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Photostability of Pharmaceutical Colorants in Opaglos® 2

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Objectives

To determine the photostability of several pharmaceutical colorants in powder state and on film coated tablets when formulated into Opaglos® 2, an Aqueous, High-Gloss Film Coating System.

Methodology

Several commonly used pharmaceutical colorants, formulated into developmental Opaglos 2 systems and coated onto solid dosage forms, were examined for their photostability according to ICH guidelines.

Colorants used in the study included:

Colorant	Color Index
Iron Oxide Yellow	CI77492
Iron Oxide Red	CI77491
Iron Oxide Brown	N/A
Riboflavin	N/A
FD&C Blue #2 Indigo Carmine	CI73015
FD&C Yellow #6 Sunset Yellow	CI15985
FD&C Red #40 Allura Red	CI16035

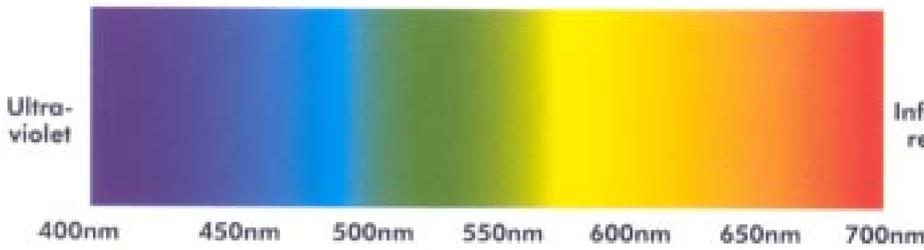
These coloring agents were chosen because of their broad regulatory acceptance and widespread use within the pharmaceutical industry. Where applicable, both the dye and lake colorant were used to compare fading. Film coating of tablets was performed in a 12" O'Hara Labcoat I from O'Hara Technologies equipped with a Spraying Systems 1/8 JAU spray nozzle. Placebo tablets of 3/8" standard convex dimensions were used in all coating runs.

Color measurements were made using a Spectrocolorimeter SF-600+ from Datacolor International. The spectrocolorimeter analyzes light energy reflected or transmitted by a sample, wavelength by wavelength. The photometric characteristics of a material are measured in the visible spectrum, and spectral graphs are produced.

In physical terms, the color of an object is measured and represented by its spectrophotometric curve. This is a graph representing the reflected or transmitted part of incident energy as a function of the wavelength, in the visible spectrum between 400 and 700 nm.

For example, if all of the wavelengths are absorbed, the color is perceived as black, whereas if all wavelengths are fully reflected (100%), white is perceived.

A graph of the visible spectrum of light is shown below with wavelengths expressed in nm.



Photostability testing was conducted in an Atlas SunChex fadeometer, Model SC-1 equipped with a xenon lamp, appropriate filters, and radiometer for measuring irradiance. Control samples (i.e. wrapped in aluminum foil) were used to distinguish between photochemical and thermal degradation.

Coated tablets were exposed in three levels of package protection: open petri dishes (unprotected), amber blister packaging, and high density polyethylene bottles (HDPE).

Powder samples were packaged in clear polyethylene bags of 2.25 mil thickness.

Sample presentation within the chamber was carefully chosen to ensure reproducibility and accuracy of measurements between samples.

In order to determine the effect of varying colorant concentration on the rate of fading, samples of coated tablets were prepared with different percentages of colorant producing dark, medium, and light colored tablets.

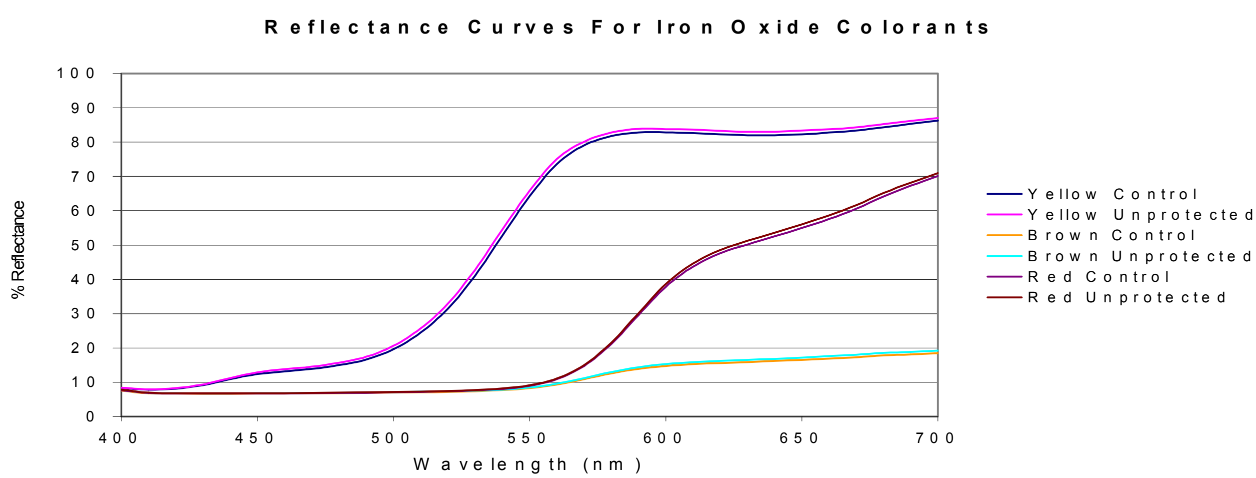
To compare rates of fading, unprotected tablets were placed in the fadeometer and pulled at regular time intervals required to give quantifiable fading. Relative active dye concentration at each time point was determined by integrating the area between the reflectance curves for the faded pigmented tablet and the uncoated white tablet between 570 and 630 nm. Results were plotted to determine the first order kinetic rate constant, k (hr^{-1}), using the equation below.

$$\boldsymbol{ln}(C/C_0) = \boldsymbol{-kt}$$

Where C/C_0 is the fraction of dye remaining at time t, and k is the first order rate constant.

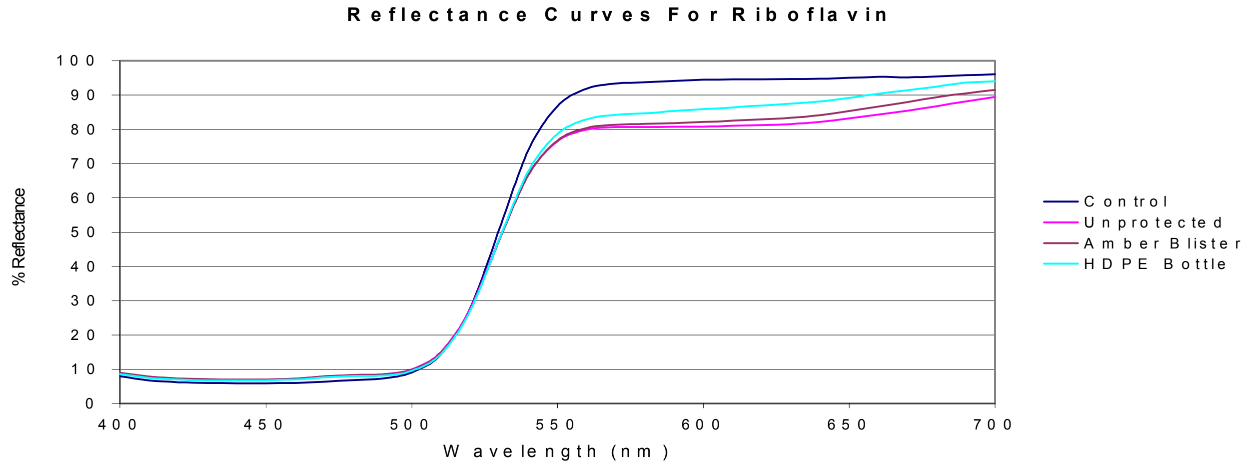
Results

Opaglos 2 With Iron Oxide



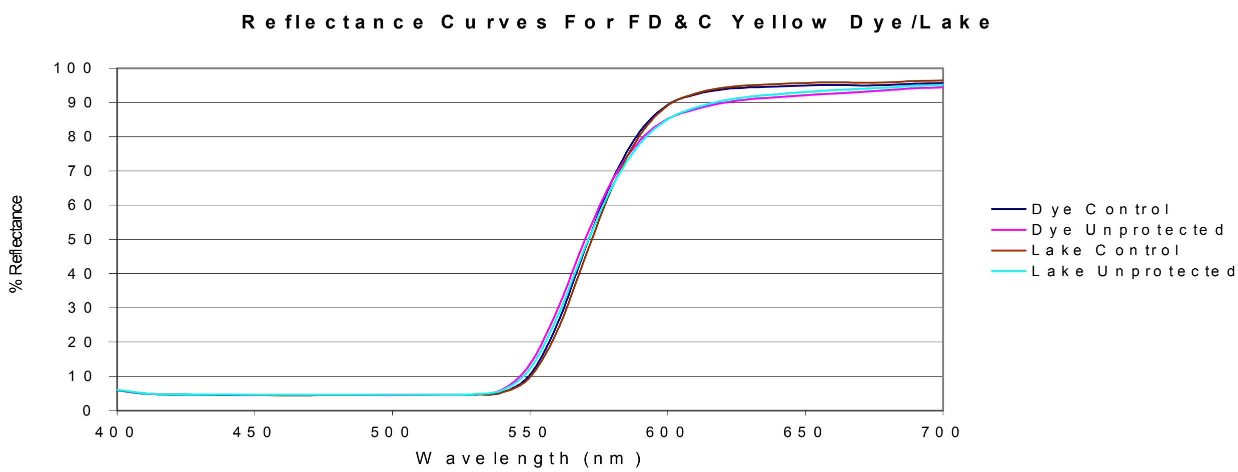
Reflectance curves for the iron oxide colorants show no change between faded and control tablets, demonstrating excellent photostability.

Opaglos 2 With Riboflavin



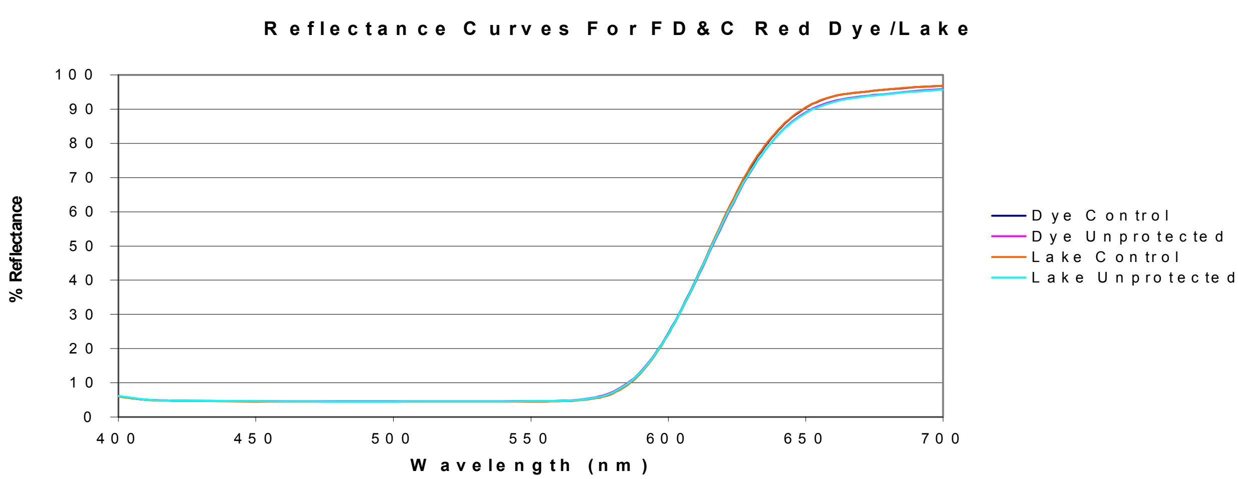
Reflectance curves for riboflavin show decreasing reflectance in the area of interest with decreasing levels of packaging protection. Even at the highest level of protection, HDPE bottle, a decrease in reflectance is observed relative to the control.

Opaglos 2 With FD&C Yellow Dye / Lake



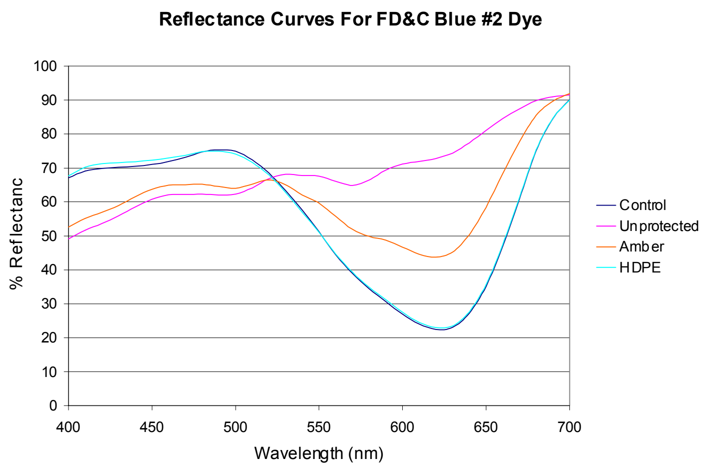
An equivalent amount of fading, as demonstrated in the reflectance curve, occurred in both the Yellow #6 dye and Lake formulations.

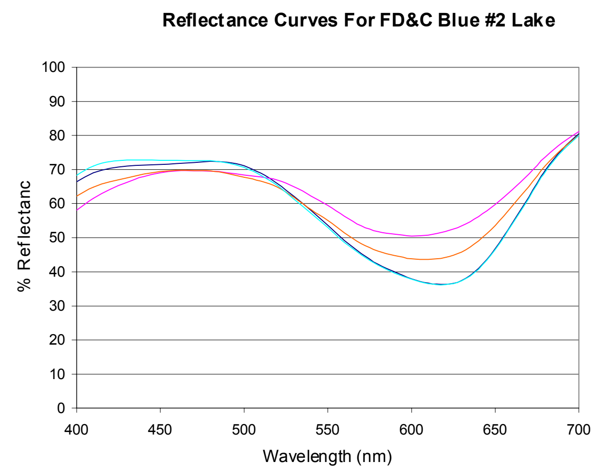
Opaglos 2 With FD&C Red Dye / Lake



The FD&C Red #40 dye and Lake exhibited good photostability even under direct exposure with no protection.

Opaglos 2 With FD&C Blue Dye / Lake

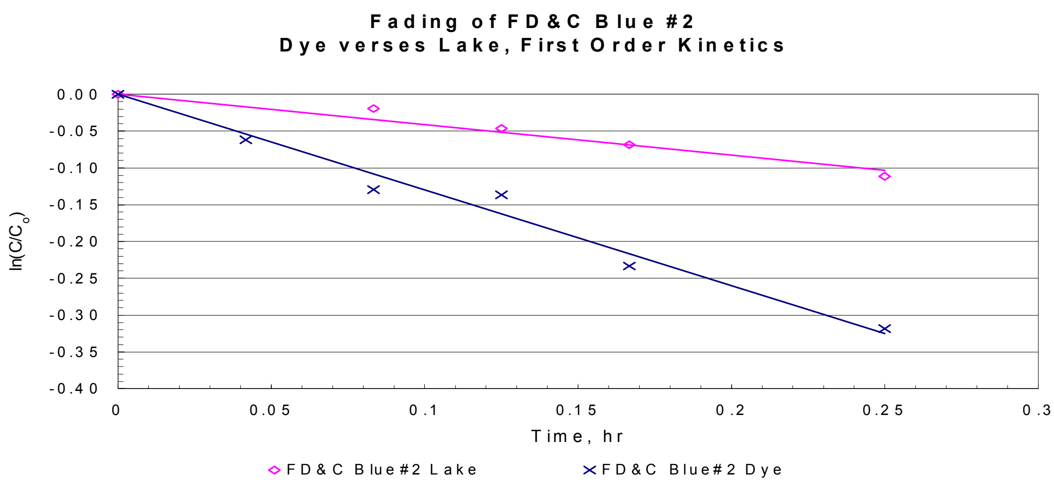




In the case of FD&C Blue #2, the Lake formulation performed significantly better than the dye-containing formulations. In both cases, the HDPE bottle provided complete protection in the presence of light. Although not shown, these observations held true for formulations containing different concentrations of Blue #2 dye and lake.

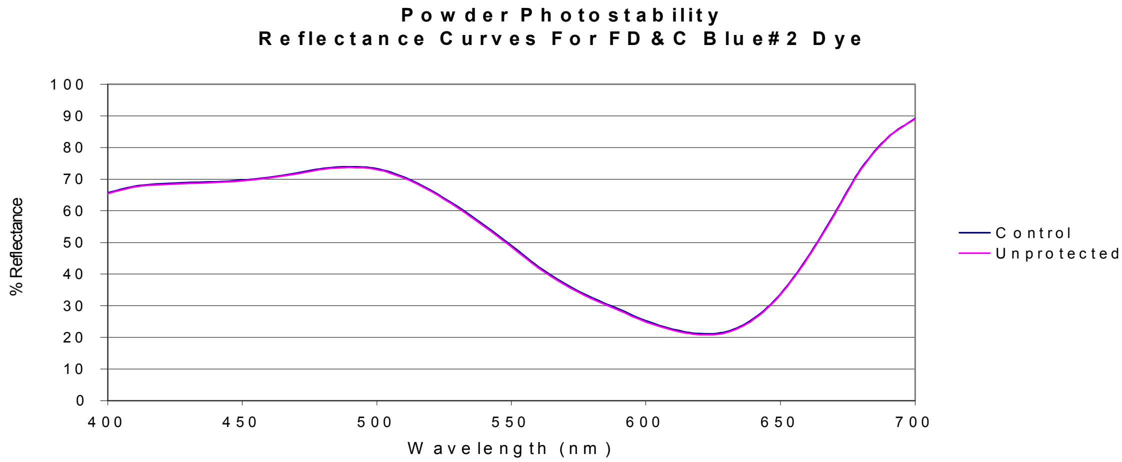
Kinetic Treatment

A further comparison of low concentration dye verses lake fading rates is shown below where the first order rate constant is the negative slope.



Colorant	Colorant Concentration	k (1/hr)
FD&C Blue #2 Dye	High	< 0.0002
FD&C Blue #2 Lake	High	< 0.00002
FD&C Blue #2 Dye	Medium	0.0007
FD&C Blue #2 Lake	Medium	0.0004
FD&C Blue #2 Dye	Low	1.3
FD&C Blue #2 Lake	Low	0.41

The relative color stability of unprotected coated tablets can be seen by comparing the first order rate constants shown above. Rates of fading were lower for lake-containing formulations. For the formulations studied, it was found that the rate constant varied inversely with the dye/lake concentration.



Exposed powders of all color formulations, when hydrated and coated onto tablets, demonstrated no change in reflectance when analyzed against controls. This is seen in the above graph of Opaglos 2 powder containing Blue #2 dye.

Additionally, no thermal degradation was noted in any samples tested in this study when control samples were analyzed against initial coated tablets.

Conclusions

In all cases, developmental Opaglos 2 dry powder formulas were found to be light-stable when packaged in standard, clear polyethylene bags.

Developmental Opaglos 2 formulations containing iron oxides, Red #40 (dye or Lake) or Yellow #6 (dye or Lake) yielded photo-stable coated tablets independent of packaging type.

Developmental Opaglos 2 formulations containing Blue #2 (dye or Lake) yielded photo-stable coated tablets when packaged in HDPE bottles.

The experimental methods described here provide a fast and accurate assessment of the relative color stability of various colorants formulated in Opaglos 2.