

of a concentrate may not affect the viscosity of the resulting foam in exactly the same manner. Surface viscosity and surface area are dominant factors in the viscosity of the pressurized foam.

The pressure rheometer can be a useful tool for studying aerosol concentrates containing propellants. Since foam-producing systems are generally emulsions or micellized solutions, determining the rheological properties of concentrates before pressurization is of limited value. Commercial pressure rheometers have become available since this research was begun. However, the magnetic clutch unit (introduced by the Polyscience Corp., Evanston, Ill.) for use with the Rotovisco viscometer requires a sample size of approximately 1 l., which makes it unattractive for product-development work. The Viscoclav MA attachment to the Contraves rheometer (Oikon Corp., Stanford, Conn.), which also utilizes a magnetically driven bob, employs a much smaller (10 ml.) sample.

It is important that cosmetic and pharmaceutical aerosol chemists investigate their pressurized systems using techniques such as those described in this paper if meaningful rheological data are to be generated.

SUMMARY AND CONCLUSIONS

The design of a device for modifying a commercially available rotational viscometer to measure the rheological properties of fluids under pressure is described.

Data presented for simple aerosol concentrate soap formulations revealed pseudoplastic properties which could not always be correlated with the flow properties of the resultant foams. This lack of

correlation may be attributable to the role that surface viscosity (rather than bulk viscosity) plays in determining foam consistency.

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Titanium Dioxide Lakes I: Prepared from Certified Water-Soluble Dyes and Employed in Color-Coating Tablets

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Abstract □ Titanium dioxide, ranging in particle size from 0.005 to 0.040 μ , has been investigated as an adsorbate in the manufacture of lake dyes from certified water-soluble dyes. The manufacturing technique for the titanium dioxide lakes and the pharmaceutical application in color-coating tablets have been demonstrated and discussed in conjunction with automatic spray coating.

Keyphrases □ Titanium dioxide lakes—preparation □ Lakes, water-soluble dyes—titanium dioxide adsorbate □ Spray drying—titanium dioxide lake preparation □ Color coating, tablets—titanium dioxide lakes

Color lakes, prepared in liquid suspension, have been extensively employed pharmaceutically for coloring sugar-coated tablets. There are advantages for using the color lakes rather than the water-soluble dyes, which are well known to the coating expert. These advantages consist of: significant time reduction for the color-coating operation, greater color stability, and greater color uniformity for consecutive batches (1). The majority of color lakes are manufactured by employing alumina as the adsorbate material interacted with various dyes. Commercial lakes are available

as micronized powders that render better color dispersion in liquid suspensions than if not so treated.

Color-concentrate suspensions prepared from color lakes are commercially available and are extensively used by the pharmaceutical industry for coloring sugar-coated tablets.

The purpose of this study was to determine the acceptability of titanium dioxide as an adsorbate material for color lake manufacture from water-soluble dyes. The titanium dioxide selected is referred to as "fumed" and possesses a submicron particle size. The ultimate goal of this project was to prepare extemporaneously color lakes for tablet coating.

EXPERIMENTAL

Materials—Fumed titanium dioxide¹ was selected for study as an adsorbate in the manufacture of color lakes because it possesses a suitable particle-size range from 0.005 to 0.040 μ . Titanium dioxide USP differs significantly from the fumed material with

¹ Titanium Dioxide P-25, DeGussa, Inc., Kearny, N. J.; Cab-O-Ti, Cabot Corp., Boston, Mass.

regard to the particle-size range and the quantity of soluble titanium salts. Commercial titanium dioxide USP, which is used as an opaquing agent with soluble and insoluble dyes in tablet coating, is unsuitable for this purpose (2). The imbalance of electrostatic charges on the surface and particle-size dimensions of the titanium dioxide USP causes agglomerates to form which prevent significant physical or chemical surface interaction with the dyes. The water-soluble dyes employed in this project were: F.D. & C. Red No. 3, F.D. & C. Blue No. 1, F.D. & C. Yellow No. 5, F.D. & C. Violet No. 1, and F.D. & C. Green No. 3. In addition, surface-active agents, *i.e.*, polyoxypropylenepolyoxyethylene condensates;² binding agents, *i.e.*, partially hydrolyzed polyvinylacetate;³ and acidifying agents, *i.e.*, hydrochloric, acetic, tannic, and citric acids, were also employed in the manufacture of the color lakes.

Color Lakes Composition and Method of Manufacture—The following color lakes were prepared with modification of the composition as an indication of the versatility of this method for preparing color lakes. Numerous lakes have been prepared; however, only one example of each modification is described in the text. The component quantities indicated are representative of 1 kg. of finished color lake.

Type 1	Percent by Weight
Fumed titanium dioxide P-25	96
F.D. & C. Violet No. 1	4

The F.D. & C. Violet No. 1 was dissolved in 500 ml. of distilled water. The fumed titanium dioxide was dispersed in 2000 ml. of water and maintained in a state of agitation employing a Kady colloid mill⁴ with a rotor of 12,000 r.p.m. The dye solution was added to the titanium slurry and milled for 30 min. The resultant color slurry was filter pressed and washed with distilled water to remove soluble titanium salts. The slurry was then vacuum dried and stored in suitable glass containers.

Type 2	Percent by Weight
Fumed titanium dioxide P-25	75
F.D. & C. Red No. 3	20
Surface-active agent (Pluronic F-68)	5

The F.D. & C. Red No. 3 was dissolved in 2 l. of distilled water. The fumed titanium dioxide was dispersed in 700 ml. of distilled water and maintained in a state of agitation by employing a Kady colloid mill. The dye solution was added to the titanium slurry and milled for 30 min. The surface-active agent (Pluronic F-68) in 1 l. of distilled water was added to the color slurry. The color slurry and 1% acetic acid-ethanolic solution was then simultaneously pumped in equal portions into a Nerco-Niro portable laboratory spray dryer⁶ employing a Sigmamotor pump.⁶ The heated chamber of the spray dryer was maintained at 175° inlet and 75° outlet temperatures. The color lake obtained was then vacuum dried for 6–8 hr. at 45° and stored in a suitable glass container.

Type 3	Percent by Weight
Fumed titanium dioxide P-25	89.5
F.D. & C. Blue No. 1	5.0
Surface-active agent (Pluronic F-68)	0.5
Partially hydrolyzed polyvinylacetate	5.0

The F.D. & C. Blue No. 1 was dissolved in 2 l. of distilled water. The fumed titanium dioxide was dispersed in 900 ml. of distilled water and maintained in a state of agitation by employing a Kady colloid mill. The dye solution was added to the titanium slurry and milled for 30 min. Then the partially hydrolyzed polyvinylacetate in 1 l. of hot distilled water was added to the color slurry. The surface-active agent (Pluronic F-68) was dissolved in 300 ml.

Table I—Pertinent Operational Details of the Automatic Color-Coating Operation Employing the Titanium Color Lakes

Coating pan speed	26 r.p.m.
Air inlet temperature	55°, 150 c.f.m.
Air exhaust temperature	35°, 200 c.f.m.
Liquid nozzle (DeVilbiss)	AV 1115-D-S
Air nozzle (DeVilbiss)	491-D
Color-coating suspension temperature	55°
Liquid pressure	30 p.s.i.
Air pressure	20 p.s.i.
Spraying time	30 sec.
Dwell time	4 min.
Drying time	6.5 min.
Color coat weight	25–35 mg./tablet
Number of applications	8–12
Color coating time	100–120 min.

of distilled water and was added with thorough agitation. The color slurry was then spray dried in the same manner as described in Type 2; however, the acetic acid-ethanolic solution was eliminated from the procedure.

Fumed alumina⁷ was also employed in exactly the same manner as with Types 1, 2, and 3, which gave similar results as obtained with the fumed titanium dioxide.

Color-Coating Suspension—Fumed titanium dioxide lakes were employed to prepare coating suspensions that were applied to sized or smoothed tablets. As outlined in Method 2, extemporaneous preparation of the color lake with a sucrose syrup (71% w/w) was used to obtain a color suspension for pan-coating tablets. The composition of the color suspensions and two procedures for manufacture are outlined as Methods 1 and 2.

Method 1	Per 3 l.
Titanium dioxide color lake described as Type 2	60.0 g.
Polyvinylpyrrolidone	15.0 g.
Sucrose syrup 71% w/w to	3.0 l.

Sixty grams of color lake described as Type 2 was dispersed in 2.8 l. of sucrose syrup (71% w/w) in which 15 g. of polyvinylpyrrolidone was dissolved. The resulting suspension was milled, employing the Kady colloid mill for 30 min. The color suspension was brought to volume, and was then suitable for application to smooth-coated tablets.

Method 2	Per 10 kg.
Fumed titanium dioxide	0.100 kg.
F.D. & C. Violet No. 1	0.004 kg.
F.D. & C. Green No. 3	0.001 kg.
F.C. & C. Yellow No. 5	0.015 kg.
Titanium dioxide USP	0.100 kg.
Distilled water	2.000 kg.
Sucrose, granular	5.000 kg.
Sucrose syrup 71% w/w <i>q.s. ad.</i>	10.000 kg.

The F.D. & C. dyes were dissolved in 1 l. of distilled water. The fumed titanium dioxide was dispersed in 1 l. of sucrose syrup (71% w/w). The liquids were then placed in the Kady colloid mill and milled for 1 hr. Five kilograms of sucrose was added to the Kady mill vessel and milled until solution was obtained. The titanium dioxide USP was mechanically milled in 1 l. of distilled water and then was added to the color lake suspension. The resulting color suspension was brought to volume with sucrose syrup (71% w/w) and milled an additional 15 min.

The resulting color suspension was then applied to 25 kg. of smoothed tablets which were contained in a rotating coating pan. The tablets employed in this project had a 180-mg. core weight and 250-mg. smooth-coat weight. The tablet cores were 8 mm. in diameter and had a deep concave shape. The coating pan employed was the Manesty CP-2 which has a 91.44-cm. (36-in.) diameter. The coating pan was equipped with four baffles as described by Lachman (3). The color-coating suspension was sprayed, using an apparatus similar to that described by Steinberg (4). A DeVilbiss

² Pluronic F-68, Wyandotte Chemical Corp., Wyandotte, Mich.

³ E. I. du Pont de Nemours & Co., Wilmington, Del.

⁴ Kinetic Dispersion Corp., Buffalo, N. Y.

⁵ Nichols Engineering & Research Corp., New York, N. Y.

⁶ Sigmamotor, Inc., Middleport, N. Y.

⁷ Aluminum Oxide C, DeGussa Inc., New York, N. Y.; Alon C, Cabot Corp., Boston, Mass.

automatic spray gun (AGB504) equipped with an internal mixing nozzle was employed in this study. Pertinent parameters of the automatic color-coating operation are outlined in Table I.

Color Fastness of the Color Lakes—The permanency of the color lakes prepared from fumed titanium dioxide and the soluble dyes was tested using a centrifuge technique. One gram of color lake was suspended in 30 ml. of water and submitted to centrifugal force at 5000 r.p.m. for 5 min. The supernatant liquid was poured off and observed for color-leaching tendencies. The same color lake was resuspended in 30 ml. of water and centrifuged. In most cases, negligible transfer of the dye to the aqueous media occurred during the first step but was absent after the second treatment.

Dispersibility of the Color Lakes—The dispersibility of the color lakes when in an aqueous suspension was determined by employing sedimentation-rate analysis. Commercially available lakes were used as a control for this study. Two grams of color lake was suspended in 100 ml. water and placed in a 100-ml. graduated cylinder. The commercial lakes settled out about five times as rapidly as those prepared and indicated poor dispersibility. The color lake particles containing fumed titanium had greater resistance to the force of gravity, which was evidenced by its flocculated state

RESULTS AND DISCUSSION

Fumed titanium dioxide was employed in this investigation as an adsorbate for color lakes. The application results from a physico-chemical reaction of the submicron material with water-soluble dyes. This results from the strong attractive forces existing between the positive-charged fumed inorganic dioxide and the negative-charged dye particles. The fumed material ranges in particle size from 0.005 to 0.040 μ , and thus it possesses a surface area (B.E.T. method) from 35 to 100 m.²/g. (5). The absence of permanent interaction between titanium dioxide USP and dyes without permanency of lake formation is well known to the dye chemist (6).

The traditional method for color lake formation involves the coprecipitation of a soluble dye with a selected, hydrated, inorganic oxide or freshly precipitated salt such as calcium sulfate or barium sulfate. This method is not applicable for titanium dioxide lake formation from the USP grade material since it does not have the necessary physical characteristics of the traditional lake adsorbates. Titanium dioxide USP used for pigmentary purposes results in particle aggregation and a deficient pigment having less than optimum dispersibility and decreased properties, *i.e.*, tinting strength. This causes the titanium pigments to possess the following undesirable qualities: poor dispersibility, aeration, and fast settling, which interfere with excellence in their pharmaceutical use. The titanium dioxide lakes which were prepared from the fumed material resulted in a lake particle having optimum pigmentary properties, notably tinting strength, and demonstrated improved dispersibility.

As a result of fumed titanium dioxide's smaller particle size as compared with the USP grade, when it was dispersed in an aqueous medium it appeared relatively transparent and exhibited a much lower tinting strength.

When the fumed titanium dioxide was dispersed in an aqueous medium, it showed an isoelectric point at pH 6.5. Fumed titanium dioxide differs from the regular opacifying grades, because it possesses a substantial positive surface charge which causes it to interact exceptionally well with negatively charged particles, *i.e.*, soluble dyes. Acidification of the titanium dioxide-dye slurry when preparing the color lake permitted greater dye inclusion, since the potential of the titanium dioxide is higher at a low pH. The isoelectric point should be avoided in lake formation because it would provide the lowest potential. The acidified dyes are poorly soluble in water, and the color lake formed was evaluated as more permanent. An important aspect of the titanium lakes is that strong acids such as hydrochloric and acetic may be employed to fix the

dye without causing the adsorbate to dissolve, as would occur with alumina. When a particular acid was varied in the treatment of the dye adsorbate, different shades of a specific color were obtained.

The spray-dried titanium lakes had a particle-size range similar to those obtained by a micronizing process and fall in a range from 1 to 10 μ as demonstrated by photomicroscopy. Excellent dispersibility of these color lakes in water was observed when compared with the commercially available color lakes prepared by jet-milled micronization.

An opaque gel structure formed during the extension of the dye on the fumed titanium dioxide. Addition of the dye caused a thickening of the fumed titanium slurry almost instantly, provided that the amount of dye was either in excess or sufficient to saturate the dye-adsorbing capacity of the fumed material. When the amount of titanium dioxide in the slurry was about 1% w/w and the dye about 1–2% w/w, a change occurred, a shifting from a colloidal suspension to a dense precipitate at the saturation point. If the dye saturation point was just reached, the lake obtained was easily separated by centrifugation; however, those slurries with a deficiency or excess of dye behaved like colloidal suspensions, and it was extremely difficult to separate the lakes from the dispersion medium by centrifugation. This phenomenon varied with the chemical structure of the dye considered.

The method of choice in the manufacture of the titanium lakes was the employment of the spray-drying technique which included preacidification before atomization into the spray-drying chamber. The inlet and outlet temperatures of the spray dryer were based on the composition of the dispersion media. The viscosity of the slurry prior to spray drying was decreased by using either inorganic or organic acids. If strong acids were employed, it was imperative that they were volatile at the inlet temperature of the spray dryer. The color fastness of these titanium dioxide lakes prepared by spray drying exhibited exceptional permanency of the dye-adsorbate interaction.

The color lakes prepared in this study were suspended in sucrose syrup (71% w/w), and the certified dye content, in certain cases, was utilized at 0.4% w/v. The color suspension was then applied to rounded, rotating tablets, and the tablets required about 8–12 applications to be considered acceptable from a color and physical appearance standpoint. The coating suspension permitted a reduction of the color-coating operation when compared with conventional dye solutions. The advantages of this process for coating tablets are: uniform color dispersion, consecutive batch reproducibility, extemporaneous preparation of color lakes, and the necessity of only 8–12 applications of the color suspension to obtain maximum color tone.

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