Opadry® TF
TiO2 Free Formulated Film Coatings

Colorcon®

Evaluation of a TiO2-Free PVA-based Film Coating System with Improved Opacity and Color Uniformity

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Introduction

Film coatings include materials to provide opacity, help with color matching, and protect active ingredients from light-induced degradation. Titanium dioxide (TiO2), classified as E171 when used as a pigment in foods, is considered the best, preferred whitener and opacifier for pharmaceutical and nutraceutical applications. Since the use of TiO2 as a food additive was suspended in Europe in 2022, companies are required to explore alternative materials to replace TiO2 with the same or similar functionalities. However, most TiO2-free (TF) PVA-based coating systems available on the market have significantly lower opacity and color uniformity compared to HPMC-based systems. As a result, most available TF systems with good opacity in the market are HPMC-based. The objective of this study was to evaluate a novel, fully formulated Opadry® TF, TiO2 Free High Opacity PVA-based coating with improved opacity and color uniformity.

Objectives

- To evaluate the opacity and color uniformity of a new PVA-based TiO2 Free film coating system
- To prove that the optimized Opadry TF, TiO2 Free High Opacity PVA-based film coating system has improved results compared to a non-optimized PVA-based TiO2 free system

Methods

Opacity Testing:

In this study, a black film coating was applied to 350mg placebo tablets (at 15% solids, 3% weight gain) and then these black tablets were used for opacity testing of the following white film coating systems:

1. Opadry II, PVA-based formulation containing TiO2
2. Opadry TF, PVA-based formulation replacing all TiO2 with calcium carbonate (non-optimized)
3. Opadry TF, TiO2 Free High Opacity PVA-based system (Optimized)

Each formulation was top-coated at 20% solids onto 3 kg of black sub-coated placebos in a 15” fully perforated side-vented coating pan from O’Hara Technologies (Labcoat II). Samples were taken at 3, 4, and 5% theoretical weight gains (WG). The top-coated black tablets were measured using a Datacolor spectrophotometer and the L-values were recorded (n=10). The L-value indicates the lightness of the sample from 0 to 100, with higher numbers representing whiter and therefore, more opaque film coat. All three formulations were coated using the same parameters which are shown in Table 1.

Color Uniformity Testing:

In this study, all three formulation systems were tested with FD&C Blue #2 Aluminum Lake (Blue #2). Each formulation was coated at 20% solids onto 17kg of 500mg acetaminophen caplets in a 24” fully perforated side-vented coating pan from O’Hara Technologies (Labcoat II). Samples were taken at 3, 4, and 5% theoretical weight gains. The Datacolor spectrophotometer was used to measure ΔE (DE) values for each individual caplet (n=20) versus a reference standard (5%WG average). In this case, DE values greater than 2.5 suggest that non-uniformity of color would be visually apparent. All three formulations were coated using the same parameters which are shown in Table 1.

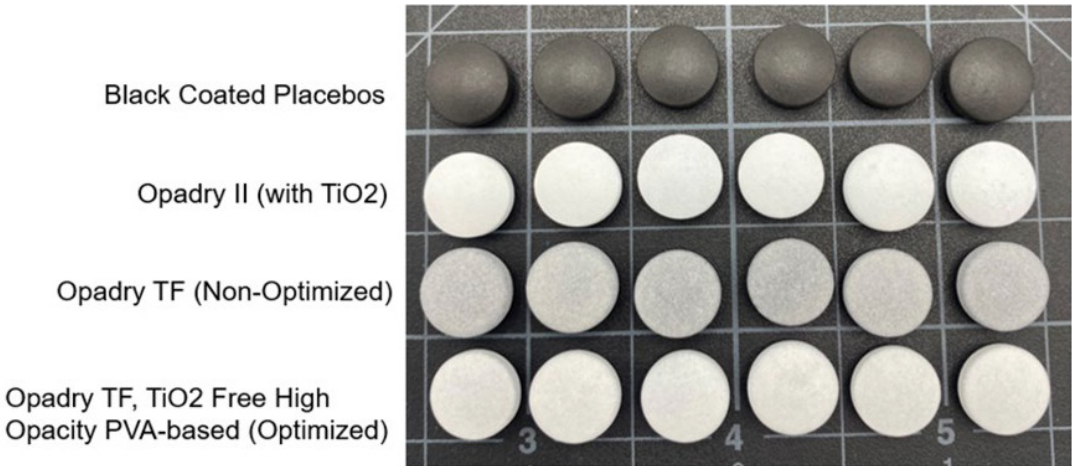
Table 1: Coating Parameters for the Three Formulations

Process Parameters	Opacity Testing	Color Uniformity Testing
Batch Size (g)	3000	17000
Spray Rate (g/min)	18-20	60
Dispersion solids (%/w/w)	20	20
Bed Temperature (°C)	45	45
Inlet Air Temperature (°C)	60	62
Air Flow (cfm/m^3/hr)	165	265
Number of Spray Guns	1	2
Pan Speed (rpm)	18	14
Atomization Air (psi)	20	30
Pattern Air (psi)	20	30

Results

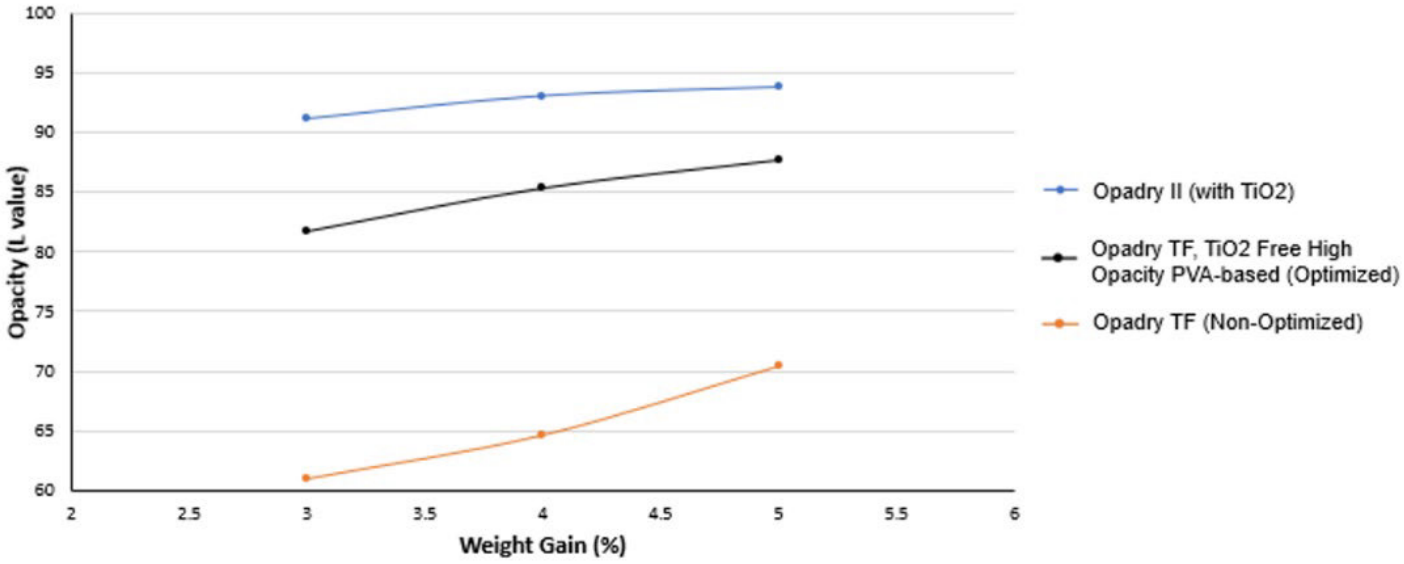
Opacity Testing:

Figure 1: Tablets with 4% Weight Gain Topcoat on Black Coated Placebos



- The optimized Opadry TF and Opadry II with TiO2 look white, suggesting that both systems have sufficient opacity and whiteness to hide the color of the black sub-coat.
- The optimized TF formulation is slightly darker than Opadry II.
- The non-optimized Opadry TF system has a significant dark grey tint suggesting poor opacity

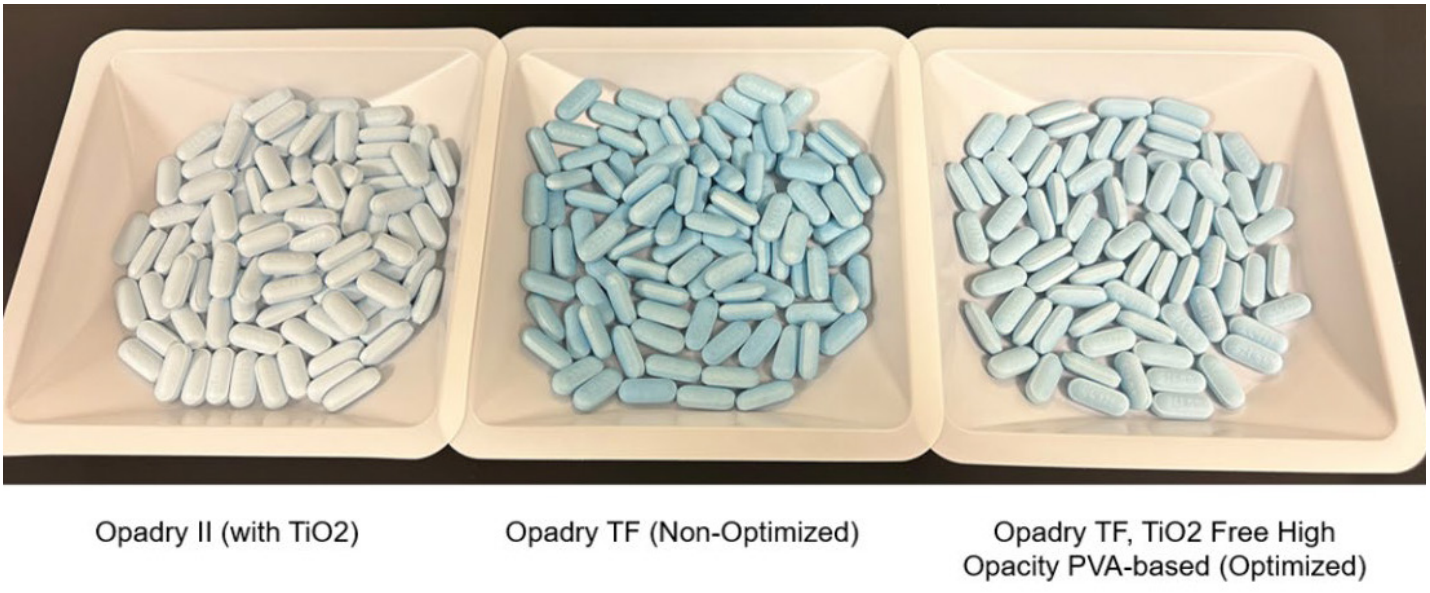
Figure 2: L-Values for Black Sub-coated Placebos with Topcoats at Different Weight Gains



- Opadry II with TiO2 has significantly better opacity compared to the non-optimized Opadry TF.
- The optimized Opadry TF, TiO2 Free High Opacity PVA-based formulation is much closer in opacity to the Opadry II with TiO2.
- The optimized Opadry TF has significantly better opacity compared to the non-optimized Opadry TF.
- These results match the visual observations as shown in Figure 1.

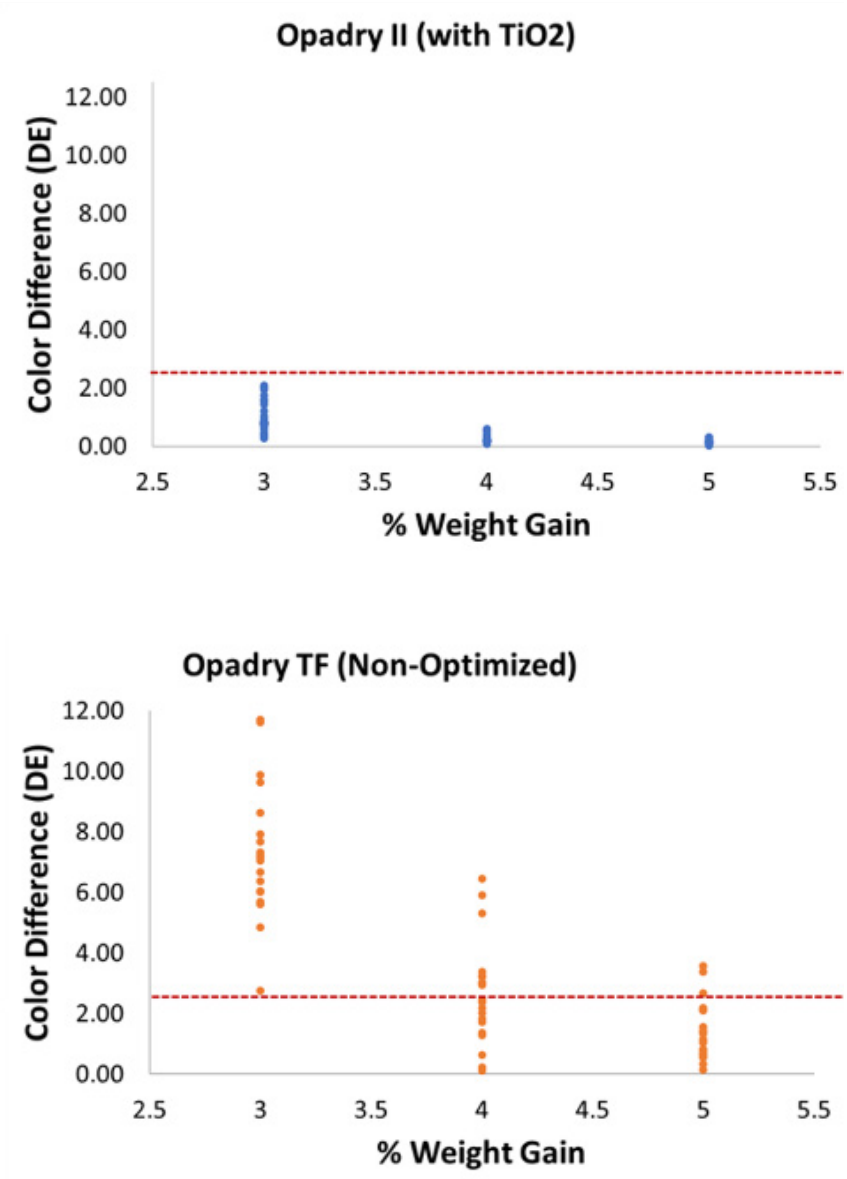
Color Uniformity Testing:

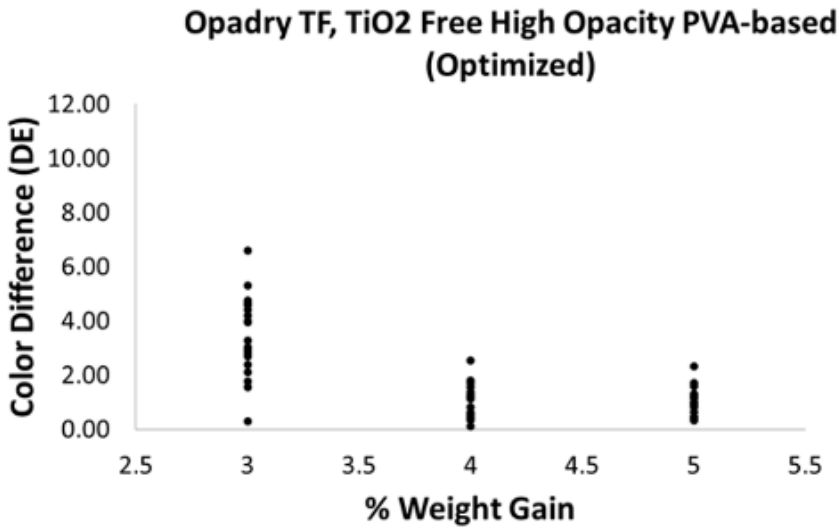
Figure 3: Acetaminophen Caplets with 4% Weight Gain



- Opadry II with TiO2 has a very light, pastel blue color appearance
- The non-optimized Opadry TF is a vibrant blue.
- The optimized Opadry TF is a lighter blue than the non-optimized Opadry TF and is closer in color-matching to Opadry II.
- Opadry II with TiO2 and optimized Opadry TF have good visual color uniformity.
- The non-optimized Opadry TF has poor visual color uniformity.

Figure 4: DE Values for Acetaminophen Caplets Coated with Blue #2 Formulations at Different Weight Gains





- Opadry II with TiO2 has the best color uniformity, reaching the acceptable limit (DE < 2.5) at 3% WG with little variation within samples.
- The non-optimized Opadry TF requires more than 5% WG to reach sufficient color uniformity and has much larger variation within samples.
- The optimized Opadry TF has good color uniformity, reaching the acceptable limit at 4% WG and lower variation at all weight gains compared to the non-optimized Opadry TF.

Conclusions

- The new optimized Opadry TF, TiO2 Free High Opacity PVA-based coating achieves good opacity and color uniformity at 4% WG. This is a significant improvement compared to other PVA-based TF systems using calcium carbonate as replacement of TiO2.
- The formulation was designed specifically to meet customer demands, and to prepare for any possible regulatory changes in Europe regarding the use of TiO2 in pharmaceutical products.