Measurement of Surface Color and Color Difference of Tablet Colorants by Tristimulus Colorimetry

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Abstract □ The surface color of a series of color dispersions containing from one to three FD&C or D&C dyes suspended in a sucrose syrup was examined using tristimulus colorimetry. CIE (x, y) and Hunter (a, b) chromaticity data, determined directly from an integrating sphere colorimeter or from reflectance spectra and suitable calculations, were used to order materials by color on expanded chromaticity diagrams. Color difference was evaluated quantitatively from Hunter (a, b) data using the Judd color difference formula. Quality control specifications were established either by defining areas of acceptable color by applying limits to the chromaticity coordinates of color standards or by requiring the Judd color difference to be less than a specific number of National Bureau of Standards standard units. This method eliminates the subjective character of color evaluation and permits the quantitation of visual color difference. These differences can be used, in conjunction with defined color standards, to develop color specifications for tablet colorants, finished tablets, and liquid and cream pharmaceutical preparations.

Keyphrases □ Color difference and surface color—measurement of tablet colorants by tristimulus colorimetry □ Tristimulus colorimetry—measurement of surface color and color difference of tablet colorants □ Chromaticity data—surface color of series of FD&C and D&C color dispersions, tristimulus colorimetry □ Colorimetry, tristimulus—surface color and color difference of tablet colorants

Many pharmaceutical tablets are coated with sugar suspensions of FD&C and D&C dyes for purposes of aesthetics, identification, and stability. Since it is desirable that all tablets coated with a specific colorant appear to be the same color, it is important that the coating material be of uniform and consistent color. The evaluation of surface color is usually a subjective test, dependent only on the ability of an individual to discriminate color differences visually.

Because the eye is not an analytical instrument, it is not capable of precisely defining color or of consistently discriminating small differences in color between two similar substances. The eye also possesses only a limited memory for color, and the visual storage of color data is, therefore, extremely difficult. Visual color determinations are complicated further by the fact that different individuals perceive the same color differently, and even the same individual often describes a single color in a different manner at different times.

Subjective color determination usually involves a visual comparison of the sample with some arbitrary color standard. This procedure necessitates reliance on color standards that are subject to change with time and are not permanent records of color. As a result, methods often involve the frequent redefinition of color standards which can lead eventually to a gradual, but significant, change in acceptable color. There is, therefore, a necessity to define color in absolute terms and to develop a numerical method of color evaluation.

Spectrophotometric techniques for the evaluation of surface color are not new. Trichromatic color measurement (tristimulus colorimetry) has been used successfully in the paint, textile, and plastic industries for many years (1, 2). Some work also has been reported on color determination and color control in the food industry (3, 4). More recently, colorimetry has been employed in the determination of color stability of pharmaceutical tablet formulations (5–18) and in the production of color matches for solid dosage forms (19–21). This work describes the measurement of surface color by tristimulus colorimetry and the determination of color specifications for the routine control of tablet colorants.

THEORY

Any color can be matched by an appropriate mixture of three selected radiations, usually saturated red (700 nm), green (546 nm), and blue (436 nm) (19). This phenomenon of three-color mixing and matching is attributed to the existence of a triple-receptor system in the eye, where the entire range of color sensations is derived from variations in the magnitude of responses in three forms of cone receptors. The spectral components of a beam of light entering the eye are combined additively when focused on the cone receptors of the retina, so an additive color mixture system must provide the basis of color measurement (20). A system has been developed by the Commission Internationale de l'Eclairge (CIE) in terms of the amounts of three defined stimuli which, when mixed in fixed proportions, produce a complete color match with some established standard. The tristimulus values (X, Y, and Z) of any sample are defined as the magnitudes of these three standard stimuli needed to produce a color match.

When a colored surface is illuminated by a standardized illuminant and the flux incident on that reflecting surface has the spectral energy distribution, P_λ, the tristimulus values of the reflected light are given by (19):

$$X = \int_0^\infty \bar{x}_\lambda P_\lambda \rho_\lambda \, d\lambda \Big/ \int_0^\infty \bar{y}_\lambda P_\lambda \, d\lambda \simeq \sum_{380}^{770} \bar{x}_\lambda P_\lambda \rho_\lambda \Big/ \sum_{380}^{770} \bar{y}_\lambda P_\lambda \quad \text{(Eq. 1)}$$

$$Y = \int_0^\infty \bar{y}_\lambda P_\lambda \rho_\lambda \, d\lambda \Big/ \int_0^\infty \bar{y}_\lambda P_\lambda \, d\lambda \simeq \sum_{380}^{770} \bar{y}_\lambda P_\lambda \rho_\lambda \Big/ \sum_{380}^{770} \bar{y}_\lambda P_\lambda \quad \text{(Eq. 2)}$$

$$Z = \int_0^\infty \bar{z}_\lambda P_\lambda \rho_\lambda \, d\lambda \Big/ \int_0^\infty \bar{y}_\lambda P_\lambda \, d\lambda \simeq \sum_{380}^{770} \bar{z}_\lambda P_\lambda \rho_\lambda \Big/ \sum_{380}^{770} \bar{y}_\lambda P_\lambda \quad \text{(Eq. 3)}$$

where ρ_λ is the reflectance, $\rho_\lambda = 1.000$ for 100.0% reflectance, and $\bar{x}_\lambda$, $\bar{y}_\lambda$, and $\bar{z}_\lambda$ are the spectral tristimulus values (distribution coefficients) of the equal energy spectrum that have been determined from color matching experiments. Since the products $\bar{x}_\lambda P_\lambda$, $\bar{y}_\lambda P_\lambda$, and $\bar{z}_\lambda P_\lambda$ for the standard sources are used frequently, tables of these products have been prepared with normalized $\bar{y}_\lambda$ distribution coefficients so that $\int_0^\infty \bar{y}_\lambda P_\lambda \, d\lambda = 100.000$[1]. The Y tristimulus value is a direct measure of the percent luminance of the colored surface. The chromaticity coordinates of the reflected light are calculated as follows:

[1] The normalized energy-weighted distribution coefficients for numerous illuminants including the S_c and D-6500 sources and the spectral distribution coefficients have been tabulated by CIE and are found in the literature (Ref. 20, pp. 316–330).

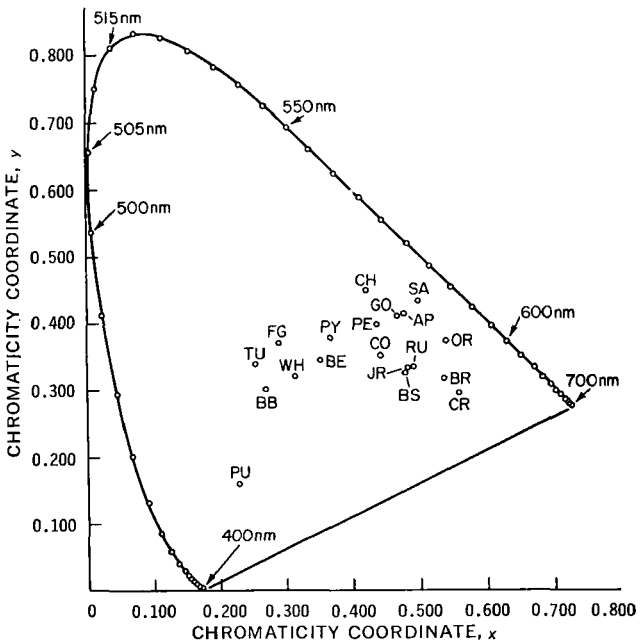

Figure 1—*An* (x, y) *chromaticity diagram prepared from the 1931 CIE chromaticity coordinates for a field subtending 2° (Ref. 19, p. 316). The colorants listed in Table I are located by their* (x, y) *coordinates to define the region of the diagram where real colors are found.*

$$x = X/(X + Y + Z) \qquad \text{(Eq. 4}a\text{)}$$

$$y = Y/(X + Y + Z) \qquad \text{(Eq. 4}b\text{)}$$

The x and y chromaticities can then be employed as coordinates to locate the position of the sample in a two-dimensional chromaticity diagram.

The separation of points on the chromaticity diagram represents real differences in color. Color difference determinations are, however, complicated because significant differences in (x, y) chromaticity values do not necessarily produce significant visual differences in color for all spectral regions (21). As a result, a nonuniform distribution of colors on the chromaticity diagram is obtained.

To produce a more uniform distribution of colors, a transformation of the chromaticity diagram is required such that the distance between any two colors is a direct measure of their visual differences. One transformation that has been widely used is the Hunter (a, b) scale. The (a, b) coordinates of a sample are derived from the (x, y) chromaticity coordinates by the following expressions (22):

$$a = [17.5Y^{1/2}][1.02(x/y) - 1.0] \qquad \text{(Eq. 5)}$$

$$b = [5.927Y^{1/2}][x + 2.181y - 1.0]/y \qquad \text{(Eq. 6)}$$

A more uniform color diagram is obtained when a and b are employed as the coordinates of the chromaticity diagram.

Several methods are available for determining color difference quantitatively. The Judd color difference formula is widely used, especially in the form shown in Eq. 7 (23):

$$\Delta E = [\Delta L^2 + \Delta a^2 + \Delta b^2]^{1/2} \qquad \text{(Eq. 7)}$$

where $\Delta L = [10Y_1^{1/2}] - [10Y_2^{1/2}]$, $\Delta a = a_1 - a_2$, $\Delta b = b_1 - b_2$, and the color difference, ΔE, is expressed in National Bureau of Standards (NBS) units. The NBS unit, the color difference seen when $\Delta E = 1$, is about three times smaller than can be perceived visually under the best conditions and corresponds to a chromaticity change of 0.0015–0.0025 in x and y for points in the center of the (x, y) diagram.

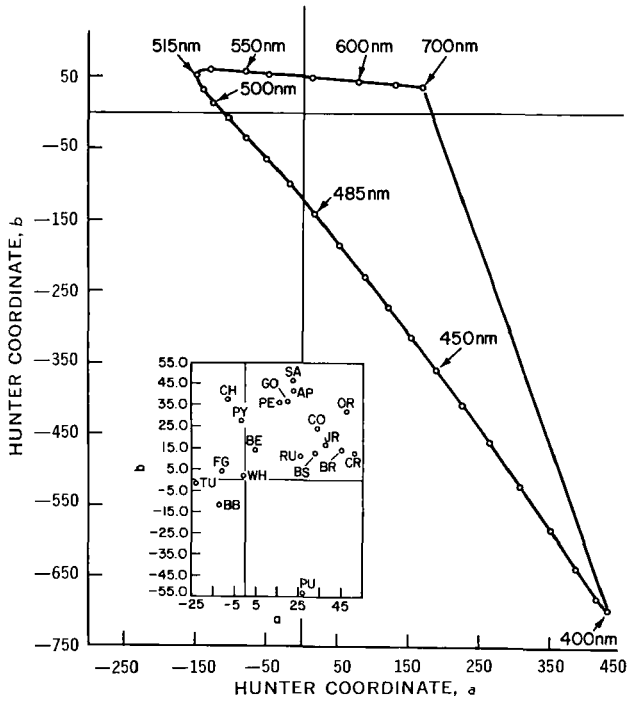

Figure 2—*Hunter* (a, b) *diagram prepared from the 1931 2° CIE chromaticity coordinates using the transformations shown in Eqs. 5 and 6. The expanded portion of the diagram shows the location of the colorants listed in Table I.*

EXPERIMENTAL

The color dispersions investigated were purchased commercially[2]. Each dispersion contains from one to three D&C or FD&C dyes adsorbed on alumina and suspended in a mixture of sucrose syrup, titanium dioxide, and sodium benzoate.

Spectral samples were prepared by spreading 5-μm layers of the suspension on chromatography paper[3] with a Bird applicator[4]. Reflectance spectra for all samples were obtained over the 380–770-nm wavelength region using a reflectance spectrophotometer[5] equipped with a tungsten lamp. Spectra were recorded against vitrolite reference plates[6]. The reflectance due to the reference was determined by running two matched vitrolite plates, and corrections for this reflectance always were made before the tristimulus values were calculated. Tristimulus and chromaticity data were calculated from reflectance values using Eqs. 1–4*b* and the CIE 1964 10° energy-weighted distribution coefficients for the D-6500[7] standard illuminant[8].

Hunter (a, b) coordinates and some tristimulus data were obtained using the CIE 1931 2° field and the standard illuminant, S_c[9], with a direct readout colorimeter[10] equipped with a tungsten-halogen lamp and novoil filters[11]. All samples were examined using the colorimeter large sample beam and 1.9-cm (0.75-in.) aperture.

[2] Colorcon, Inc., West Point, Pa.
[3] Whatman 3MM chromatography paper.
[4] Precision Gage and Tool Co., Dayton, Ohio.
[5] Beckman DB-G spectrophotometer with reflectance attachment, Beckman Instruments, Fullerton, Calif.
[6] Beckman Instruments, Fullerton, Calif.
[7] The Colorimetry Commission of CIE has defined standard spectral distributions at various color temperatures, and the source D-6500, with a color temperature of 6500°K, has been selected as typical of average daylight (Ref. 19, p. 7).
[8] Individual calculations were made at 10-nm intervals over the 770–380-nm wavelength region, and a summation of these was made to evaluate X, Y, and Z. The energy-weighted distribution coefficients used are tabulated in the literature (Ref. 19, pp. 316–330).
[9] The 1931 CIE source S_c, with a color temperature of 6700°K, approximates average daylight. The source consists of a gas-filled tungsten lamp used in conjunction with two color filters (Ref. 19, p. 309).
[10] Gardner XL-10, Gardner Laboratory, Inc., Bethesda, Md.
[11] Gardner Laboratory, Inc., Bethesda, Md. The novoil filters absorb UV light and simplify measurements on fluorescent samples.

Table I—(x, y) and (a, b) Chromaticity Data for Colorants

Sample	Color	Composition[a]	x[b]	y	$10Y^{1/2}$	a	b
AP	Apricot	Y5, Y6	0.474 ± 0.0002	0.415 ± 0.0001	77.3 ± 0.06	22.5 ± 0.10	41.7 ± 0.06
BB	Baby blue	B1, Y5	0.269 ± 0.0004	0.302 ± 0.0002	78.0 ± 0.06	72.0 ± 0.06	−11.3 ± 0.10
BE	Beige	B2, R2, Y5	0.351 ± 0.0001	0.346 ± 0.0002	79.4 ± 0.10	5.0 ± 0.06	14.2 ± 0.06
BR	Brick red	R7, R36	0.536 ± 0.0028	0.318 ± 0.0010	35.1 ± 0.06	44.7 ± 0.06	14.3 ± 0.06
BS	Burnt sienna	B2, R3, Y5	0.477 ± 0.0000	0.326 ± 0.0000	38.5 ± 0.06	32.7 ± 0.06	12.7 ± 0.06
CH	Chartreuse	G3, Y5	0.418 ± 0.0004	0.449 ± 0.0005	72.6 ± 0.07	−6.5 ± 0.05	37.9 ± 0.11
CO	Coral	R3, Y5	0.441 ± 0.0004	0.353 ± 0.0003	69.8 ± 0.06	33.7 ± 0.15	24.5 ± 0.06
CR	Cranberry	R3, Y5, Y6	0.557 ± 0.0010	0.296 ± 0.0006	32.2 ± 0.06	50.8 ± 0.25	12.5 ± 0.12
FG	Forest green	B1, V1, Y5	0.289 ± 0.0006	0.371 ± 0.0019	29.1 ± 0.12	−10.5 ± 0.12	4.0 ± 0.15
GO	Gold	R2, Y5, Y6	0.468 ± 0.0004	0.411 ± 0.0000	70.7 ± 0.10	19.7 ± 0.06	36.9 ± 0.06
JR	Jasper red	R2, R3, Y5, Y6	0.481 ± 0.0004	0.334 ± 0.0001	46.3 ± 0.06	37.4 ± 0.15	16.8 ± 0.06
OR	Orange	R3, Y5	0.538 ± 0.0005	0.375 ± 0.0006	57.9 ± 0.06	47.3 ± 0.12	32.2 ± 0.06
PE	Peach	Y5, Y6	0.434 ± 0.0001	0.398 ± 0.0002	81.1 ± 0.06	16.0 ± 0.06	36.3 ± 0.06
PU	Purple	B1, V1, Y5	0.229 ± 0.0008	0.160 ± 0.0013	34.2 ± 0.43	27.0 ± 0.32	−53.1 ± 0.65
PY	Pale yellow	Y5	0.367 ± 0.0002	0.378 ± 0.0000	93.7 ± 0.06	−1.6 ± 0.06	28.0 ± 0.06
RU	Rust	R2, R3, R36	0.489 ± 0.0018	0.336 ± 0.0020	30.8 ± 0.11	25.9 ± 0.06	11.4 ± 0.06
SA	Saffron	Y5	0.496 ± 0.0004	0.435 ± 0.0005	77.0 ± 0.20	22.2 ± 0.35	46.4 ± 0.17
TU	Turquoise	B1, V1, Y5	0.253 ± 0.0004	0.338 ± 0.0005	56.0 ± 0.17	−23.1 ± 0.17	−1.1 ± 0.10
WH	White	B2	0.314 ± 0.0001	0.322 ± 0.0000	95.4 ± 0.28	−0.6 ± 0.06	2.4 ± 0.11

[a] Samples are dispersions of FD&C or D&C lakes in sucrose suspensions containing titanium dioxide and sodium benzoate. B1 = FD&C Blue No. 1, B2 = FD&C Blue No. 2, G3 = FD&C Green No. 3, R2 = FD&C Red No. 2, R3 = FD&C Red No. 3, R7 = D&C Red No. 7, R36 = D&C Red No. 36, V1 = FD&C Violet No. 1 (delisted), Y5 = FD&C Yellow No. 5, and Y6 = FD&C Yellow No. 6. [b] The (x, y) and (a, b) data were obtained with a colorimeter having a field subtending 2° and using the standard illuminant S_c.

RESULTS AND DISCUSSION

The 1931 CIE (x, y) spectral chromaticity coordinates are plotted in Fig. 1, and the Hunter (a, b) transformation of these coordinates is shown in Fig. 2. The curved portion of both diagrams represents the loci of spectral colors. Pure white for illuminant S_c is located near the center in each diagram with coordinates x = 0.3100, y = 0.3161 and a = 0.031, b = −0.042 (24). Sample colors are represented by points lying within the spectral boundary. The effect of the Hunter transformation is to shorten the green region (550–490 nm) and to expand the blue region (490–400 nm), producing a more uniform chromaticity diagram.

Once a color is located on a chromaticity diagram by its (x, y) coordinates, an additional property of the color, dominant wavelength, can be defined (25). The dominant wavelength is determined by drawing a line from the white point through the color point to intersect the spectral locus at some specific wavelength. For colors lying below the white point, *i.e.*, in the purple and maroon regions, the dominant wavelength is the complimentary wavelength found by drawing a line from the color point through the white point to intersect the spectrum locus.

To evaluate surface colors quantitatively and to locate these colors on both the (x, y) and (a, b) chromaticity diagrams, data for a series of color dispersions were obtained (Table I). Relative standard deviations were calculated for both (x, y) and (a, b) chromaticity coordinates for all samples and were found to be less than ±1.2% for most colorants. Chromaticity data are highly reproducible and, therefore, useful for the determination of small color differences. The data from Table I are plotted on the (x, y) diagram (Fig. 1) and the expanded portion of the (a, b) chromaticity plot shown in Fig. 2. Both diagrams locate materials by color. Colors on the Hunter (a, b) diagram are noticeably more separated, especially in the red–yellow and blue–green regions. As a consequence, very similar colors, *e.g.*, BS, JR, and RU and AP and GO, are more easily distinguished on the (a, b) than on the (x, y) chromaticity plot. Since the Hunter (a, b) scale was designed to create a more uniform measurement of color difference, equal increments in either a or b produce nearly the same visual color difference in the red as in the green and blue regions of the diagram.

Small differences in color were evaluated using three color suspensions, the chartreuse material (CH), the purple suspension (PU), and the white colorant (WH). Color data were obtained either directly, using an integrating sphere colorimeter, or from reflectance spectra and suitable calculations using Eqs. 1–4*b* (Table II). A two-way analysis of variance showed the data for all samples of each of the three colorants to be significantly different from each other. In addition, the statistical analysis showed 10 replicate determinations of color data for a single sample to be not signifi-

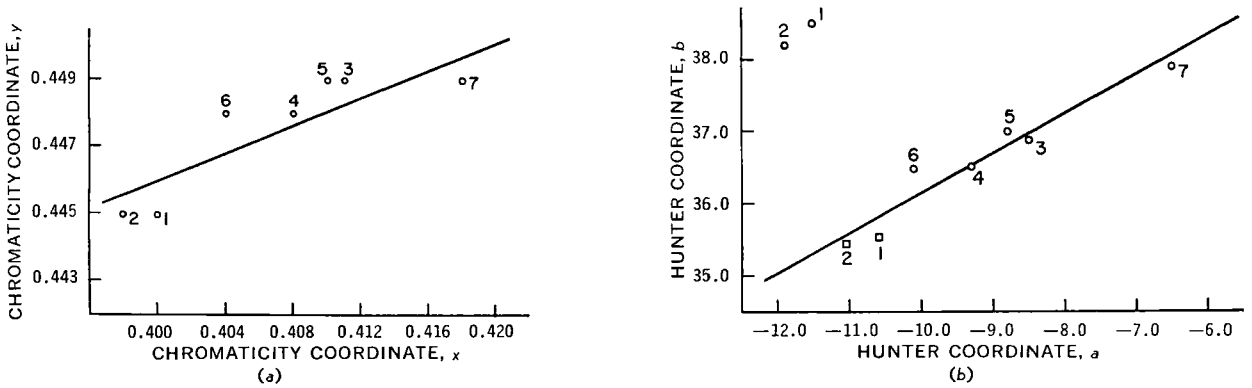

Figure 3—(a) *Expanded* (x, y) *chromaticity diagram for the chartreuse material (CH). Chromaticity coordinates were obtained using the 1931 CIE 2° energy-weighted distribution coefficients for illuminant* S_c. (b) *Expanded Hunter* (a, b) *diagram for the chartreuse colorant (CH). The* (a, b) *coordinate values were determined for the 1931 CIE 2° field data and the standard illuminant* S_c. *Key:* ○, *experimental data; and* □, *calculated data.*

Table II—(x, y) and (a, b) Chromaticity Data for Samples of Three Colorants

Colorant	Sample	x	y	$10Y^{1/2}$	a	b
CH[a]	1[b]	0.400	0.445	78.6	−11.5	38.6
	2[b]	0.398	0.445	78.0	−11.9	38.2
	3	0.411	0.449	72.2	−8.5	36.9
	4	0.408	0.448	72.0	−9.3	36.5
	5	0.410	0.449	72.5	−8.8	37.0
	6	0.404	0.448	72.9	−10.1	36.5
	7	0.418 ± 0.0004	0.449 ± 0.0005	72.6 ± 0.06	−6.5 ± 0.04	37.9 ± 0.13
PU[c]	1	0.238	0.207	43.1	16.1	−43.0
	2	0.236	0.182			
	3	0.238	0.187	38.2	24.3	−51.2
	4	0.237	0.178	36.4	26.1	−54.0
	5	0.235	0.185	37.1	24.3	−52.2
	6	0.238	0.192	39.8	21.9	−49.9
	7	0.236	0.194			
	8	0.234 ± 0.0016	0.190 ± 0.0006	40.5	22.8	−53.6
	9	0.238	0.185			
	10	0.233	0.173	34.2 ± 0.40	27.0 ± 0.29	−53.1 ± 0.61
WH[c]	1	0.318	0.336	92.6	−0.7	4.0
	2	0.325	0.340	91.1	0.0	6.0
	3	0.324	0.340	91.9	−0.1	5.8
	4	0.325	0.341	90.9	−0.6	5.5
	5	0.314 ± 0.0003	0.330 ± 0.0002	95.4 ± 0.23	−0.5 ± 0.03	2.4 ± 0.07
	6	0.311	0.328	92.9	−1.2	0.5

[a] The (x, y) and (a, b) data were obtained with a colorimeter having a field subtending 2° and using the standard illuminant S_c. [b] The (x, y) data were converted to (a, b) data using Eqs. 5 and 6 with $10Y^{1/2} = 72.4$, and the following results were obtained: Sample 1, $a = -10.6$, $b = 35.6$; and Sample 2, $a = -11.0$, $b = 35.4$. These values are used only for illustrative purposes. [c] The (x, y) data were obtained from reflectance spectra and suitable calculations using 10° energy-weighted distribution coefficients for the D-6500 standard illuminant. The (a, b) data were obtained with a colorimeter having a 2° field and using the standard illuminant S_c.

cantly different. As a result, small differences in color between different samples of a single colorant are real and not a consequence of experimental error.

The chartreuse material (CH) is a mixture of FD&C Yellow No. 5 and FD&C Green No. 3 in a sugar suspension. Seven discrete samples of this material were examined, and the expanded chromaticity diagrams, prepared by plotting the (x, y) and (a, b) data from Table II, are shown in Figs. 3*a* and 3*b*. The positions of the samples on the diagrams define their color. The line drawn on the (x, y) plot represents the direction of color shading found for these samples, from green at the lower left to yellow at the upper right. The (a, b) plot is more complex, since five of the seven points lie on a straight line which again defines color shading from green at the lower left to yellow at the upper right, while two points, representing the color positions of Samples 1 and 2, lie significantly off this line. Closer examination of the data and the expressions for the (a, b) transformations provides an adequate explanation. Equations 5 and 6, for the conversion of (x, y) to (a, b) data, include the term $Y^{1/2}$, which is a measure of the lightness of the sample. A linear (a, b) relationship is expected from a linear (x, y) relationship only when the $Y^{1/2}$ term remains constant. The data in Table II show that all samples except 1 and 2 have nearly the same $[10Y^{1/2}]$ (average $[10Y^{1/2}]$ for Samples 3–7 is 72.4). If the average value of $[10Y^{1/2}]$ found for Samples 3–7 is used to convert the (x, y) to (a, b) data for Samples 1 and 2, the resulting values lie on the line. Consequently, (a, b) data and their associated chromaticity diagrams have the advantage of discriminating not only differences in surface color but also differences in sample lightness.

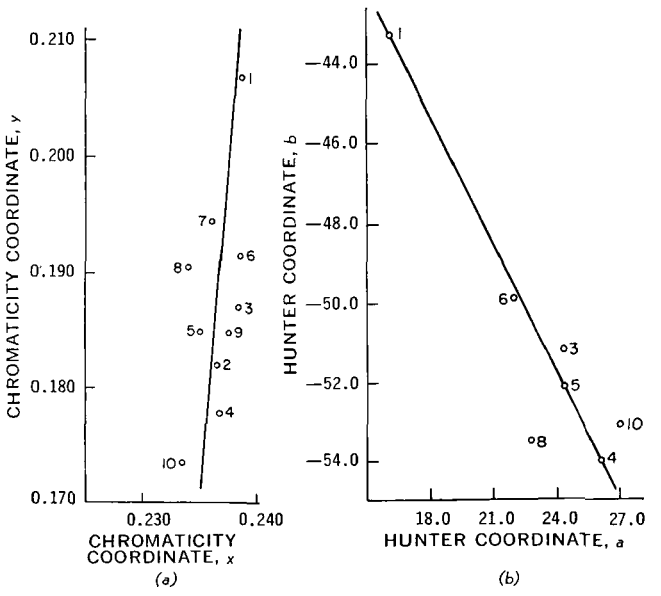

Figure 4—(a) *Expanded* (x, y) *chromaticity diagram for the purple color dispersion (PU) using the CIE 1964 10° energy-weighted distribution coefficients and the D-6500 illuminant.* (b) *The expanded Hunter* (a, b) *diagram for the purple material (PU). Coordinate values were determined for standard illuminant* S_c *and the 1931 2° field data.*

Chromaticity diagrams also can be used for the quality control evaluation of surface color and for the establishment of acceptable limits of color variation. The method can be illustrated using the data for the chartreuse material in Table II and Figs. 3*a* and 3*b*. Those samples of the chartreuse material considered to have acceptable color as judged subjectively were identified and located on the chromaticity diagrams. In this example, only Samples 3–6 were thought to be acceptable; Samples 1 and 2 were considered too green and Sample 7 too yellow. An area of acceptable color was created by placing limits on the (x, y) and (a, b) coordinates: for the (x, y) diagram, $0.402 \leq x \leq 0.414$ and $0.446 \leq y \leq 0.450$; for the Hunter (a, b) diagram, $-7.2 \leq a \leq -10.7$ and $35.5 \leq b \leq 37.7$.

If a reference standard is established for any surface color, all further subjectivity in color difference measurement can be eliminated by employing the color difference formula shown in Eq. 7. Color difference can be expressed in NBS units, and limits of acceptability for a sample when compared to a standard also can be defined in NBS units rather than by a subjective examination. For example, Sample 4 of the chartreuse material was designated as the reference standard and acceptable samples were required to have color differences less than 3 NBS units when calculated relative to the standard. Suitable calculations using Eq. 7 showed Samples 1, 2, and 7 to have color differences of 7.3, 6.8, and 3.2 NBS units, respectively, while Samples 3, 5, and 6 had differences of only 0.92, 0.87, and 1.2 NBS units, respectively. Samples 1, 2, and 7, since they differed from the standard by more than 3 NBS units, did not have acceptable surface colors.

A series of samples of the purple colorant (PU), a sugar suspension of three FD&C dyes (Blue No. 1, Yellow No. 5, and Violet No.

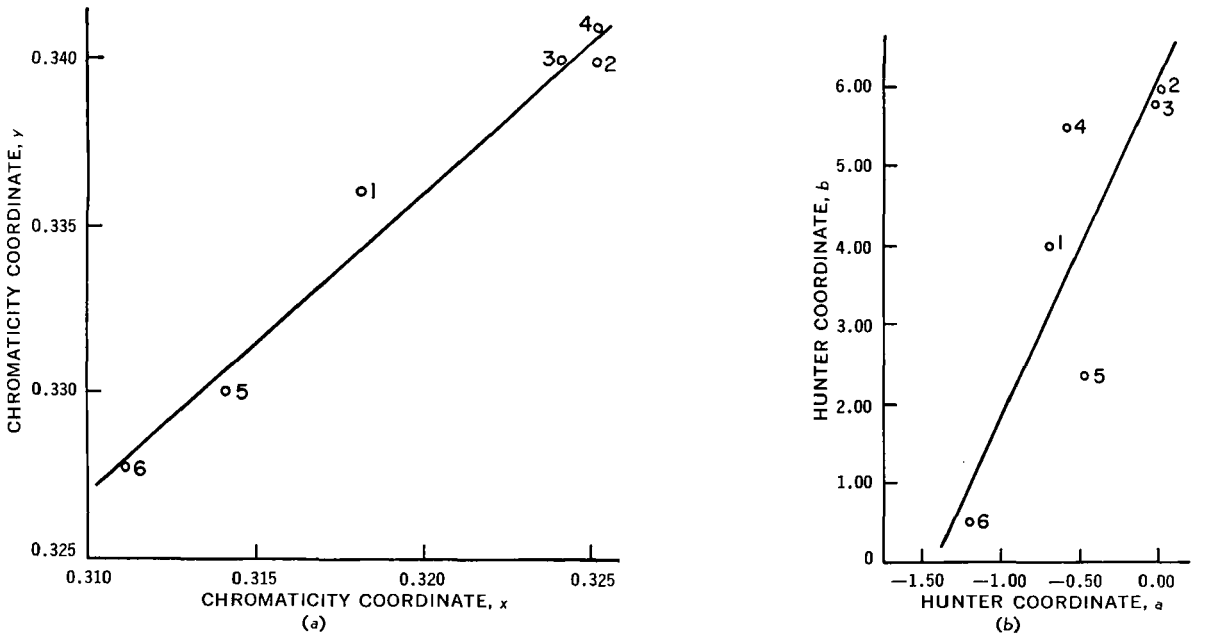

Figure 5—(a) *Expanded* (x, y) *chromaticity diagram for the white color dispersion (WH). Coordinates were evaluated using the 1964 10° energy-weighted distribution coefficients for the illuminant D-6500.* (b) *Expanded Hunter* (a, b) *diagram for colorant (WH). Coordinates were obtained for illuminant* S_c *and the 1931 2° field data.*

1[12]) also was examined, and the color data are collected in Table II. The expanded scale chromaticity diagrams (Figs. 4*a* and 4*b*) describe the gradual shading of this material from a deep, intense purple at the lower extreme to a violet color with a distinct blue cast at the upper extreme. The line drawn through the data points on both chromaticity diagrams defines the direction of color shading as described by the dominant wavelength of the samples. As a result, the differences in the slopes of the (x, y) and (a, b) plots are directly related to the transformation of the (x, y) spectral boundary (Figs. 1 and 2). In both chromaticity diagrams, Sample 1 is significantly different from all other samples, having far more blue color. The desirable color for this purple material was selected subjectively as the color of Samples 4 and 10. Samples 1, 6, 7, and 8 were considered too blue to be acceptable.

A region of acceptable color was created by placing arbitrary limitations on the color coordinates: $0.230 \leq x \leq 0.243$ and $0.167 \leq y \leq 0.188$ and $23.3 \leq a \leq 29.3$ and $-50.5 \leq b \leq -56.5$. Under these conditions, Samples 3 and 8 became borderline cases. If Sample 10 is defined as the reference standard for the purple colorant, color difference can be evaluated in terms of NBS units using the Judd formula. The following values were obtained for Samples 1, 3, 4, 5, 6, and 8, respectively: 17.3, 5.2, 1.8, 4.1, 8.2, and 7.6 NBS units. For control purposes, a ΔE value greater than 5 will cause a sample to be rejected because of unsuitable surface color. For the data presented, only Samples 4 and 5 are unquestionably acceptable while Sample 3 is borderline.

Color data were obtained for a third dispersion, the white colorant (WH), which is a suspension of FD&C Blue No. 2 in a sucrose solution. These data are shown graphically in Figs. 5*a* and 5*b*. The linear relationships found for both the (x, y) and (a, b) chromaticity plots represent the shading of samples from the blue region at the lower left to the yellow region in the upper right. A subjective examination of the white color samples revealed that Samples 2–4 were all yellowish and were, therefore, unacceptable. Sample 5 was considered most desirable while Samples 1 and 6, although having slight yellow and blue casts, respectively, represented the limits of colorant acceptability. On this basis, the following limits on the chromaticity coordinates were established: $0.310 \leq x \leq 0.319$ and $0.327 \leq y \leq 0.337$, $-1.25 \leq a \leq -0.25$ and $0.50 \leq b \leq 4.50$. In terms of NBS units, these limits represent ±3 units around the coordinates for Sample 5.

[12] FD&C Violet No. 1 has been delisted by the Food and Drug Administration. The samples examined were several years old and did contain FD&C Violet No. 1.

CONCLUSIONS

Surface color and small differences in color are evaluated quantitatively for a series of tablet colorants from tristimulus and (x, y) chromaticity values, determined either directly from integrating sphere colorimeters or from reflectance spectra and suitable calculations. Color data are plotted to give chromaticity diagrams which function to order materials by color. These diagrams eliminate subjectivity from color evaluation and from subsequent sample acceptance or rejection by permitting the selection of a color standard and applying limits to the chromaticity coordinates to define an area of acceptable color. Since the (x, y) scale is not uniform, limits of acceptability are established independently for both the x and y coordinates and for every distinct color.

In an effort to simplify the measurement of color differences, the more uniform Hunter scale is used. Hunter (a, b) coordinates are obtained either directly from an integrating sphere colorimeter or from a transformation of the (x, y) coordinates. Expanded chromaticity diagrams prepared from the Hunter data also order materials by color and have the added advantage that the distance between any two colors can be regarded as nearly a direct measure of visual difference. The use of these uniform scales permits the definition of color difference in terms of the NBS unit, and limits of acceptability are established in terms of these units.

The compilation of tristimulus and chromaticity information provides a permanent detailed description of a colored sample and defines quantitatively the color difference between the sample and its established standard. The subjectivity of an individual in discriminating color difference is, therefore, replaced by an absolute numerical method that permits the establishment of discrete control specifications for surface colors.

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Intragranular Starch: Comparison of Starch USP and Modified Cornstarch

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Abstract □ Incorporation of starch USP or a modified cornstarch within the granules of several drug formulations was investigated. In general, the formulation containing the modified starch exhibited improved processing characteristics as well as improved tablet properties. A comparison of a granulated and a direct compression formulation of the same ingredients indicated that granulation of an active ingredient is not necessarily detrimental to its (pharmaceutical) availability.

Keyphrases □ Starch—comparison of starch USP and modified cornstarch □ Excipients—comparison of starch USP and modified cornstarch □ Disintegrants—comparison of starch USP and modified cornstarch □ Binding agents—comparison of starch USP and modified cornstarch

Direct compression of pharmaceutical tablets has become an integral part of pharmacy in recent years, and several components have been designed and marketed especially for use in such systems. For example, Manudhane *et al.* (1) discussed the use of a modified cornstarch[1] in direct compression formulas. Starch USP is a common excipient in solid dosage forms, both as a binder and as a disintegrant (2).

When cornstarch, in either of these two forms, is added to a formulation in the dry state (prior to the lubricating step), its use is that of a disintegrant. When it is incorporated into the granule, either as a paste or dry (prior to granulation with some other agent), both the binding property and the disintegrant property may be operative. It is this dual property that is of interest in this study.

This work documents a comparison of starch USP and a modified cornstarch incorporated in the granules of several drug formulations. Their processing properties and their relative pharmaceutical availabilities, as indicated by dissolution measurements, were studied.

EXPERIMENTAL

Materials—Excipients used in preparing the tablets included starch USP, a modified cornstarch[1], microcrystalline cellulose[2], spray-dried lactose[3], and magnesium stearate USP. Active ingredients included acetaminophen[4], ascorbic acid[5], chlorothiazide[5], levodopa[6], methyldopa[5], and probenecid[5].

Tablet Preparation—The active ingredients selected were all at a dosage of 500 mg, and tablet composition was identical for all drugs. The excipients were maintained constant in the experimental plan, although the formulation may not have been ideal for any one of the drugs. Batch sizes remained constant at 1000 tablets.

Granulations of 500 g of each active ingredient and 60 g of either starch USP or the modified cornstarch with a 7.0% starch paste (65°) were processed in a planetary mixer[7]. In all cases, the starch paste was prepared with starch USP. The wet granulations were manually screened through a No. 6 screen and oven dried overnight at 45°. After dry milling[8], the granulations were blended[9]

[1] Sta Rx 1500 starch, A. E. Staley Manufacturing Co., Decatur, Ill.

[2] Avicel PH 101, FMC Corp., American Viscose Division, Newark, Del.
[3] Foremost-McKesson, Inc., San Francisco, Calif.
[4] S. B. Penick & Co., New York, N.Y.
[5] Merck & Co., Rahway, N.J.
[6] Monsanto Co., St. Louis, Mo.
[7] Kitchen Aid model K-45, Hobart Manufacturing Co., Troy, Ohio.
[8] Homoloid, 0.13-cm (0.050-in.) screen.
[9] Patterson Kelley V-blender.