Influence of Sunscreening Agents on Color Stability of Tablets Coated with Certified Dyes III: FD&C Yellow No. 6

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Abstract □ The influence of a protective coating of six sunscreening agents (glyceryl *p*-aminobenzoate, benzocaine, cinoxate, homosalate, *n*-octyl salicylate, and amyl salicylate) upon the photostability of FD&C Yellow No. 6 used to color coat tablets was studied. The alcohol film-, modified sugar-, and film-coating methods were used to apply the sunscreening agents. Tablets were exposed to 1000 foot-candles of light for various times, after which reflectance measurements and visual observations were recorded. FD&C Yellow No. 6 did not follow the Kubelka–Munk equation. The order of relative stability was FD&C Yellow No. 6 > erythrosine sodium (FD&C Red No. 3) > FD&C Blue No. 1. The greatest protection against fading was afforded by benzocaine.

Keyphrases □ Sunscreening agents—effect on color stability of tablets coated with FD&C Yellow No. 6, various coating methods □ Color stability—tablets coated with FD&C Yellow No. 6, effect of sunscreening agents and various coating methods □ Stability, color—tablets coated with FD&C Yellow No. 6, effect of sunscreening agents and various coating methods □ Tablets—coated with FD&C Yellow No. 6, effect of sunscreening agents and various coating methods on color stability □ Dyes—FD&C Yellow No. 6 tablet coating, effect of sunscreening agents and various coating methods on color stability □ FD&C Yellow No. 6—tablet coating, effect of sunscreening agents and various coating methods on color stability

The influence of six sunscreening agents (salicylate, benzoate, and cinnamate types) on the color stability of tablets coated with erythrosine sodium (FD&C Red No. 3) and FD&C Blue No. 1 was reported previously (1, 2). Three different methods were developed for their application. For FD&C Red No. 3, the degree of protection was dependent not only upon the type of sunscreening agent but also upon the application method. For FD&C Blue No. 1, no sunscreening agent exhibited significant protective action.

The purposes of this study were to evaluate the influence of selected sunscreening agents on tablets coated with FD&C Yellow No. 6 and to predict the color shelflife of such coated tablets.

EXPERIMENTAL

Materials—The six sunscreening agents used were glyceryl *p*-aminobenzoate[1], benzocaine, cinoxate[2], homosalate, *n*-octyl salicylate, and amyl salicylate[3]. The dye was FD&C Yellow No. 6. All compounds were used as received without further purification.

Procedure—The preparation of tablets, the equipment, the method of regulating exposure to light, and the determination of the quantity of sunscreening agent per tablet were described previously (1).

Coating Procedure—Ten subcoats and 25 smoothing coats were applied to core tablets, in lots of 6 kg, using medium strength gelatin syrup and white subcoating dusting powder. After the tablets were completely dry, the color coating was applied. Plain coating syrup (170 g of sucrose and 100 ml of deionized water) and color syrup (0.300 g of dye in 100 ml of plain coating syrup) in the stated ratio were applied in the following order: nine coats of 25 ml each in 1:90 parts, nine coats of 30 ml each in 1:75 parts, nine coats of 32 ml each in 1:60 parts, six coats of 32 ml each in 1:20 parts, nine coats of 32 ml each in 1:10 parts, eight coats of 32 ml each in 1:4 parts, and 12 coats of 32 ml each in 1:1 parts of plain syrup and color syrup, respectively.

Application of Sunscreening Agents—Three coating techniques, alcohol film, modified sugar, and film, were used to apply the sunscreening agents to the color-coated tablets. Observations regarding the "wet" feel of tablets coated with glyceryl *p*-aminobenzoate, turbid solutions for the modified sugar-coating method, and mottled appearances of tablets coated with salicylates by the film-coating method were similar to those reported (1). The quantitative assessment of surface mottling of colored tablets as reported by Armstrong and March (3) was not performed, because it was beyond the scope of this study.

No change in hue occurred upon application of various sunscreening agents such as was reported with FD&C Red No. 3 upon the application of glyceryl *p*-aminobenzoate (1) and with FD&C Blue No. 1 upon the application of glyceryl *p*-aminobenzoate or benzocaine (2). However, a brilliant shine was obtained (even before polishing) with FD&C Yellow No. 6 upon the application of cinoxate or glyceryl *p*-aminobenzoate.

Measurement of Color Change—Adequate samples of each set of color-coated tablets were exposed to 1000 foot-candles of light and 26 ± 2° in a light cabinet. Samples were withdrawn at designated time intervals, and the reflectance of the tablets was measured using the transmittance scale. A spectrophotometer[4] and reflectance attachment unit (2) were used to measure the reflectance of individual tablets.

Measurements were made between 400 and 525 nm for each sample at appropriate wavelength intervals and at the maximum for the dye

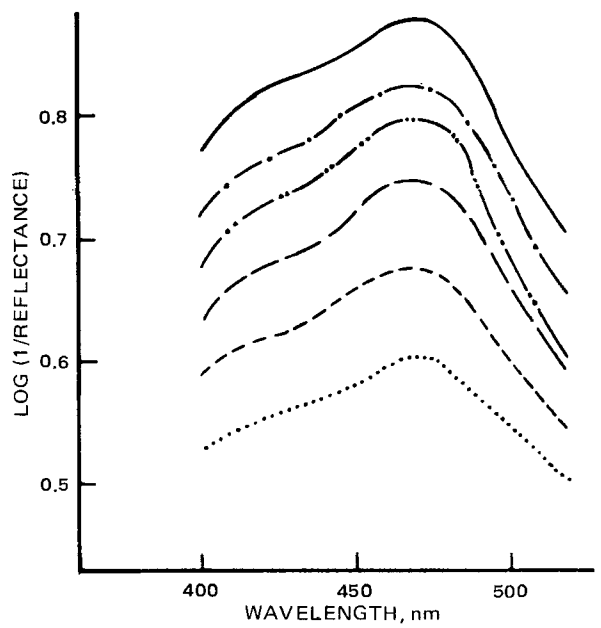

Figure 1—*Visible absorption spectra of control tablets color coated with FD&C Yellow No. 6 by film coating after intervals of storage under 1000 foot-candles of light. Key: —, initial; —·—, after 5 days; —··—, after 10 days; — —, after 20 days; - - - - -, after 30 days; and . . . . . , after 40 days.*

[1] Escalol-106, Van Dyke & Co.
[2] Giv-Tan-F, Sindar Co.
[3] Amyl Salicylate Extra, Fritsche Brother Inc.
[4] Beckman DU.

Table I—Log (1/Reflectance) Measurements of Tablets[a] Color Coated with FD&C Yellow No. 6 and Exposed to 1000 Foot-Candles of Light, with the Sunscreening Agent Applied by the Alcohol Film-Coating Method

	Log(1/Reflectance) after Exposure for				
Sunscreening Agent	Initial	8 Days	20 Days	40 Days	Initial −40 Days
Control	0.860	0.805	0.762	0.655	0.205
Glyceryl *p*-aminobenzoate	0.850	0.775	0.690	0.560	0.290
Benzocaine	0.840	0.825	0.772	0.635	0.205
Cinoxate	0.860	0.818	0.772	0.730	0.130
Homosalate	0.815	0.750	0.680	0.605	0.210
Homosalate (not polished)	0.885	0.745	0.705	0.652	0.233
n-Octyl salicylate	0.830	0.770	0.718	0.700	0.130
Amyl salicylate	0.825	0.770	0.718	0.700	0.125

[a] All tablets were polished except as noted.

Table II—Log (1/Reflectance) Measurements of Tablets Color Coated with FD&C Yellow No. 6 and Exposed to 1000 Foot-Candles of Light, with the Sunscreening Agent Applied by the Modified Sugar-Coating Method

	Log(1/Reflectance) after Exposure for				
Sunscreening Agent	Initial	8 Days	20 Days	40 Days	Initial −40 Days
Control	0.885	0.860	0.820	0.745	0.140
Glyceryl *p*-aminobenzoate	0.910	0.830	0.765	0.660	0.250
Benzocaine	0.910	0.830	0.765	0.660	0.250
Cinoxate	0.890	0.855	0.800	0.740	0.150
Homosalate	0.865	0.825	0.808	0.770	0.095
n-Octyl salicylate	0.885	0.860	0.815	0.745	0.140
Amyl salicylate	0.855	0.825	0.775	0.690	0.165
	0.920	0.818	0.818	0.752	0.168

(475 nm) (Fig 1). Color evaluation by visual observation was carried out as previously reported.

RESULTS AND DISCUSSION

The Kubelka–Munk equation:

$$\ln \theta_t = \ln \theta_t' - ktI \qquad \text{(Eq. 1)}$$

where $\theta_t = (1 - R)^2/2R$, R = reflectance at the absorbance maximum at time t, I = intensity in foot-candles, k = apparent first-order rate constant, and $\theta_t = \theta_t'$ at $t = 0$, conveniently describes the first-order degradation of various dyes, *e.g.*, FD&C Red No. 3 (1, 4) and FD&C Blue No. 1 (2). The data obtained for FD&C Yellow No. 6 plotted as log θ_t *versus* the product of time and intensity did not yield a straight line, indicating that the fading did not occur *via* a simple first-order process. The data were also plotted as $1/\theta_t$ *versus* the product of time and intensity; but this plot also failed to yield a straight line,

Table III—Log (1/Reflectance) Measurements of Tablets Color Coated with FD&C Yellow No. 6 and Exposed to 1000 Foot-Candles of Light, with the Sunscreening Agent Applied by the Film-Coating Method

	Log (1/Reflectance) after Exposure for				
Sunscreening Agent	Initial	8 Days	20 Days	40 Days	Initial − 40 Days
Control	0.880	0.814	0.748	0.605	0.275
Glyceryl *p*-aminobenzoate	0.905	0.870	0.710	0.620	0.285
Benzocaine	0.875	0.845	0.780	0.712	0.163
Cinoxate	0.860	0.845	0.790	0.690	0.170
Homosalate	0.810	0.838	0.715	0.660	0.150
n-Octyl salicylate	0.795	0.680	0.532	0.509	0.286
Amyl salicylate	0.700	0.675	0.600	0.572	0.128

Table IV—Summary of Visual Observations of Tablets Coated with FD&C Yellow No. 6 and Exposed to 1000 Foot-Candles of Light over 40 Days[a]

	Coating Type		
Sunscreening Agent	Alcohol Film	Modified Sugar	Film
Control	Noticeable fading objectionable within 30 days	1	3
Glyceryl *p*-aminobenzoate	3, S	2	2, S
Benzocaine	3	1	1
Cinoxate	2	1	1, S
Homosalate (not polished)	3	Not studied	Not studied
Homosalate	1	1	3A
n-Octyl salicylate	1	1	3A
Amyl salicylate	1	1	3A

[a] 1 = fading less than alcohol film control, 2 = fading similar to alcohol film control, 3 = fading greater than alcohol film control, 3A = fading greater than alcohol film control but with mottled appearance due to cracked film, and S = brilliant shine. All tablets were polished except as noted.

suggesting that the rate of fading did not follow a second-order equation either.

This failure to comply with the Kubelka–Munk equation prevents prediction of shelflife for color-coated tablets. However, it is possible, on the basis of reflectance measurements and visual observations, to assign an order of protection afforded by the sunscreening agents to FD&C Yellow No. 6. Reflectance measurements are reported for 0, 8, 20, and 40 days. Tables I–III show log (1/reflectance) measurements of various sets of color-coated tablets. These values are an average of two or three determinations. The range of these determinations generally varied between 0.005 and 0.010 unit [log (1/reflectance) was read off the absorbance scale]. Table IV summarizes visual observations.

Control—FD&C Yellow No. 6 exhibited sensitivity to the type of coating applied. The relative order of stability was modified sugar coating < alcohol film coating < film coating. In the absence of any

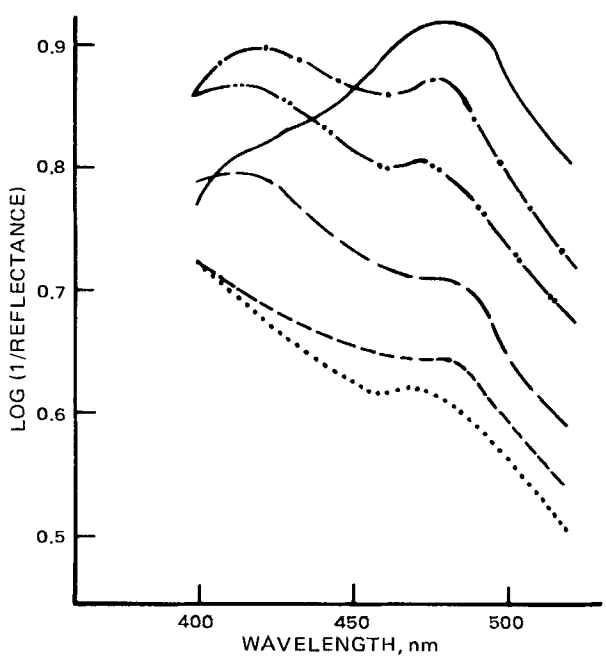

Figure 2—*Visible absorption spectra of tablets color coated with FD&C Yellow No. 6 with glyceryl* p*-aminobenzoate by film coating technique after intervals of storage under 1000 foot-candles of light. Key: —, initial; —·—, after 5 days; —··—, after 10 days; — —, after 20 days; - - - - -, after 30 days; and . . . . . , after 40 days.*

Table V—Visual Observations of Tablets Coated with Certified Dyes and Exposed to Varying Intensities of Light for up to 70 Days[a]

Days	750 Foot-Candles, Film Coating			1000 Foot-Candles, Sugar Coating		
	FD&C Yellow No. 6	FD&C Red No. 3	FD&C Blue No. 1	FD&C Yellow No. 6	FD&C Red No. 3	FD&C Blue No. 1
0—1	5	5	5	5	5	5
2—5	4	4	4	5	4	3
6—10	4	3	3	4	4	2
11—20	4	3	3	4	3	1
21—30	3	3	2	3	2	1
31—40	3	2	1	2	2	1
41—50	2	2	1	1	1	0
50—70	2	2	0	—	—	—

[a] 5 = no change, 4 = moderate change, 3 = noticeable change, 2 = poor stability, 1 = very poor stability, and 0=colorless. Material was condensed and retabulated from Ref. 5.

numerical values for rate constants or any other linear function, it is difficult to assign the relative order of stability of FD&C Yellow No. 6 with respect to FD&C Red No. 3 and FD&C Blue No. 1. Vaidya (5) assigned the following order: FD&C Yellow No. 6 > FD&C Red No. 3 > FD&C Blue No. 1 (Table V). The present findings are in general agreement with that order.

Glyceryl *p*-Aminobenzoate—FD&C Red No. 3 (1) and FD&C Blue No. 1 (2) both showed a distinct change of hue when tablets were coated by either the alcohol film-coating or the film-coating method. Although no change in hue was observed with any coating procedure in the present study, a different shade of yellow might have been produced that was not readily distinguishable by the eye. Tablets exhibited a brilliant shine (alcohol film- and film-coating method), which was retained even after 10 days of exposure to 1000 foot-candles of light. A chemical reaction between the dye and the glyceryl *p*-aminobenzoate apparently occurred, resulting in a slight shift in the maximum and a new peak at 420 nm (Fig. 2). No attempt was made to isolate the compound or to determine the reaction involved.

Benzocaine—The protective effect of the UV absorber, benzocaine, appeared most effective for FD&C Yellow No. 6 when applied as the modified sugar coat or the film coat.

Cinoxate—This compound appeared to have a distinct protective action on FD&C Yellow No. 6 when applied by the film-coating method. Only moderate fading occurred even after 40 days of exposure. A brilliant shine also was retained for up to 5 days of exposure at 1000 foot-candles of light.

Salicylates—Tablets coated with the salicylates by the film-coating method appeared mottled after 24 hr of drying due to cracking of the film. Compared to control tablets for each coating method, coating by the alcohol film method appeared to afford the best protection.

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