Impact of Opacifier Type in a Film Coating Formulation on Photostability of Tablet Ingredients

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Introduction

Film coatings impart mechanical integrity, gloss, and light and moisture protection to tablets. As consumer preferences for clean label ingredients in dietary supplements increase, this has led to the use of calcium carbonate as an alternative opacifier to titanium dioxide (TiO2) in film coating systems. The direct replacement of calcium carbonate in place of TiO2 results in a reduction of opacity and whiteness. Good opacity in film coatings is important for a variety of reasons, including the protection of ingredients that are sensitive to light. Although calcium carbonate does not have equivalent opacifying properties to TiO2, it is the second best. To overcome, Colorcon has developed an optimized TiO2 free formula that contains calcium carbonate but maintains superior opacity and whiteness. The objective of this study was to evaluate the photo-protection properties of this new, best-in-class high opacity Opadry® TF, TiO2 Free Formulated Film Coatings (CC)*.

*Also available Nutrafinish®, Titanium Dioxide Free Film Coatings for nutritional and dietary supplement products regulated as foods.

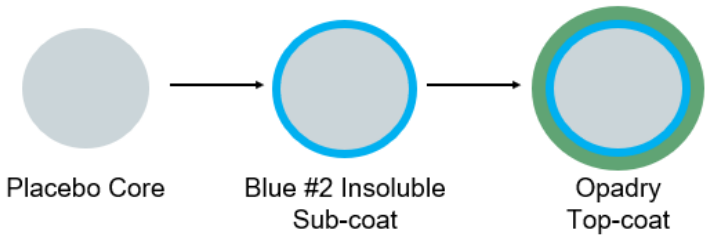
Methods

In this study, an insoluble layer containing FD&C Blue #2 Aluminum Lake (Blue #2), a pigment known to have low photostability[1], was coated onto 3.5 kg placebo tablets using an aqueous ethylcellulose dispersion (at 15% solids). This coating formulation was chosen to form an insoluble film coating layer (~50 microns) preventing any pigment leaching from the coating layer. The impact of calcium carbonate vs. TiO_2 on light protection of Blue #2 was studied using the following coating systems:

1. Opadry (TiO_2): HPMC-based formulation with titanium dioxide; 20% solids
2. High opacity Opadry TF (CC): HPMC-based formulation with calcium carbonate; 20% solids
3. Opadry (CC): HPMC-based formulation with calcium carbonate; 15% solids

Each formulation was top-coated onto 1 kg of the Blue #2 coated placebos (Figure 1).

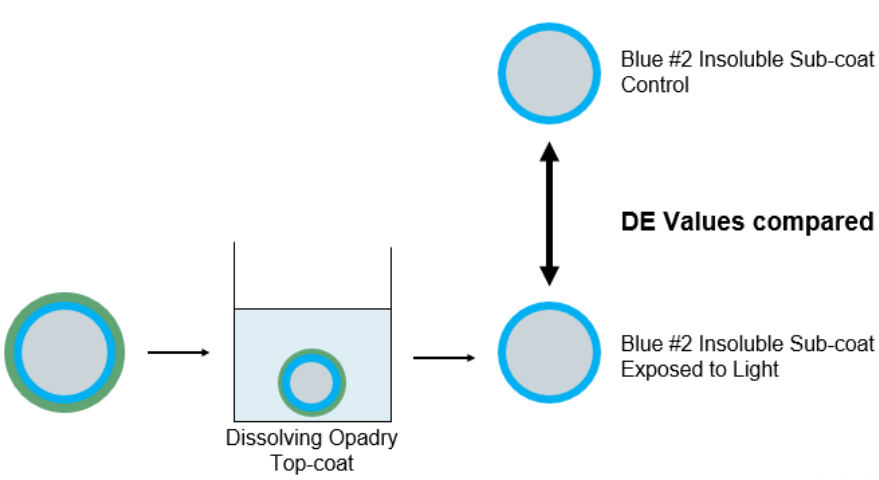
Figure 1. Coating Process



The coated tablets were exposed to light in a photostability chamber (Atlas Suntest XLS+, US) at 250 W/m² in the wavelength range of 300-800 nm. All samples were exposed at 9 hour or 22-hour periods to meet ICH UV and visible light exposure criteria.[2]

Samples tested in the light chamber included a positive control (Blue #2 tablets with no top-coat), a negative control (Blue #2 tablets with no top-coat; the petri dish was covered with aluminum foil), and the three formulations at 3%, 4% and 5% (w/w) theoretical weight gains. Ten tablets of each were placed into petri dishes and exposed to light in the chamber for 9 or 22 hours. Following light exposure, the soluble top-coat was removed by washing in 800 ml of deionized water, then dried with a paper towel to remove the remaining top-coat residue (Figure 2). Any color change of Blue #2 in the insoluble coat was measured using a Datacolor spectrophotometer and the Delta E (DE) values were compared to the standard (initial Blue #2 sub-coated placebos without top-coat). DE values greater than 2.5 suggest color change is visible to the naked eye; however, the Datacolor can detect changes that are not noticeable visually.

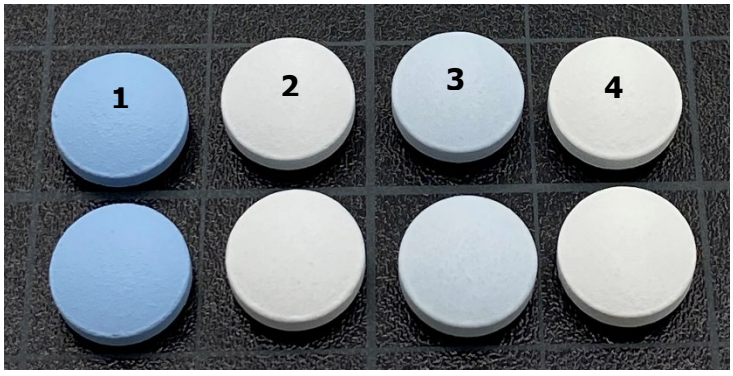
Figure 2. Testing Method



Results

Opacity and Whiteness: High opacity Opadry TF (CC) and Opadry (TiO_2) tablets look white suggesting that both systems have sufficient opacity and whiteness to hide the color of the blue sub-coat. In contrast, the Opadry (CC) tablets have a blue tint suggesting poor opacity (Figure 3).

Figure 3. Tablets with 4% Weight Gain Top-coat



(1) No Top-coat
(2) High opacity Opadry TF (CC)
(3) Opadry (CC)
(4) Opadry (TiO_2)

Method validation: All initial DE values are < 0.5, indicating that the washing method successfully removed the top-coat with no effect on the color of the sub-coat and demonstrating that the method was validated (Figure 4).

Figure 4. Tablets with 4% Weight Gain of Top-coat, Before and After Washing Method: T=0

(1) No Top-coat
(2) High opacity Opadry TF (CC)
(3) Opadry (CC)
(4) Opadry (TiO_2)

Photostability: Figure 5 shows the impact of total light exposure time on color change of the 4% WG coated tablets; with color change increasing with longer exposure to light. The three top-coated formulations have less color change compared to the sub-coat only positive control, suggesting all the coatings provided some light protection, and are always better than uncoated systems. High opacity Opadry TF (CC) has comparable light protection to Opadry (TiO_2), and both have better light protection than Opadry (CC). As previously mentioned, color change may not be visibly noticeable (Figure 6). However, color change can be detected using Datacolor (Figure 5).

Figure 5. Change in DE Values for Blue #2 Sub-coated Tablets with Top-coat at 4% WG Over Time in Photostability Chamber

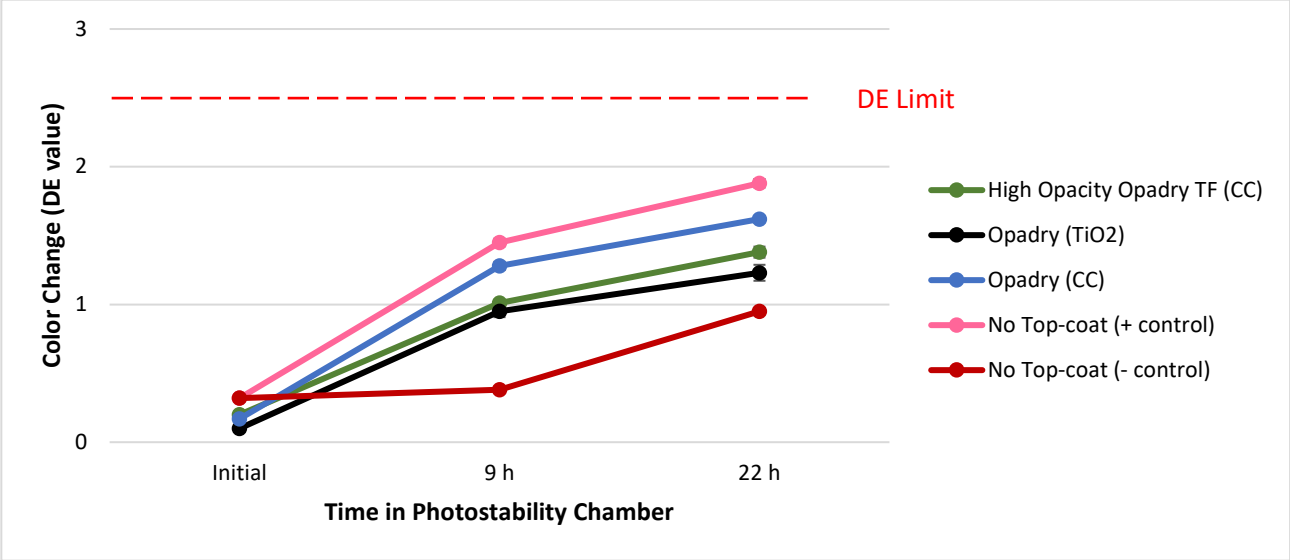
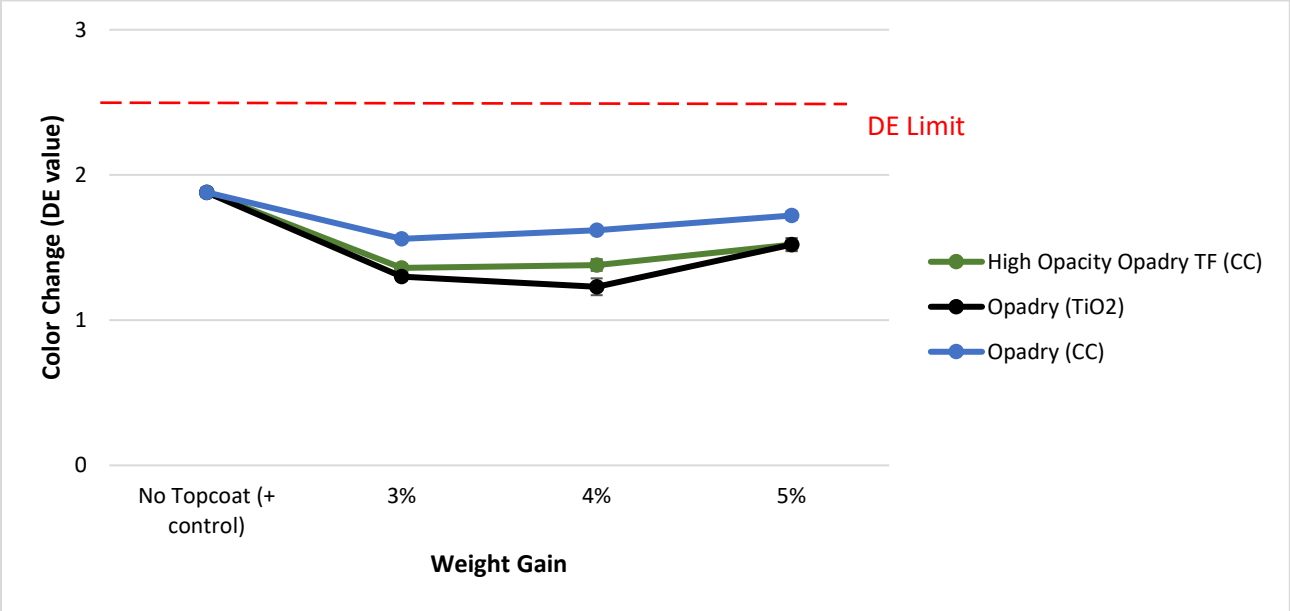


Figure 6. 4% Top-coat Weight Gain Tablets After Washing Method: T=22 Hours in Light Chamber.

(1) No Top-coat (+ve control)
(2) No Top-coat (-ve control)
(3) High Opacity Opadry TF (CC)
(4) Opadry (CC)
(5) Opadry (TiO_2)

Figure 7 shows the impact of weight gain on color change for the 22-hour exposure time. There is little difference between the various weight gains, suggesting 3% WG is sufficient for high opacity Opadry TF (CC) to provide comparable light protection to Opadry (TiO_2). This figure also shows both formulations have better light protection than Opadry (CC). Similar work has been completed using radish as the photo-labile pigment, which has worse photostability than Blue #2.[3] Data (not shown here) suggested that higher % weight gains may be needed with highly photosensitive ingredients.

Figure 7. Change in DE Values for Blue #2 Sub-coated Tablets with Top-coat at Different Weight Gains at 22 h in Photostability Chamber



Conclusions

This study showed that high opacity Opadry TF (CC) provided similar photostability protection when compared with a TiO2-based coating applied at 3% weight gain. Further work is ongoing to evaluate the impact of opacifier on photosensitive active pharmaceutical ingredients.

References

1. Downham A, Collins P. Colouring our foods in the last and next millennium. International Journal of Food and Science & Technology. 2001;35(1):5-22. https://doi.org/10.1046/j.1365-2621.2000.00373.x. Accessed May 2021.
2. U.S. Food and Drug Administration. Q1B Photostability Testing of New Drug Substances and Products Guidance Document. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q1b-photostability-testing-new-drug-substances-and-products. Accessed May 2021.
3. Mehaffey T, et al. Stability of Non-Synthetic Pigments in Fully Formulated Film Coating Systems. AAPS 2019.

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