Inhibitory Effect of Gums and Adsorbants Upon the Migration of FD&C Blue No. 1 in Lactose

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The degree of migration of FD&C Blue No. 1 on a lactose granulation column was determined. Additives to act as dye migration inhibitors were uniformly incorporated into lactose granulation columns (prior to wetting with aqueous dye solutions) and evaluated. Tragacanth (1 per cent), acacia (3 per cent), attapulgite (5 per cent), and talc (7 per cent) were effective dye inhibitors at their respective levels. Solka-Floc was shown to have dye migration tendencies, but was still not completely effective at the 9 per cent level.

VISUAL OBSERVATIONS of commercially available uncoated colored tablets reveal the need, in many instances, for an examination into the cause of lack of uniformity of the tablet color and into a method for its improvement. In a recent article (1), the operation of fluidized bed drying was reported to be an effective procedure in improving color uniformity of colored granulations. Aside from the manufacturing techniques involved in mixing, blending, and drying colored granulations, the problem appears to center on those factors influencing the uniformity of application of dyes to a granulation, the most pronounced phenomenon being migration of the dye.

When a powder or granulation previously wetted with an aqueous dye solution is being air dried, the solvent rises through the powder by means of capillary action and diffusion and evaporates at the surface. Under these conditions, a hydrophilic dye with little affinity for the powder or granulation would, if present, rise with the aqueous solvent and be deposited at the solid-gas interface. This process then could be likened to adsorption chromatography wherein a water soluble dye applied to a weak adsorbant passes through the column with the aqueous eluent.

Although texts on tableting (2, 3) recognize the problem of dye migration, no evaluation or treatment of the subject appears to have been reported. It was therefore of interest to determine quantitatively the degree of migration of a dye in a granulation being dried and to examine the inhibitory influence of several additives on dye migration during the drying process.

EXPERIMENTAL

An aqueous solution of FD&C Blue No. 1 at 0.1% concentration was prepared. To 500 Gm. of lactose U.S.P. (in a Hobart mixer, model N-50) 60 ml. of the dye solution was slowly added and mixed to a reasonably uniform color dispersion. (This required about 5 minutes.) The colored and dampened material was then hand screened through a 16-mesh stainless steel screen. Clear glass vials of uniform internal diameter (29 mm.) and of uniform height (69 mm.) were then rapidly filled in duplicate to within 5 mm. of the top of the vial with approximately 29 Gm. of colored granulation. The material was settled by gently tapping the underside of the vial. The uncovered vials were then placed to dry in a dehumidified room held to a relative humidity of 20% and a temperature of 25°.

FD&C Blue No. 1, having a relatively large degree of water solubility, was chosen as representative of the FD&C dyes commonly employed. The adsorptive abilities of the powder and its constituents must be taken into consideration, as we were

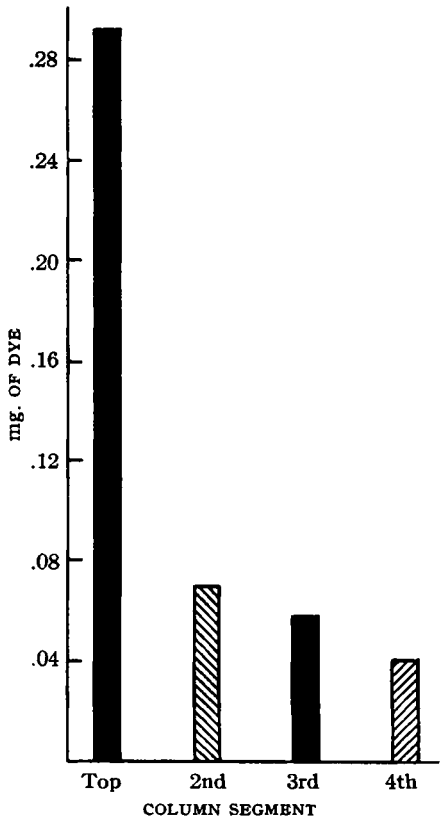

Fig. 1.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of a lactose column.

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interested in examining the migration aspects of the dye. It has been indicated by several authors (4, 5) that an inverse relationship between solubility and adsorbability appears to exist. The triphenylmethane group of dyes generally shows better water and polar solvent solubility than the azo, indigoid, and xanthene dyes. FD&C Blue No. 1, a triphenylmethane dye with three sulfonic acid groups, should serve as a dye more difficult to adsorb onto a column than other triphenylmethane dyes with fewer sulfonic acid groups. The inverse relationship of adsorption from aqueous solutions and the number of sulfonic acid groups present on a dye molecule has been reported (6).

As adsorption takes place better at lower temperatures (7), a temperature of 25° was chosen in preference to higher oven drying temperatures. A slow uniform rate of drying also precludes the possibility

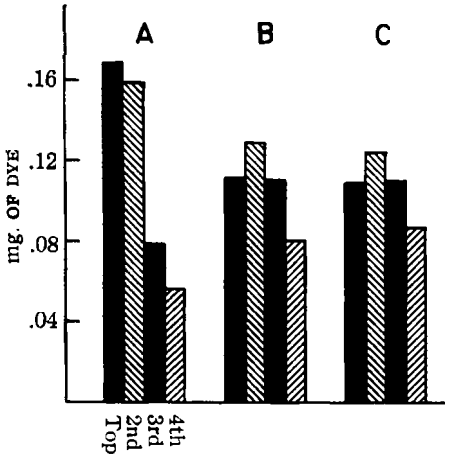

Fig. 2.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of lactose columns containing different levels of acacia. Key: A = 2%, B = 3%, C = 4%.

of "case hardening" and subsequent retention of moisture within the column.

After a period of 5 days, to permit the moisture level to drop to insignificant levels (less than 0.4% measured on a Cenco moisture balance) and to assure contact of the dye with any adsorbent that may be present, the columns of material were removed by inverting the vials and tapping the sides and glass bottoms smartly. The intact formed cylinder of granulation was then measured off into equal sections and cut with a sharp blade. Each section was then weighed and dissolved in 50 ml. of distilled water. Absorbance readings, using a Beckman model DU spectrophotometer at a wavelength of 630 mμ, were recorded and the dye concentration in milligrams per gram of lactose were calculated (see Fig. 1).

Since the dye solution is absorbed by the lactose in a sponge-like manner and since the color can be readily washed out of the granulation (as exhibited by the rapid migration of the dye), the process of coloring the lactose is said to be one of "imbibition" and not one of true dyeing (8). This suggested that "colloids which imbibe to their fullest" (9) might act to localize the color and prevent migration. "Thickeners," exemplified by acacia and tragacanth, have

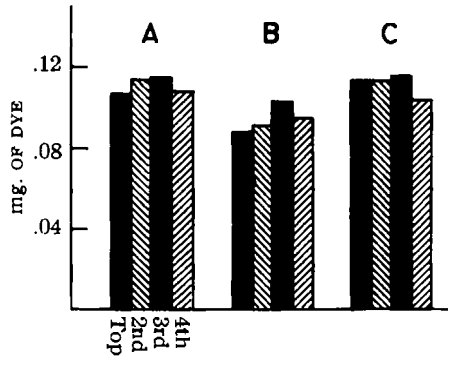

Fig. 3.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of lactose columns containing different levels of tragacanth. Key: A = 1%, B = 2%, C = 3%.

been employed in textile dyeing for just this purpose (10). As these gums readily form colloidal dispersions, they were incorporated into the columns of lactose in an attempt to inhibit the migration of the dye.

Solka-Floc, a purified wood cellulose, has been listed as an organic adsorbant (11); this material also has the property of absorbing moisture. These properties led to the inclusion of Solka-Floc as an additive to be evaluated.

Adsorptions of dyes on mineral substances have been amply described in the literature (12). Based on their dispersed position throughout a lactose granulation, it was thought that inert adsorbants, such as talc and activated attapulgite, might adsorb and hold the dyes in place, thereby preventing migration of a hydrophilic dye as the water surfaced and evaporated.

The experimental procedures employed to eval-

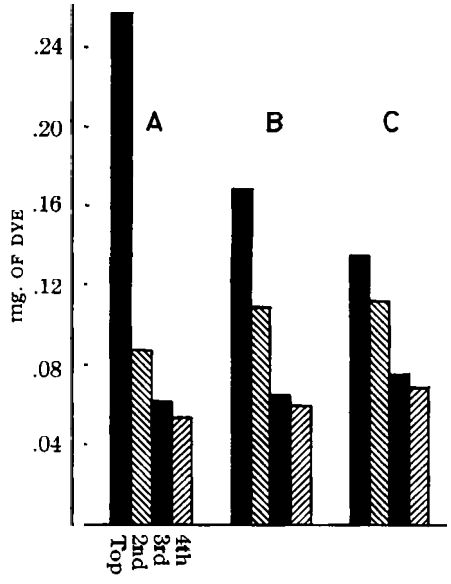

Fig. 4.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of lactose columns containing different levels of Solka-Floc. Key: A = 3%, B = 6%, C = 9%.

uate the effect of gums and adsorbants on the migration of dyes were the same as described above, except that each column now contained a uniformly incorporated additive. The calculated concentrations of the prepared dye solutions added to the different granulations was not exactly 0.1% for each solution prepared. It is the relative dye concentration found within each individual column, however, that points to the degree of migration. A level of 3% was first chosen to establish a basis for comparison. Additional concentration levels of the additives were then incorporated and evaluated in an attempt to determine that level which would be effective in inhibiting the migration of the dye.

RESULTS AND DISCUSSION

Figures 2–6 offer a visual representation of the results. Uniformity of height of the bars indicates

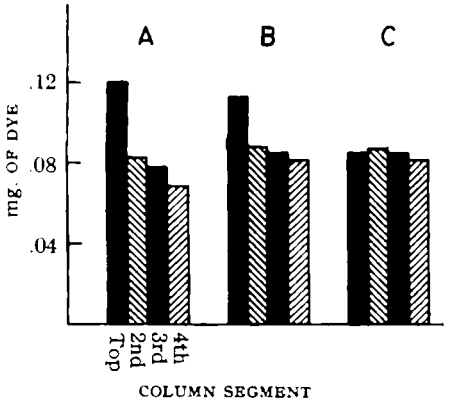

Fig. 5.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of lactose columns containing different levels of talc. Key: A = 3%, B = 5%, C = 7%.

the ideal situation of uniformity of color throughout the columns.

Figure 4 reveals the concentration of dye found in the upper portions of the column expressed as per cent of total dye recovered from the column.

Acacia, at the 3% level, inhibited the migration of FD&C Blue No. 1 in our lactose column. Tragacanth appears to be equally effective at the 1% level. The adsorbants, talc and attapulgite, were also effective, but required a greater concentration of additive than that required for the gums. Approximately 5% of activated attapulgite was comparable in effect to 7% talc. Solka-Floc exhibited migration inhibiting tendencies as shown by the inverse relationship between concentration of additive and con-

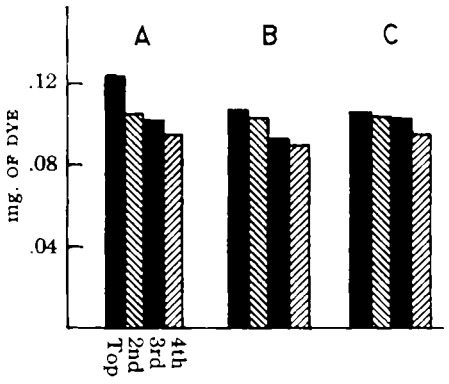

Fig. 6.—Concentration in mg./Gm. of FD&C Blue No. 1 in various segments of lactose columns containing different levels of attapulgite. Key: A = 3%, B = 4%, C = 5%.

centration of dye into the upper portions of the column. However, complete inhibition was not found at the 9% level of additive. Surface area of adsorbant may be a factor influencing the relative abilities of the various additives to inhibit dye migration, but this has not yet been evaluated.

It would seem from the above that gums and adsorbants can be successfully employed to inhibit the migration of FD&C Blue No. 1 on a lactose column. In the order or effectiveness, it has been found that 1% tragacanth is roughly equivalent to 3% acacia, which is approximately equivalent to 5% attapulgite or 7% talc. Extrapolation of the data in Fig. 4 indicates that Solka-Floc at the 12–15% level might also be an effective dye migration inhibitor. Thus, it appears that incorporation of selected gums and mineral adsorbants into formulations of wet granulations inhibits the migration of dyes.

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