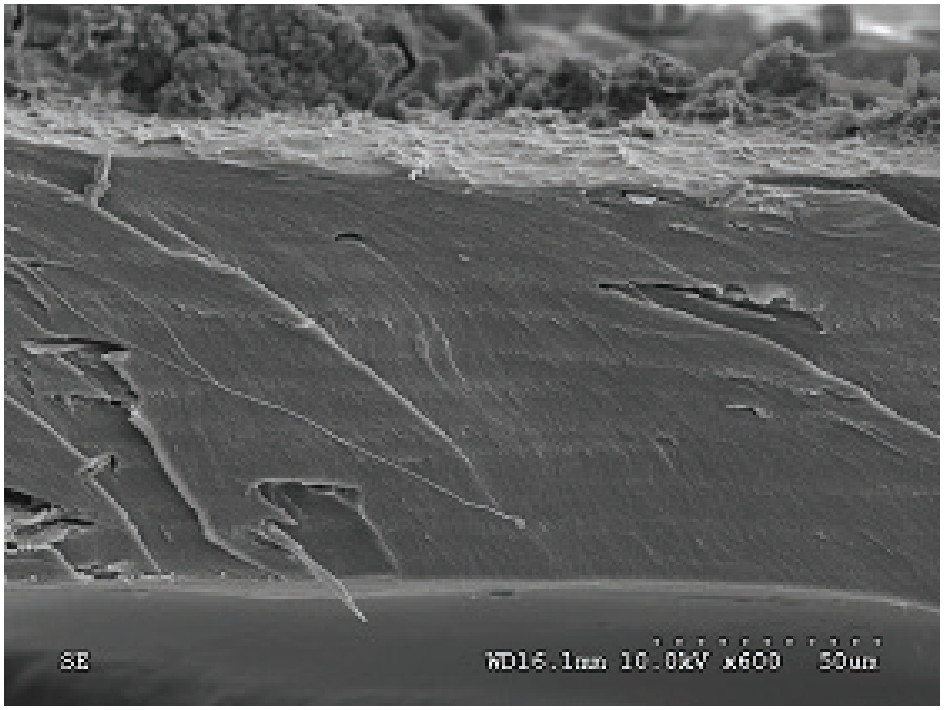


Figure 3. . Cross-Section View (600X) of Opadry CA Coating (acetone:water, 90:10 w/w, 10% WG)



Similar zero order drug release profiles were obtained for glipizide osmotic tablets irrespective of the co-solvent ratios used to prepare the Opadry CA solutions (f_2 = 81) (**Figure 4**). **Figure 5** shows that drug release rate decreased with increasing SPM coating weight gain and that water concentration in the co-solvent had minimal impact on the drug release rate.

Figure 4. Glipizide Release Profiles from PPOP Tablets (Opadry CA at 10% WG)

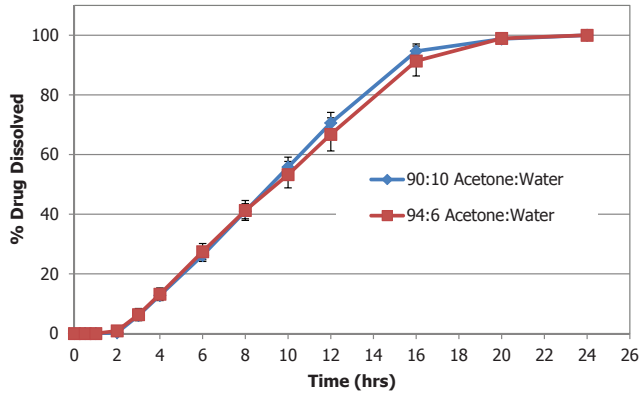
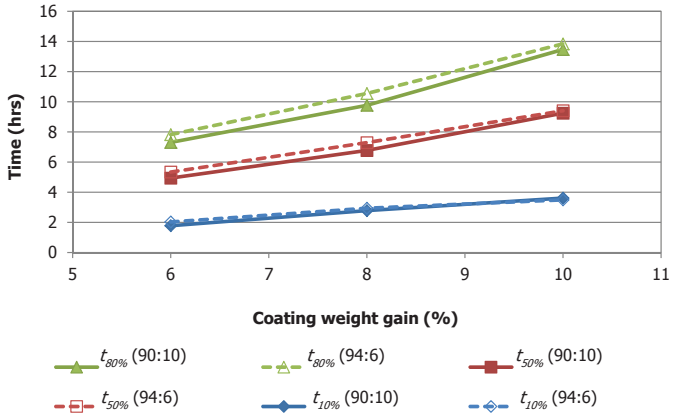


Figure 5. Comparison of Three-Point Dissolution Data ($t_{10\%}$, $t_{50\%}$, $t_{80\%}$) for Glipizide Osmotic Tablets



Conclusions

Opadry CA was successfully applied in production scale coating equipment at a batch size of 70 kg. Coating process conditions of reduced gun-to-bed distances, low-to-moderate air pressures, lower product bed temperature and higher spray rates were confirmed in the scale-up trials. The osmotic tablets demonstrated excellent membrane clarity and robust drug release regardless of the co-solvent ratios.

References

1. S.L. Shamblin, Controlled release using bilayer osmotic tablet technology: reducing theory to practice, In: H. Wen, K, Park, Oral Controlled Release Formulation Design and Drug Deliver: Theory to Practice. 2010; John Wiley & Sons, Inc., 129-153.
2. Martin L, et al. Investigation of Critical Process Parameters for Coating Push-Pull Osmotic Pump Tablets with Opadry CA. AAPS Annual Meeting and Exposition, 2012.
3. Deng H, et al. The Influence of Opadry® CA Weight Gain and Solvent Ratio on Performance of Push-Pull Osmotic Pump Tablets. 39th Annual Meeting and Exposition of Controlled Release Society, 2012.