Measurement of a Color Gamut Obtained from FD&C Colorants

By ALLAN M. RAFF

A method is illustrated to determine what colors may be achieved utilizing the FD&C aluminum lakes as colorants. Lakes were mixed with a tablet excipient, compressed, and the reflectance was measured. A color solid was constructed at fixed values of lightness. Reduction in the color solid caused by limitations imposed by Federal regulations and pharmaceutical requirements is also illustrated. The use of such a technique aids in making color matches and defines the extent of realizable colors.

THE PURPOSE OF this study is threefold. First, it illustrates a method whereby the pharmaceutical formulator can define the gamut of colors he may achieve with a given set of colorants in any pharmaceutical dosage form as long as the color of the dosage form can be measured instrumentally. Second, it establishes the color gamut of the FD&C aluminum lakes. They were chosen as representative of a class of colorants important in taking full advantage of the techniques of direct tablet compression (1, 2). Third, this study further serves to illustrate the need for considering colorants as more than spectrophotometric curves. They also possess varying degrees of physical and chemical stability, tinctorial power, etc. (3, 4).

An introduction and orientation to the basic concepts utilized in this study are contained in an appendix[1] and bibliography of a previous article (5).

Instrumentation.—The instrumental approach to color matching, and more specifically the use of the spectrophotometer for industrial color formulation, is the method chosen in most instances.

Davidson and Hemmendinger (6–8) have developed several instruments to expedite the work involved in spectrophotometric color matches based upon a two-constant theory of pigment mixtures (9–11). Others, such as Billmeyer, *et al.* (12, 13), and later Alderson, *et al.* (14), described the use of large digital computers as an aid in color formulation. Saltzman (15) described the use of a pigment library as an aid in pigment identification and color matching. Duncan (16) investigated the mechanisms of color production and derived a set of formulas for the prediction of color matches.

The making of a spectrophotometric color match can only be achieved when the same colorants that are present in the color sample are used in the preparation of the pharmaceutical dosage form. It is often stated that *color* matching is best attained by *colorant* matching (17).

In the case of color matching in industrial pharmacy we assume that we are definitely going to get a metameric[2] color match. The reason for this assumption is as follows. The pharmacist is shown a color sample on a paper that was achieved with printing inks, or he is given the liquid dosage form of a drug from which it is now desired to make a tablet, or someone just happens to be wearing a tie that has an "appealing" color. In the case of the color samples being made from printing inks in the first example, and textile dyes in the last, it is obvious that these dyes cannot be used in the preparation of pharmaceutical products. In the example of the liquid dosage form, it was made with water-soluble dyes and, while these may be used, they defeat the purpose of direct compression. If we further assume that in the majority of cases we are only trying to match the colors of our own products, and not those of our competitors, then we already know the exact colorant composition of the color in the liquid and do not need to resort to spectrophotometry for color matching. One would also have the problem here of differences in the attributes of the appearance modes (18, 19) of a liquid with a transmitted color *versus* a tablet with a reflected color. The color may not appear the same even with the same colorant formulation, achieved with or without a spectrophotometer. When a nonmetameric match cannot be made it is necessary to resort to colorimetry (6).

In other words, the industrial pharmacist in his role as a colorist faces problems that may be more acute than those of the colorist in the paper coating, printing, textile, ceramic, plastic, or paint industry. At the present time the U. S. Food and Drug Administration (FDA) lists only 11 FD&C coal-tar dyes (20). Others, in the D&C category, have a more tenuous existence and may eventually be decertified. Since the number of colorants is so limited (and if we add further limitations such as the requirement for a dry colorant for direct tablet compression), the primary question in the development of a color for a new product should be "What colors are available to us?" not "Can we make a match of a color standard using different colorants?" It is for this reason that this example of a color gamut is presented.

Color Gamut.—A color gamut, or color solid, is of value because it enables one to tell, with a minimal amount of effort, whether a color standard can be matched.

A color solid may be constructed because color

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[1] Available from the author.

[2] A metameric match is one that does not appear to match under all conditions of illumination.

can be considered as a three-dimensional system. These dimensions may be described in the terminology of the Munsell (21) system or that of the C.I.E. (22, 23) system. The first dimension, "hue" (Munsell), is that attribute which distinguishes a red from a green. In the C.I.E. system this is the dominant wavelength. The second dimension is "value" (Munsell), or "lightness" (C.I.E.), the lightness compared with a gray scale from white to black. It may be thought of as the attribute which allows the differentiation of light from dark colored objects (17). The third dimension is "chroma" (Munsell), "purity" (C.I.E.) or saturation, the "redness" of a red as it goes from a dull brick red to a brilliant scarlet (15).

There are a number of additional attributes which will affect the appearance of a colored object, such as size, shape, sparkle, transparency, glossiness, and luster (19). While these factors cannot be ignored, they were, in a sense, eliminated from this experiment by evaluating all colors in tablets with the appearance modes having the same attributes.

While the number of colors perceived may be considered as infinite, those available to the industrial pharmacist are probably more severely limited than in any other field. Aside from all the natural factors that limit the available colors—such as their toxicity, light fastness, and chemical reactivity—the pharmaceutical industry may use only those colorants approved by the FDA (20). In the case of the FD&C aluminum lakes, only nine FD&C dyes are utilized in their manufacture.

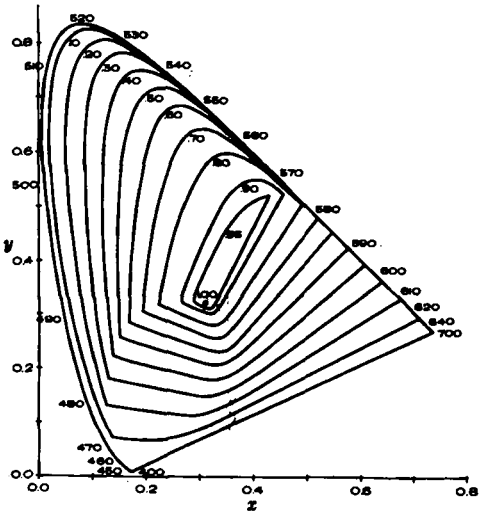


Fig. 1.—The (x, y) chromaticity diagram of the C.I.E. system. The parts of the spectrum locus are identified by wavelength in mμ. The region bounded by this locus and the straightline (purple border) joining its extremes represent all chromaticities producible by actual stimuli. Within the outermost locus are the contours of theoretically realizable surface colors at various levels of lightness. Illuminant "C" assumed. [From MacAdam, D. L., (25).]

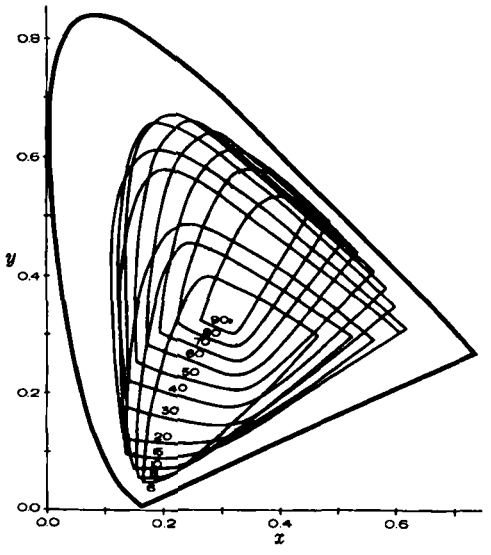


Fig. 2.—MacAdam limits modified by surface reflection factor. [From Atherton, E., and Peters, R. H., (27).]

Limitations.—Before defining the color gamut of these nine colorants, the theoretical limitations should first be examined.

Figure 1 illustrates a chromaticity diagram. All mixtures of the spectrum colors lie within the area enclosed by the solid line. The area contains all the real colors (18, 22, 23).

MacAdam developed the theory of the maximum visual efficiency of colored materials (24) and then subsequently (25) showed what surface colors are theoretically realizable. One of his diagrams is reproduced in Fig. 1. It is obvious that even without the limitation of specific colorants being introduced the color gamut has lessened.

The further limitations to the gamut of surface colors were studied for fabrics by Vickerstaff (26) and for paints by Atherton and Peters (27). The modifications in the range of realizable surface colors for materials such as paints, or compressed tablets with a glossy surface, are a result of the fact that no surface absorbs 100% of the incident light. Figure 2 contains the modifications in the MacAdam diagram when surface reflectance is taken into account.

The studies cited had as their objective the description of the theoretically realizable surface colors in order to determine where best to expend

TABLE I.—DATA OBTAINED ON FIRST SERIES OF TABLETS COLORED WITH FD&C BLUE NO. 2 ALUMINUM LAKE, CONCENTRATED

Concn., % w/w	Tristimulus Value			Chromaticity Coordinates		Lightness (Percentage)	Munsell Value V_T
	X	Y	Z	x	y		
0.00	0.9784	1.0025	1.1320	0.3143	0.3220	100.25	9.91
0.01	0.9020	0.9247	1.1447	0.3066	0.3144	92.47	9.60
0.10	0.7325	0.7506	1.0024	0.2947	0.3020	75.06	8.83
1.00	0.4120	0.4194	0.6920	0.2704	0.2753	41.94	6.92
10.00	0.1420	0.1375	0.3040	0.2434	0.2356	13.75	4.26
100.00	0.0230	0.0185	0.0584	0.2302	0.1852	1.85	1.41

future research efforts. The problem was to determine those areas of color in which new colorants should be made available. All industries have in common the need and desire for colorants that will be light and at the same time saturated or intense. Such studies as these are of great value in this respect.

However, in the pharmaceutical industry the problem is somewhat different since we have little to say about the development of additional colorants. This is solely within the province of the chemist, tempered by economics, and constantly scrutinized by the Federal government. In the sense in which colorants are legally defined, the problem then becomes one of determining the color gamut defined by specific materials under a given set of conditions.

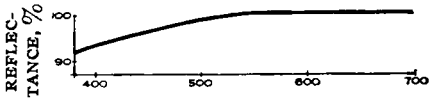


Fig. 3.—Reflectance curve of tablet containing no colorants.

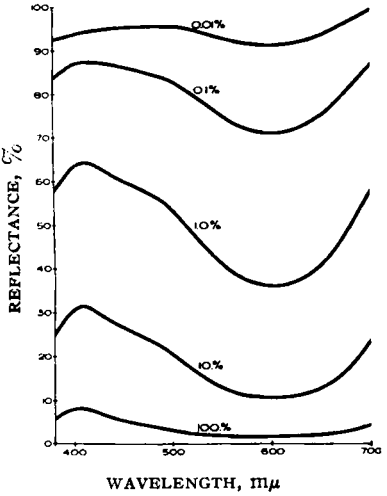


Fig. 4.—Reflectance curves of tablets containing various percentages of FD&C Blue No. 2 aluminum lake, concentrated.

EXPERIMENTAL

Materials.—A spray dried basic tablet granulation (28) having the following formulawas used.

Calcium sulfate, dihydrate	90.585% w/w
Solka Floc, BW-100	4.950
Acacia	3.465
Magnesium stearate	1.000

Two series of National Aniline FD&C aluminum lakes were used. The dye content of one series was nominally 15%; that of the other, designated by the manufacturer as "Concentrated," was nominally 40%. Other manufacturers produce these aluminum lakes in other concentrations; the data of the following experiments are not perfectly valid for any concentrations other than those described. The colorants evaluated were the aluminum lakes of the following FD&C dyes: Violet No. 1, Blue No. 1 and No. 2, Green No. 1, Yellow No. 5 and No. 6, and Red No. 2, No. 3, and No. 4.

Equipment.—A Mikro-Samplmill fitted with a No. .010 HB screen; Carver hydraulic press; Hobart mixer, K4-B; punch and die ($1^1/_2$ in., flat face, bevel edge) for Stokes model F tablet press; and G.E. recording spectrophotometer with Librascope integrator (29) were utilized.

Preparation of Tablets.—Five batches of tablets were prepared: FD&C aluminum lake 0.01%, *A;* 0.10%, *B;* 1.0%, *C;* 10.0%, *D;* 100.0%, *E;* with basic granulation *q.s.* in each.

A series of logarithmic dilutions was chosen to

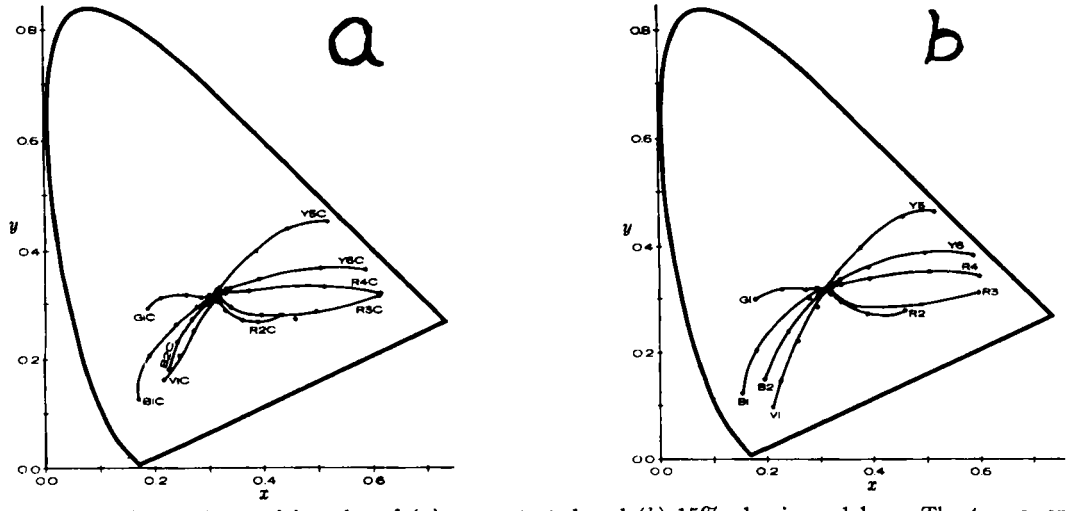
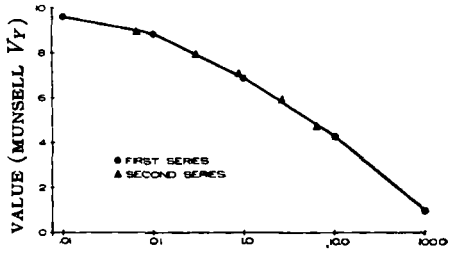


Fig. 5.—C.I.E. chromaticity plot of (*a*) concentrated and (*b*) 15% aluminum lakes. The traces, or curved lines, represent chromaticity loci of a concentration series of the lakes measured individually. Key for *a:* B1C = FD&C Blue No. 1; B2C = FD&C Blue No. 2; V1C = FD&C Violet No. 1; R2C = FD&C Red No. 2; R3C = FD&C Red No. 3; R4C = FD&C Red No. 4; Y6C = FD&C Yellow No. 6; Y5C = FD&C Yellow No. 5; G1C = FD&C Green No. 1; aluminum lakes, concentrated, respectively. Key for *b:* B1 = FD&C Blue No. 1; B2 = FD&C Blue No. 2, V1 = FD&C Violet No. 1; R2 = FD&C Red No. 2; R3 = FD&C Red No. 3; R4 = FD&C Red No. 4; Y6 = FD&C Yellow No. 6; Y5 = FD&C Yellow No. 5; G1 = FD&C Green No. 1; aluminum lakes, 15%, respectively.



PER CENT CONCENTRATION OF FD&C BLUE NO. 2, AL. LAKE, CONCD., IN TABLETS

Fig. 6.—Concentration of FD&C Blue No. 2 aluminum lake, concentrated, in tablet *vs.* Munsell value level.

by Davidson (31) was utilized, and the tristimulus value, Y, which is also a function of lightness, was converted to the Munsell value function V_Y (32). These values were then plotted against their respective concentrations (Fig. 6).

Using the graph of Fig. 6, concentrations were determined which would yield values of V_Y from 9 down to that value that could be obtained using no more than 1% of pure dye content in a tablet. Tablets were then made having those concentrations determined by the use of the graph of Fig. 6. The tristimulus values, chromaticity coordinates, lightness, and values for V_Y, are shown in Table II.

The color solid could have been illustrated at

TABLE II.—DATA OBTAINED ON SECOND SERIES OF TABLETS COLORED WITH FD&C BLUE NO. 2 ALUMINUM LAKE, CONCENTRATED

Concn., % w/w	Tristimulus Value			Chromaticity Coordinates		Lightness (Percentage)	Munsell Value V_Y
	X	Y	Z	x	y		
0.065	0.7443	0.7622	1.0117	0.2956	0.3027	76.22	8.89
0.290	0.5681	0.5815	0.8601	0.2827	0.2893	58.15	7.95
0.900	0.4391	0.4472	0.7178	0.2737	0.2788	44.72	7.11
2.600	0.2787	0.2802	0.5177	0.2589	0.2603	28.02	5.82
6.200	0.1752	0.1723	0.3623	0.2468	0.2427	17.23	4.71

cover effectively the psychological value scale. This scale has an exponential relationship to perceived lightness (30). These dilutions also allowed each series to be plotted on a single graph which permitted a ready comparison of the changes in the curves that resulted from changes in concentrations.

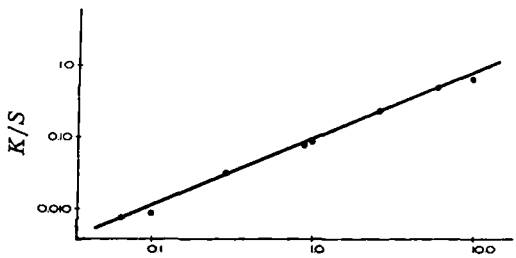
In formulas *A–D* the colorant was mixed with the basic granulation in the Hobart mixer and then passed through the Mikro-Samplmill. The material was then placed in a punch and die assembly in the Carver press and compacted at a pressure of 12,000 p.s.i. For the compaction of the pure aluminum lake it was necessary only to coat the die with a lubricant prior to compaction to effect the release of the tablet.

Each tablet was marked so that the upper surface could be measured in every case. This was necessary because the upper tablet face had a greater gloss than the lower face due to the nature of compaction in the Carver press.

Measurement of Tablets.[3]—The reflectance of the tablets was measured using a G.E. recording spectrophotometer equipped with a Librascope integrator using illuminant C. The specular component was not measured. Magnesium oxide was the white standard. The tristimulus values, chromaticity coordinates, lightness, and values for V_Y (see below) for FD&C Blue No. 2, aluminum lake, concentrated, are shown in Table I.

Figure 3 shows the reflectance curve of a tablet containing no colorant; Fig. 4 shows the reflectance curves of the tablets containing FD&C Blue No. 2, aluminum lake, concentrated. Similar curves were obtained for each colorant. The results of this initial series are plotted in Fig. 5. It can be seen that the color gamut is greatly reduced from that shown in Fig. 2.

Continuing to use the results obtained from FD&C Blue No. 2 aluminum lake, concentrated, as an example, a modification of a method developed



PERCENTAGE CONCENTRATION OF FD&C BLUE NO. 2, AL. LAKE, CONCD. IN TABLETS

Fig. 7.—Concentration of FD&C Blue No. 2 aluminum lake, concentrated in tablet *vs.* absorption coefficient/scattering coefficient (K/S). Reflectance measured at 410 mμ.

various levels of reflectance rather than at Munsell values. In this case the value of K/S[4] would be plotted *versus* concentration as shown in Fig. 7 and the concentrations required to obtain the desired levels of reflectance determined.

The reflectance curves of the second series of tablets containing FD&C Blue No. 2, aluminum lake, concentrated, are shown in Fig. 8.

Figure 9 is composed of a series of contours at Munsell value 9. This is what is possible when there is a limitation concerning the colorants which may be used and a further restriction that the maximum concentration may not exceed 1% of pure dye content. The other systems are shown at the same value level for comparison.

Color Matching.—It is obvious from Fig. 9 that the color gamut at this value level 9 is far less than the theoretical limits. This is equally true at all other value levels. For example, at a value of 4 there is only a single point because no other colorant was this dark at a pure dye concentration of less than 1%. Another restriction was the use of only the aluminum lakes as colorants without using a black, such as carbon black. This meant that the values

[3] The author thanks Messrs. Best, Leary, Seeber, and Croce of National Aniline Division, Allied Chemical Corp., for their assistance in having the spectrophotometric measurements of the tablets made.

[4] $K/S = (1 - R_\infty)^2/2 - R_\infty$, the Kubelka-Munk function (9).

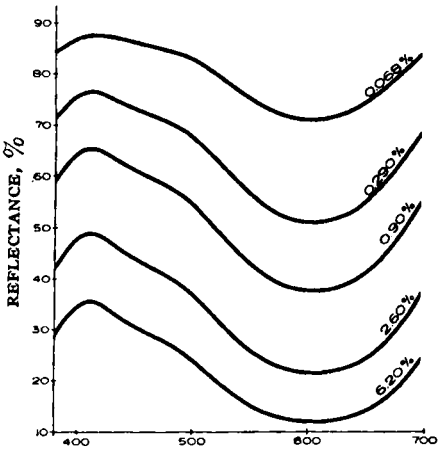


Fig. 8.—Reflectance curves of tablets containing various percentages of FD&C Blue No. 2 aluminum lake, concentrated.

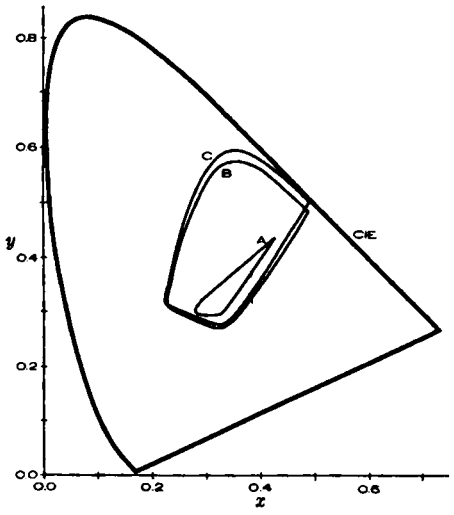


Fig. 9.—Contours at Munsell V_Y = 9. Key: contour *A*, limit of aluminum lakes; contour *B*, limit of Atherton and Peters; contour *C*, limit of MacAdam; contour C.I.E., limit of spectral colors.

were modified solely by the amount of colorant in the tablet formulation. Additional experiments are now in progress that will determine the maximum saturation of each colorant and will also utilize a carbon black to vary the lightness of each colorant. This should serve to enlarge the color gamut. However, the system will have to be evaluated for reproducibility of color from batch to batch as a function of the dispersion of the carbon black.

The principal usefulness of such a color mixture diagram is that it enables one to obtain from measurements, using either spectrophotometers or abridged spectrophotometers, information about the range of hues obtainable without actually making all the necessary physical combination of hues. Duncan (16) showed that the recording of the position of a color on the C.I.E. diagram enabled a determination of whether it would be possible to make a match with the colorants available. "In general, the theory indicates that any color can be reproduced when its chromaticity coordinates fall within an area that is generated by drawing lines connecting the points representing the chromaticity coordinates of the colorants being used. If the color to be reproduced falls outside of such an area, it is sufficient evidence that the color cannot be produced with the colorants available" (33). It must be kept in mind at all times that color is a three-dimensional concept, so it is necessary to consider the lightness of the proposed color as well as the hue and saturation. For this reason, the color gamut described here is shown at definite levels of lightness.

For matching a color, the procedure would then be as follows. The color to be matched would be measured in a spectrophotometer, and the chromaticity coordinates and lightness value determined. This point would be plotted on the correct level of reflectance (or V_Y) to see whether it lies within the area. If it does not lie within the area, there is little likelihood that any match, metameric or nonmetameric, can be achieved. If the point does lie within the area, then it may be achieved by utilizing those colorants that bound it.

DISCUSSION

The color gamut in Fig. 9 shows that in this case there is relatively little opportunity to make a light and a saturated color in a tablet at the same time. If one further restricts the colorant concentrations to the more usually used concentrations of 0.1%, the color gamut then contains only pastel colors.

The curve of the colorant traces (Fig. 5) indicates that, as the concentration of the colorants is increased, both the hue and the lightness value change. Unlike the color additive mixture of lights—hue, value, and chroma for pigments are not independent properties, nor are their changes predictable *a priori*.

More extensive discussions of the usefulness of color grids are given by Evans (34) and Saltzman (33) as well as those cited earlier. The making of color matches having the minimum metamerism possible with a given set of colorants has been aided by the development of a tristimulus difference computer by Davidson and Hemmendinger (35, 36). The instrument permits the application of the relation between the tristimulus values and concentration without any precalibration except that involving the spectral measurement of the component pigments.

SUMMARY

Color matching in industrial pharmacy, as in other fields, is a difficult problem. However, in pharmacy, exact matches, which can only be made with the same colorants as those of the standard, are the exception rather than the rule. Considering this fact and that industrial pharmacists have relatively few colorants—and these cannot be used indiscriminately—then it behooves us to define the gamut of colors available to us for such dosage forms as liquids, compressed and coated tablets, etc. Having this information will then allow a quick determination of whether a color sample can be matched to any extent.

"It is necessary that this problem be recognized so that a great deal of difficulty may be avoided in asking for an exact match where it is evident, from the

difference between the two colorant systems, that different colorants must be used and therefore an exact match is not obtainable" (3).

REFERENCES

(1) Hollidge, K. B., talk presented at western regional meeting of the Pharmaceutical Mfgs. Assoc., 1961.
(2) Kibbe, W., *Drug Cosmetic Ind.*, **88**, 170(1961).
(3) Saltzman, M., *SPE Tech. Papers*, **8**, (1962).
(4) Saltzman, M., *Offic. Dig. Federation Soc. Paint Technol.*, **35**, 245(1963).
(5) Raff, A. M., THIS JOURNAL, **52**, 291(1963).
(6) Davidson, H. R., and Hemmendinger, H., paper presented at the Fifth International Color meeting, Dusseldorf, Germany, 1961.
(7) Davidson, H. R., and Hemmendinger, H., *SPE Tech. Papers*, **8**, (1962).
(8) Davidson, H. R., and Hemmendinger, H., *J. Opt. Soc. Am.*, **48**, 281(1958).
(9) Kubelka, P., and Munk, F., *Z. Tech. Physik.*, **12**, 593 (1931).
(10) Kubelka, P., *J. Opt. Soc. Am.*, **38**, 448, 1067(1948).
(11) Fink-Jensen, P., Congres' FATIPEC III, Belgium, 1955.
(12) Billmeyer, F. W., Jr., Beasley, J. K., and Sheldon, J. A., *J. Opt. Soc. Am.*, **50**, 70(1960).
(13) Billmeyer, F. W., Jr., *ibid.*, **50**, 137(1960).
(14) Alderson, J. V., Atherton, E., and Derbyshire, A. N., *J. Soc. Dyers Colourists*, **77**, 657(1961).
(15) Saltzman, M., *Dyestuffs*, **43**, 57(1959).
(16) Duncan, D. R., *J. Oil Colour Chemists' Assoc.*, **32**, 296 (1949).
(17) Judd, D. B., "Color in Business, Science and Industry," John Wiley & Sons, Inc., New York, N. Y., 1951, p. 331.
(18) Committee on Colorimetry, Opt. Soc. Am., "The Science of Color," Thomas Y. Crowell Co., New York, N. Y., 1953.
(19) Committee on Colorimetry, Opt. Soc. Am., *J. Opt. Soc. Am.*, **33**, 552(1943).
(20) *Federal Register*, **28**, 317(1963).
(21) Munsell, A. H., "A Color Notation," 9th ed., Munsell Color Co., Baltimore, Md., 1941.
(22) Commission Internationale de l'Eclairage, Proceedings of the 8th Session, Sept., 1931, Cambridge University Press, Cambridge, England, 1932.
(23) Hardy, A. C., "Handbook of Colorimetry," The Technology Press, Cambridge, Mass., 1936.
(24) MacAdam, D. L., *J. Opt. Soc. Am.*, **25**, 249(1935).
(25) *Ibid.*, **25**, 361(1935).
(26) Vickerstaff, T., *Proc. Phys. Soc. (London)*, **57**, 15 (1945).
(27) Atherton, E., and Peters, R. H., Congres' FATIPEC III, Belgium, 1955.
(28) Raff, A. M., Robinson, M. J., and Svedres, E. V., THIS JOURNAL, **50**, 76(1961).
(29) Davidson, H. R., and Imm, L. W., *J. Opt. Soc. Am.*, **39**, 942(1949).
(30) Murray, H. D., "Colour in Theory and Practice," Chapman & Hall, Ltd., London, England, 1952.
(31) Davidson, H. R., *J. Opt. Soc. Am.*, **45**, 216(1955).
(32) Nickerson, D., *Am. Dyestuff Reptr.*, **39**, 541(1950).
(33) Saltzman, M., *Dyestuffs*, **44**, 217(1960).
(34) Evans, R. M., "An Introduction to Color," John Wiley & Sons, Inc., New York, N. Y., 1948.
(35) Davidson, H. R., and Hemmendinger, H., *J. Opt. Soc. Am.*, **51**, 1459; abstract WB17, (1961).
(36) Clement, L. A., *Color Eng.*, **1**, 10(1963).

Effect of Cortisone on the Minimal Carcinogenic Dose$_{50}$ of Methylcholanthrene in Albino Mice

By RALPH T. MANCINI, RONALD F. GAUTIERI, and DAVID E. MANN, JR.

The administration of 0.4 mg. of cortisone acetate per 30 Gm. of body weight, injected subcutaneously five times a week over a 16-day period (12 injections) during the initial phase of the experiment, caused a slight decrease in the incidence of methylcholanthrene-induced tumors. The CF-1 albino mice used in this experiment also exhibited a definite retardation or even a significant decrease in body weight during the 16-day period of cortisone acetate administration. However, when cortisone acetate was withdrawn, the mice gained weight rapidly. At the termination of the experiment, the groups of mice which had received cortisone (Groups B and C) exhibited a mean weight approximately equal to that of the control groups.

THE ISOLATION of cortisone from the adrenal cortex by Kendall, *et al.* (1), Reichstein (2), and Wintersteiner and Pfiffner (3) in 1936 was followed by the extraction and identification of approximately 45 additional steroids, five of which—besides cortisone—exhibited significant physiological activity: corticosterone, 11-desoxycorticosterone, 11-dehydrocorticosterone, 17-α-hydroxycorticosterone (hydrocortisone), and 17-hydroxy-11-desoxycorticosterone. Of these, cortisone has been subjected to the most thorough clinical evaluation in such diverse conditions as arthritis, leukemia, Addison's disease, allergic states, skin diseases, and ophthalmic disorders. In addition, the influence of the steroid on carcinogenesis has been studied.

One of the earliest experiments to determine the effects of cortisone on the growth of malignant tumors in mice was conducted in 1944 by Heilman and Kendall (4). They showed that the administration of cortisone in drinking water inhibited lymphosarcomas, while withdrawal caused the initiation of carcinogenesis. However, growth was not reversed by the subsequent readministration of cortisone. Other investigations have demonstrated that cortisone exerted a temporary inhibition of ependyomas (5), lymphosarcomas (6), adenocarcinomas (7), and rhabdomyosarcomas (8).

In a study conducted by Baserga and Shubik (9), it was observed that cortisone reduced the

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