A Novel Method to Evaluate Moisture Barrier Performance of Opadry® Film Coating Systems On-Tablet

Authors: Daniel To, Jason Teckoe and Ali Rajabi-Siahboomi

Colorcon, Inc. Harleysville, PA 19438, USA | DVS Symposium 2018 Poster Reprint

Introduction

Many active pharmaceutical ingredients and drug products are sensitive to moisture, which can lead to degradation or poor product performance on stability. Immediate release film coating systems that offer moisture barrier protection are used to improve the stability of these moisture sensitive drug products. In this study a novel on-tablet test methodology has been developed to characterize the moisture barrier performance of fully formulated, immediate release film coating systems using dynamic vapor sorption (DVS).

Methods

Materials

The moisture barrier properties of a novel fully formulated, PEG-free, immediate release PVA based film coating system (Opadry® amb II) was compared to four commercially available film coating systems, Opadry®, Opadry® II, Opadry® 200 and Opadry® amb (Colorcon Inc., USA). Round biconvex placebo tablets (10 mm) composed of lactose (69.4%), Starch 1500® partially pregelatinized maize starch (15.0%), microcrystalline cellulose (15.0%), magnesium stearate (0.5%) and fumed silica (0.1%) were used as a model core.

Tablet Coating

The fully formulated film coating systems were coated onto 2.5 kg of round biconvex placebo tablets (10mm) in a 15” fully perforated Labcoat I (O’Hara Technologies Inc., Canada) coating pan to 2, 3 and 4% weight gain (WG). The solids concentration and spray rate were adjusted to the recommended values to enhance coating uniformity and prevent sticking, shown in Table 1. The inlet air temperature was adjusted to achieve a bed temperature of 45°C, while all other parameters were kept constant. The airflow, pan differential pressure, pan speed, gun to bed distance, atomization and pattern air pressures were maintained at 300 m^3/hr, 18 rpm, 11.4 cm, 1.4 bar and 1.4 bar, respectively.

Table1. Tablet Coating Process Parameters

Formulation	Opadry amb II	Opadry	Opadry II	Opadry 200	Opadry amb
Inlet Air Temp (C°)	64	68	64	64	60
Spray Rate (g/min)	20	20	20	20	20
% Solids	20	15	20	20	20

Dynamic Vapor Sorption

The moisture uptake of coated and uncoated tablets was evaluated in a DVS Intrinsic (Surface Measurement Systems Ltd., USA). The tablets were initially dried at 40°C and 0%RH, until an equilibrium dry condition of less than 0.0002% weight loss per min was obtained for 10 minutes. The tablets were then exposed to a 40°C and 75%RH environment and the moisture uptake recorded as a function of time until the rate of change in moisture uptake rate was less than 0.0002%, over a 10-minute period. A steady state moisture uptake rate was determined from the slope of the predominantly linear portion of the moisture uptake profile. The on-tablet water vapor transmission rate (WVTR) through the coating was determined by normalizing the steady state moisture uptake rate by the tablet surface area. The on-tablet WVTR of at least three tablets from each coating trial was determined and the average value and standard deviation were reported.

$$\text{On — tablet WVTR} = \frac{\left(\frac{dm}{dt}\right)_{SS}}{SA}$$

Where

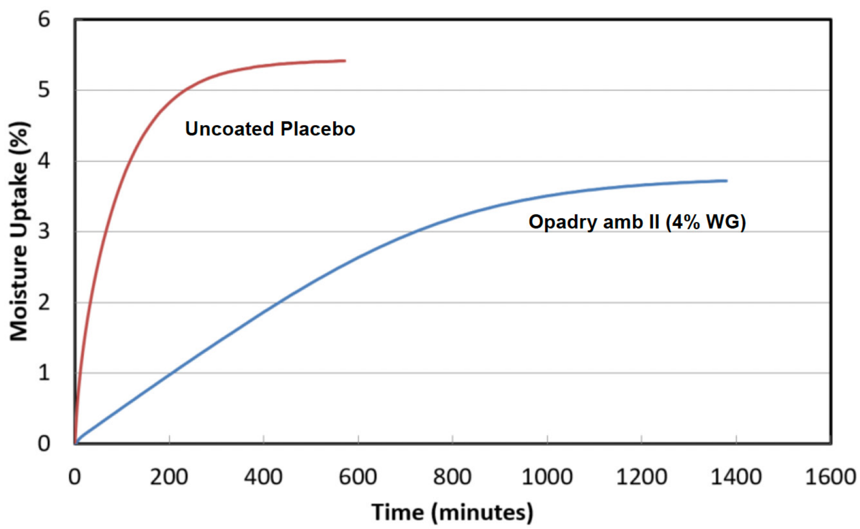
$\frac{\left(\frac{dm}{dt}\right)_{SS}}{SA}$ = steady state moisture uptake tare (g/day); SA = Surface area (m2)

Results

Comparison of Uncoated and Film Coated Tablets

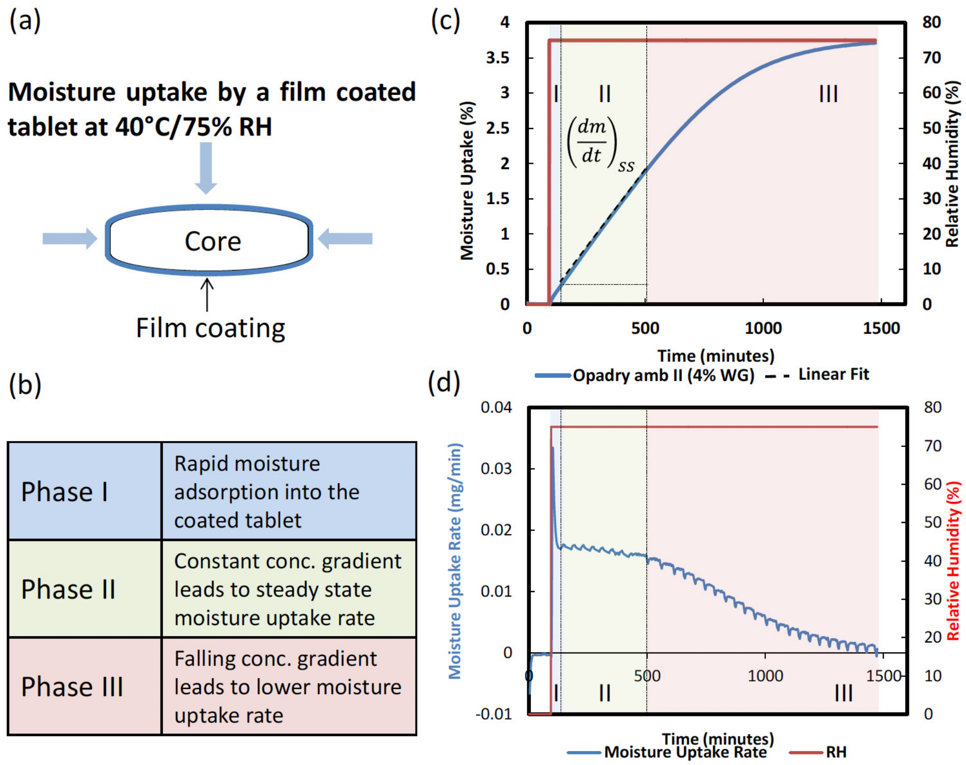
Typical moisture uptake profiles of an uncoated placebo tablet and one coated with Opadry amb II are shown in Figure 1. The slow uptake of moisture into the film coated tablet in comparison to the uncoated placebo indicates that diffusion through the film coating was the limiting factor for moisture uptake.

Figure 1. Moisture Uptake Profile of Uncoated and Opadry amb II Coated Placebo Tablets at 40°C/75%RH



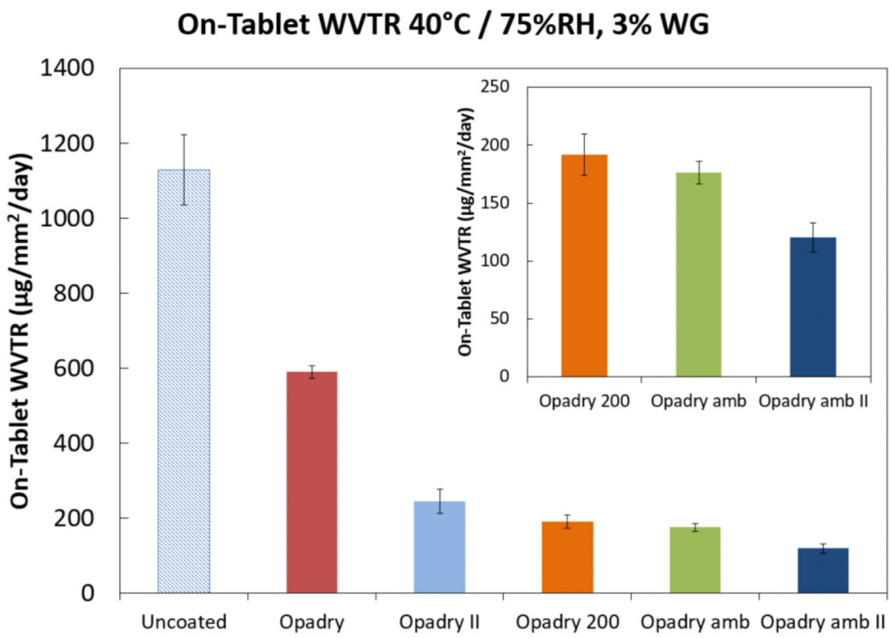
Close examination of the moisture uptake rate of the Opadry amb II coated tablet, depicted in Figure 2, shows that moisture uptake occurs in three phases. Immediately after being exposed to the humid environment a sharp increase in the moisture uptake rate was observed where moisture rapidly adsorbed onto the film coated tablet. This was followed by a period where the moisture uptake rate was constant for nearly 500 minutes and approached a steady state value. The steady state moisture uptake rate was determined from the slope of a line fitted to this portion of moisture uptake profile. In the final phase, the moisture uptake rate slows as the moisture level across the film increased and the concentration gradient is no longer constant.

Figure 2. Three Phases of Moisture for the Opadry amb II Coated Tablet (4% WG) (a) Schematic Indicating Moisture Uptake, (b) Description of Phases, (c) Moisture Uptake Profile and (d) Moisture Uptake Rate



The moisture barrier properties of the film coating systems at 3% WG on placebo tablets are compared in Figure 3. All the film coating systems provided some moisture protection in comparison to the uncoated tablet, as shown by the on-tablet WVTR values; Opadry amb II offered the best moisture barrier performance. The on-tablet WVTR value for this system was an order of magnitude lower than the uncoated tablet and offered 30% reduction in moisture transmission rate than the existing lead moisture barrier product, Opadry amb.

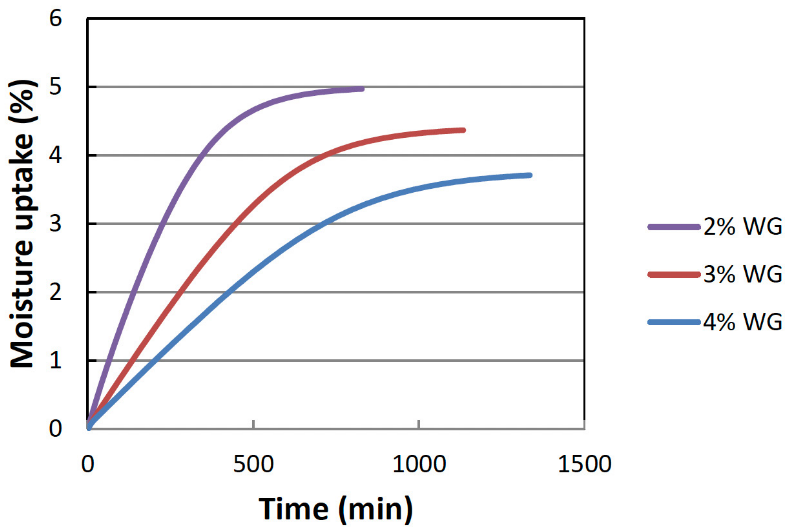
Figure 3. Influence of Formulation on On-Tablet WVTR



Influence of Coating Weight Gain

The influence of coating WG on the moisture barrier performance of Opadry amb II was evaluated. The typical moisture uptake profile of tablets coated to 2, 3 and 4% WG as a function of time is shown in Figure 4. At higher weight gains the steady state portion of the moisture uptake rate had a lower slope and remained linear for a longer time period, indicating enhanced moisture protection than the lower WG samples.

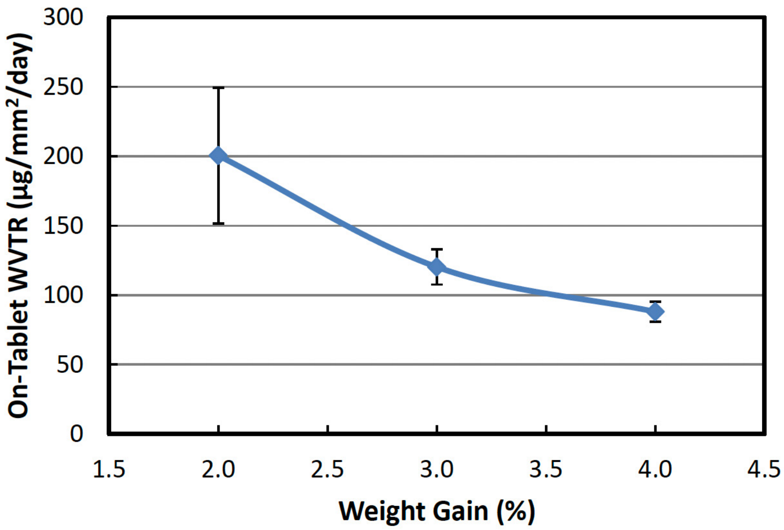
Figure 4. Moisture Uptake Profiles of Tablets Coated with Opadry amb II at 2, 3 and 4% WG.



The average on-tablet WVTR values derived from the moisture uptake profiles are described in Figure 5. At 2% WG Opadry amb II has the potential to provide moisture barrier protection with an on-tablet WVTR value of 201 ± 49 μg/mm²/day, however increased variability at this low WG limits the robustness of the moisture barrier performance.

Increasing the coating level to 3% WG reduced both the average value and the variability to 120 ± 13 μg/mm²/day. Further increasing the coating level to 4% WG offered the most robust moisture barrier performance with an on-tablet WVTR value of 88 ± 7 μg/mm²/day.

Figure 5: Influence of Coating WG on the Moisture Barrier Performance of Opadry amb II



Conclusions

A novel method based on dynamic vapor sorption was successfully used to study the on-tablet moisture barrier performance of a range of film coating systems. In addition to determining moisture transmission rate, it was also possible to demonstrate that increasing the coating WG up to 4% provided a significant enhancement to the moisture barrier performance of the coating.

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North America	Europe/Middle East/Africa	Latin America	India	China
+1-215-699-7733	**+44-(0)-1322-293000**	**+54-1-5556-7700**	**+91-832-6727373**	**86-21-61982300**

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