Stability Evaluation of Two Non-Synthetic Pigments for Use in Fully Formulated Film Coating Systems

Charles Cunningham, Chris Neely and Thomas P. Farrell

Colorcon Inc., Global Headquarters, 275 Ruth Road, Harleysville, PA 19438 USA; www.colorcon.com/about/contact

Purpose

There is an increasing interest in the use of non-synthetic pigments in film coating formulations for dietary supplements and pharmaceuticals. Since non-synthetic pigments are typically derived from natural sources, color variability and color stability in formulated coating systems is a concern. In addition to assessing the stability of the pigment on the coated tablet, it is also necessary to examine the color stability of the pigments in the pre-formulated coating material in order to ensure reproducible color over a potentially extended material storage period. The purpose of this study was to evaluate the color stability of two non-synthetic pigments in model pre-formulated film coating systems under accelerated storage conditions.

Methods

Purple carmine and beta carotene pigments were formulated into three coating systems at a 7% w/w usage level. (**Table 1**).

Table 1. Materials Used in the Study

Coating Formulations (Colorcon Inc. West Point, PA)	Polymer Base
Opadry,® Complete Film Coating System	Hypromellose
Opadry II,® High Performance Film Coating System	Polyvinyl alcohol
Opadry® NS, Complete Film Coating System for Nutritional Supplements	Cellulosics
Pigments (CHR Hansen, Milwaukee, WI)	**Color**
Purple carmine CC-5000-L-P-B	Purple
Beta carotene BC-100Y-WSP	Bright yellow

The coating formulations (1kg) were packaged in fiber cartons with sealed polyethylene liners and stored in the dark at 30°C / 65% RH and 40°C / 75% RH for 6 months. At 1.5 month intervals, samples of the stored film coating formulations were reconstituted in deionized water (Di H2O) and applied to white Lanetta cards using a Bird Film Applicator (150 µm). The cards were dried in a 50°C oven for 10 minutes then measured for color change.

Each coating formulation was also applied on 350 mg placebo tablets (to a 3.0% weight gain) , in a 12" fully-perforated pan (Labcoat I, O'Hara Technologies). The coated tablets were packaged in foil-sealed 100 cc HDPE bottles (50 tablets per bottle) and stored in the dark at 30°C / 65% RH and 40°C / 75% RH for three months. The coated tablets were measured monthly for color change.

Both the powder and coated tablet samples were tested for color change using a Datacolor 600 spectrophotometer (Datacolor, Lawrenceville, NJ) employing the Commission Internationale de l'Eclairage (CIE) L* a* b* system. The total color difference (ΔE) from the target reference color was determined by calculating the distance between two points in the color space using the following equation:

$$\Delta E^* = [(L^*1 - L^*2)^2 + (a^*1 - a^*2)^2 + (b^*1 - b^*2)^2]^{1/2}$$

Results

Formulated Powder Stability – Purple Carmine

The specification limit for color change was NMT 3.5 ΔE for the formulations containing purple carmine. After 6 months storage at 40°C / 75% RH, none of the coating systems containing purple carmine exceeded 2.5 ΔE in color difference. (**Figure 1**). Samples stored for 6 months at 30°C / 65% RH did not exceed 1.6 ΔE (**Figure 2**).

Figure 1. Color Change of Formulated Powders Containing Purple Carmine (40°C / 75% RH)

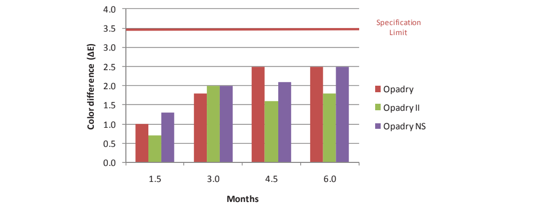
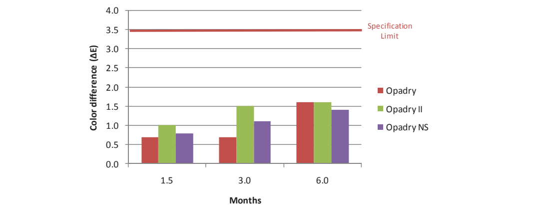


Figure 2. Color Change of Formulated Powders Containing Purple Carmine (30°C / 65% RH)



The purple carmine pigment exhibited good stability in either storage condition irrespective of formulation type. These results indicated that coating formulations containing this pigment will remain within specification for up to 2 years.

Formulated Powder Stability – Beta Carotene

The beta carotene pigmented formulations exhibited significant color change and all exceeded the specification (3.0 ΔE) after 3 months storage at 40°C / 75% RH (**Figure 3**). After 6 months at 30°C / 65% RH storage conditions, the beta carotene formulations were visually comparable to the reference but only the Opadry NS formulation met the instrumental color change specification with a 0.8 ΔE (**Figure 4**).

Figure 3. Color Change of Formulated Powders Containing Beta Carotene (40°C / 75% RH)

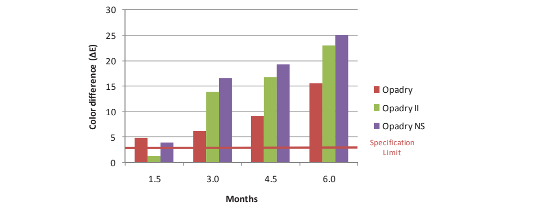
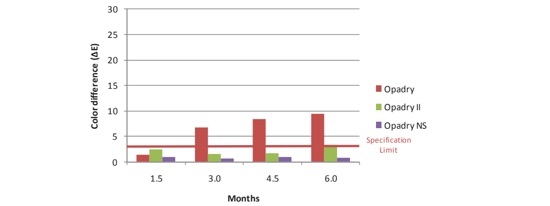


Figure 4. Color Change of Formulated Powders Containing Beta Carotene (30°C / 65% RH)



The beta carotene pigment exhibited poor color stability at the 40°C / 75% RH storage condition. At 30°C / 65% RH, the results were significantly better, but showed that the color stability could be formulation dependent. This pigment could be qualified for use in some types of coating formulations, but longer term stability studies would need to be conducted to further assess product shelf life and proper storage conditions.

Coated Tablet Stability – Purple Carmine

The specification limit for color change was NMT 3.5 ΔE for the coated tablets containing purple carmine. After 3-months storage at 40°C / 75% RH, none of the coated tablets exceeded 1.5 ΔE in color difference. (**Figure 5**). Coated tablets stored for 3 months at 30°C / 65% RH did not exceed 1.0 ΔE (**Figure 6**).

Figure 5. Color Change of Coated Tablets with Purple Carmine (40°C / 75% RH)

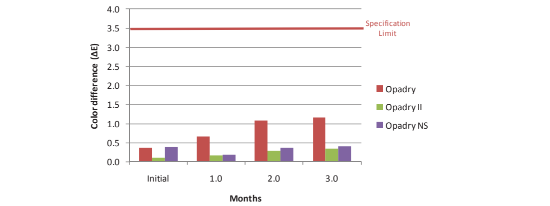
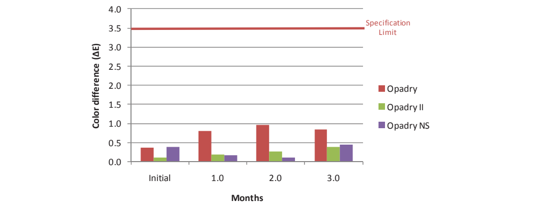


Figure 6. Color Change of Coated Tablets with Purple Carmine (30°C / 65% RH)



The tablets with purple carmine pigment exhibited good stability in either storage condition irrespective of formulation type. These results provide confidence that this pigment would be stable in the intended end use film coating application.

Coated Tablet Stability – Beta Carotene

The specification limit for color change was NMT 3.0 ΔE for the coated tablets containing beta carotene. After just 1-month storage at either 40°C / 75% RH or 30°C / 65% RH, all coated tablets failed the color change specification (**Figures 7 and 8**).

Figure 7. Color Change of Coated Tablets with Beta Carotene (40°C / 75% RH)

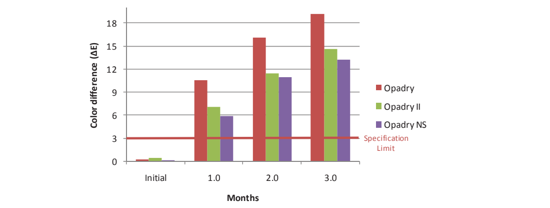
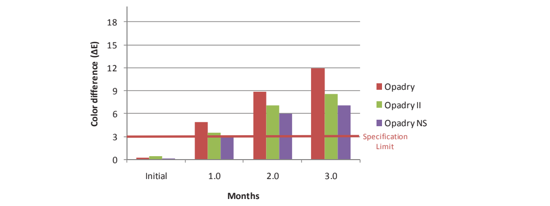


Figure 8. Color Change of Coated Tablets with Beta Carotene (30°C / 65% RH)



The coated tablets with beta carotene pigment exhibited poor color stability at both storage conditions. Significant fading of the tablets was observed visually and instrumentally. Although the tablet samples were stored in the dark, beta carotene is prone to oxidation induced decomposition as well as light sensitivity.[1] Prior to the use of this pigment in film coating applications, further studies should be conducted to determine optimum packaging and storage conditions that would reduce the potential for color change.

Conclusions

The non-synthetic pigments evaluated in this study differed significantly in their stability under accelerated storage conditions. In addition to storage conditions, formulation of the film coating base also affected stability. The stability of non-synthetic pigments in film coating systems must be carefully evaluated in order to determine proper product shelf life and appropriate packaging and storage conditions. As a result of this study, the purple carmine pigment was successfully qualified for use in fully formulated film coating systems and complemented previously qualified non-synthetic pigments (**Figure 9**). Studies are continuing on additional non-synthetic pigments.

Figure 9. Examples of Coated Tablets Employing Stable Non-synthetic Pigments Including Purple Carmine

References

1. H. Morais P. Rodrigues C. Ramos E. Forgács T. Cserháti J. Oliveira; Effect of ascorbic acid on the stability of β–carotene and capsanthin in paprika (Capsicum annuum) powder, Nahrung / Food Research, Volume 46, Issue 5, 1 September 2002, Pages: 308–310.