Applications of Opadry® CA, A Fully Formulated Cellulose Acetate Based Coating System for Osmotic Pump Tablets

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Purpose

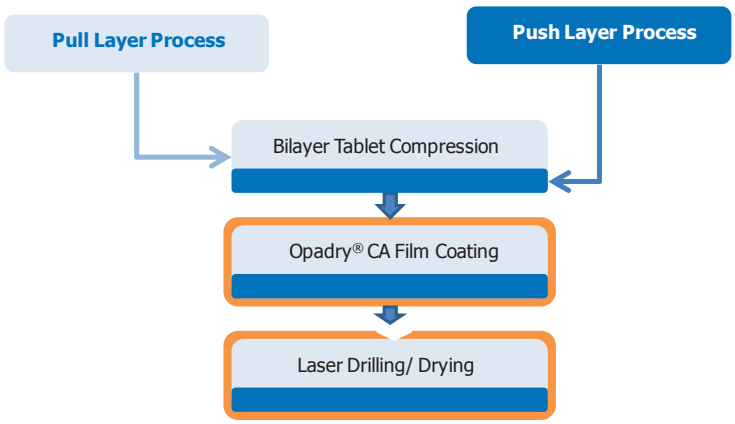
Osmotic pumps have gained significant interest in oral solid dosage form development mainly due to their ability to deliver drugs at constant rates (zero order release) independent of media pH and hydrodynamics of the surrounding media.[1-5] In general, the drug release rate from an osmotic pump is governed by the osmotic potential created by soluble components within the core and the surrounding medium, and the permeability of the semipermeable membrane (SPM) coating.[2] The purpose of the present study was to investigate the equivalence of Opadry CA to conventional multi-step preparations in coating application and performance of push-pull osmotic pump (PPOP) tablets. In addition, the stability of the Opadry CA formulation and the resulting PPOP tablets were assessed.

Methods

Tablet Preparation

The manufacturing process for push-pull osmotic pump tablets is shown in Figure 1.

Figure 1. Manufacturing Process for Push-Pull Osmotic Pump Tablets



Coating Substrates: glipizide bilayer tablets, 10 mg dose, 330 mg tablet weight
Coating Materials: Opadry CA coating systems
Solvents: acetone, water

Coating Solution Preparation:

a) One-step method: Opadry CA was added directly to acetone-water co-solvent and mixed for 45 mins (Figure 2)

b) Multi-step method: cellulose acetate (CA) was dissolved separately in acetone and polyethylene glycol (PEG) in water, followed by adding the aqueous PEG solution to the organic CA solution (Figure 3). The solutions were mixed for 75-110 min, depending on the CA/PEG and acetone/water ratios.

Figure 2. Opadry CA Solution Preparation

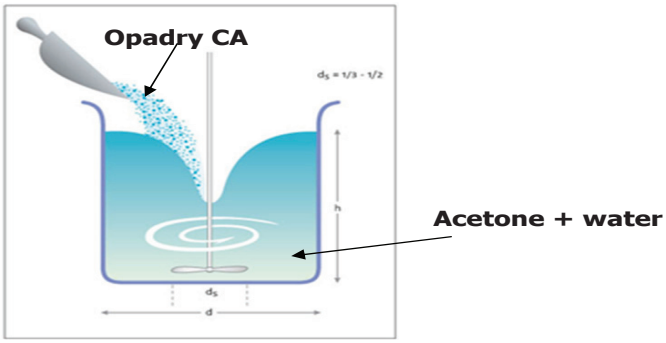
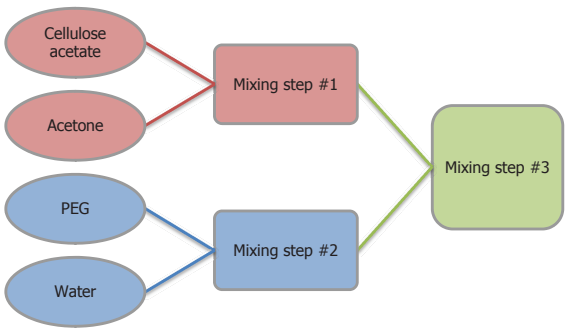


Figure 3. Conventional Method of CA Solution Preparation



Organic Coating: Vector Hi-Coater LDCS (Vector, USA) using a 2.5 L side-vented coating pan (coating param-

Table 1. Coating Process Parameters

Process Parameters	Value
Batch size (kg)	1.5
Gun-to-bed distance (inch / cm)	2.5 / 6.3
Inlet temperature (°C)	41 - 43
Exhaust temperature (°C)	30 - 33
Product temperature (°C)	26 - 29
Airflow (cfm / m^3/hr)	80 / 136
Fluid delivery rate (g/min)	29 - 30
Atomizing air pressure (psi / bar)	21.0 / 1.4
Pattern air pressure (psi / bar)	7.5 / 0.5
Pan speed (rpm)	18
Theoretical weight gain (%)	10

Drying: Vacuum oven at 40°C for 24 hr

Laser Drilling: 0.5 mm delivery orifice on the pull layer side of PPOP tablets (Cobalt 250, InkCupsNow, USA)

Top-Coat: Opadry® II, 6% WG (6% was required to obscure the laser drilled orifice)

Characterization and Drug Release

The total solution preparation time and turbidity (UV-Visible spectrometer, Agilent Technologies, USA) were recorded for each method. The resulting PPOP tablets were evaluated for drug dissolution. In addition, Opadry CA (CA : PEG 3350 = 9:1 w/w) and the coated PPOP tablets (Opadry CA at 10% WG with and without top-coat) were stored at 40°C/75% RH (with or without desiccant) for 6 months. At each time interval, formulated blends were examined for moisture content, CA content and coating assessment. PPOP tablets were evaluated for drug assay and drug release. Dissolution method: USP Apparatus II, at 50 rpm with sinkers in 900 mL of simulated intestinal fluid (SIF, pH 7.5) without enzyme at 37 ± 0.5°C

Results

Solution Preparation Time and Turbidity

Opadry CA coating systems at various CA : PEG ratios easily dissolved into acetone-water mix within 45 min, compared to longer preparation times (75-110 min) required for the multi-step method (Table 2). Clear coating solutions of low turbidity (absorbance at 400 nm, CA : PEG = 9:1 w/w) were obtained with both preparation methods, and were stable for at least 4 hours after preparation (Figure 4).

Table 2. Solution Preparation Time: Opadry CA One-Step Method vs. Conventional Multi-Step Method (at 7.0% Solids Content)

CA : PEG	Acetone : Water	Solution Preparation Time (min)	
		One-Step	Multi-Step
9:1	90:10	30	75
9:1	94:6	30	100
8:2	90:10	30	80
8:2	94:6	45	110
7:3	90:10	30	80
7:3	94:6	45	110

Figure 4. . UV Absorbance of CA solutions at 7% Solid Contents: Opadry CA Solution 1 (Acetone:Water = 96:4 w/w); Opadry CA Solution 2 (Acetone:Water = 90:10 w/w)

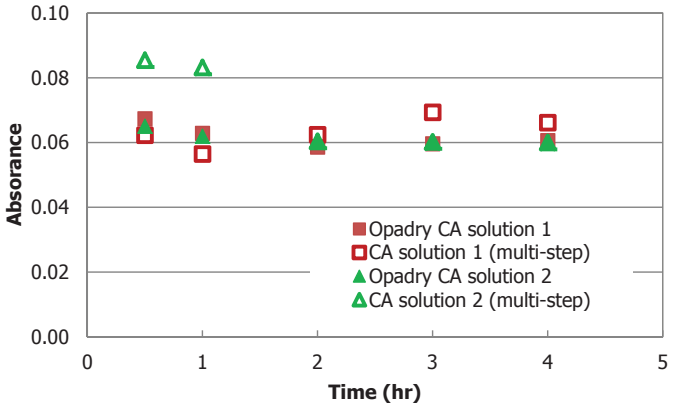
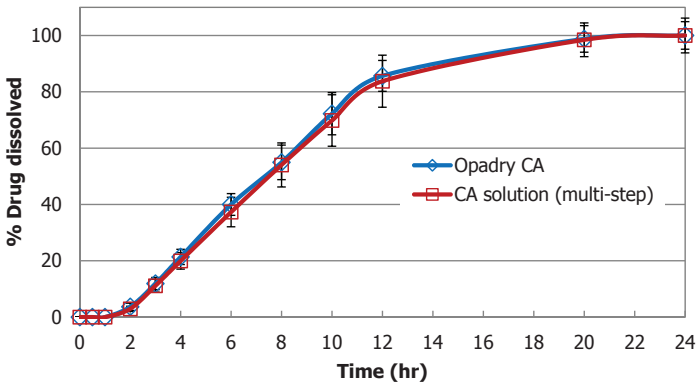


Figure 5. Drug Release Profiles from Glipizide PPOP Tablets Coated with CA Solution: (CA : PEG 3350 = 9:1 w/w, Acetone: Water = 90:10 w/w) Prepared by One-Step (Opadry CA) or Multi-Step Method (n = 6, f_2 = 87)



Drug Release

Figure 5 shows similar drug release profiles (f_2 = 87) from glipizide PPOP tablets coated with CA solutions, irrespective of preparation method, indicating that the quality of SPM, hence PPOP performance, is comparable for both methods.

Opadry CA Powder Stability

The moisture content was consistently low for Opadry CA powder samples (CA : PEG 3350 = 9:1 w/w) during the 6-month storage at 40°C/75% RH (Figure 6). All powder samples exhibited reproducible CA content (RSD < 0.5%). Figure 7 shows that Opadry CA coating system had excellent stability and provided similar drug release profiles (f_2 = 67-90) when applied to glipizide bilayer tablets. Furthermore, use of desiccant improved the stability of Opadry CA and subsequently the dissolution performance of the PPOP tablets (f_2 = 90 vs. f_2 = 67).

Figure 6. Moisture Content of Opadry CA Powder, Accelerated Storage Condition

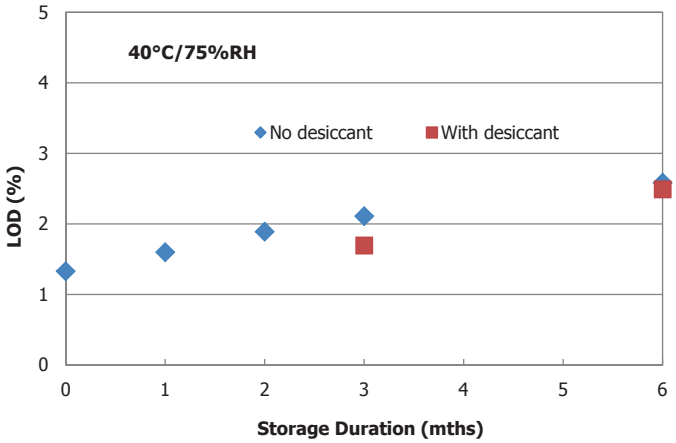
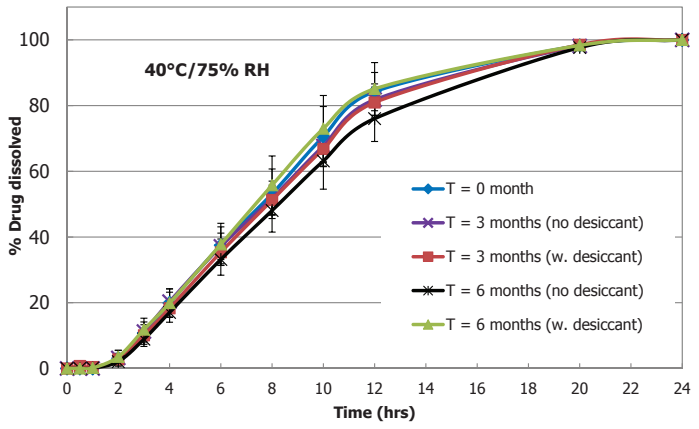


Figure 7. Drug Release Profiles from Glipizide PPOP Tablets Coated with Opadry CA Stored in Accelerated Storage Condition (f_2 = 67-90) (n = 6)

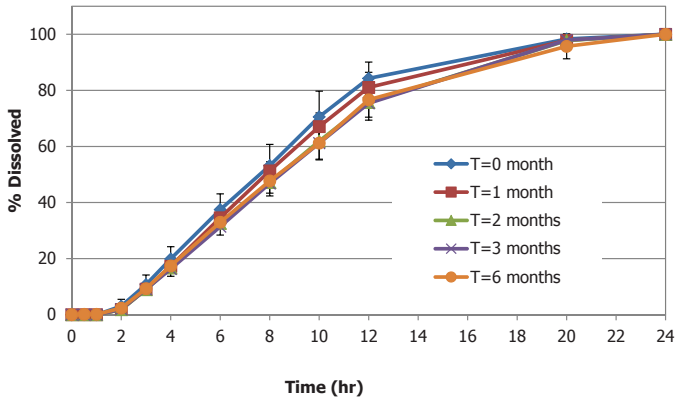


Opadry CA Coated PPOP Tablet Stability

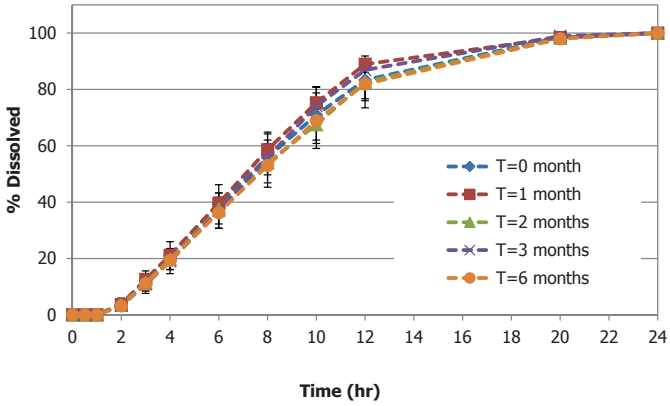
Opadry CA coated PPOP tablets exhibited excellent stability after 6 months at accelerated storage condition as shown in Figures 8 (A) and 8 (B). Application of the top-coat led to slightly better similarity in drug release profiles (f_2 = 83-84 for top-coated PPOP vs. f_2 = 63-81 for PPOPs without top-coat), while the presence of desiccant had minimal effect on drug release. This could be attributed to the moisture barrier property of Opadry 85F system as a top-coat. In addition, all PPOP tablets had good drug content uniformity (n = 10, %RCA = 0.05-0.47%).

Figure 8. Drug Release Profiles from Opadry CA Coated Glipizide PPOP Tablets after Storage in 40°C/75%RH Stability Chamber With No Desiccant (n=6)

(A) No Top-Coat (f_2 = 63–81)



(B) With Top-Coat (f_2 = 83–84)



Conclusions

Opadry CA, a fully formulated semipermeable membrane coating system, exhibited similar performance to the conventional system while providing significant time savings in coating solution preparation. Both the Opadry CA powder and coated PPOP tablets showed excellent stability through 6 months at 40°C/75% RH. The results demonstrated an easy-to-use and stable coating system that can be customized to achieve desired drug release profiles from osmotic tablets, reproducibly.

References

1. V. Malaterre, et al. Oral osmotically driven systems: 30 years of development and clinic use, *European Journal of Pharmaceutics and Biopharmaceutics*, 73 (2009) 311-323.
2. 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
3. P. Patel, S. Missaghi, T. Farrell and A. Rajabi-Siahboomi, Effect of Semipermeable Coating Composition and Opadry Top-Coating Systems on Performance of Push-Pull Osmotic Pump Tablets of a Practically Water Insoluble Model Drug. AAPS Annual Meeting and Exposition, Washington DC, USA, Oct. 2011.
4. L. Martin, H. Deng, S. Missaghi, T. Farrell and A. Rajabi-Siahboomi, Investigation of cellulose acetate polymer viscosity and coating solution concentration on performance of Opadry CA coated push-pull osmotic pump (PPOP) tablets, 39th CRS annual meeting and exposition, Quebec City, Canada, July 2012
5. H. Deng, L. Martin, S. Missaghi, T. Farrell and A. Rajabi-Siahboomi, The influence of Opadry CA weight gain and solvent ratio on performance of push-pull osmotic pump tablets, 39th CRS annual meeting and exposition, Quebec City, Canada, July 2012