of the material (Fig. 1C) in the biological extract with added internal standard.

Table I shows the urinary analysis of I in the rabbit as a function of time. The cumulative urinary excretion indicates the half-life of excretion of the intact drug to be approximately 15 hr. Significantly, the animal excreted less than 1% of the drug in its native form. Evidently, its long acting characteristic must be attributed to its biotransformation into active metabolites.

REFERENCES

(1) R. E. Billing and R. E. McMahon, *Fed. Proc. Abstr.*, **32**, 764 (1973).

(2) R. N. Booher, *J. Med. Chem.*, **18**, 266 (1975).

(3) J. H. Jaffe and E. C. Senay, *J. Am. Med. Assoc.*, **216**, 1303 (1971).

(4) A. Zaks, M. Fink, and A. M. Freedman, *ibid.*, **220**, 811 (1972).

(5) G. L. Henderson, B. K. Wilson, and D. H. M. Lau, *Clin. Pharmacol. Ther.*, **21**, 16 (1977).

(6) M. M. Kochhar, P. P. Davidson, and R. S. Bhushan, *Res. Commun. Chem. Pathol. Pharmacol.*, **16**, 251 (1977).

(7) C. G. Hammar, B. Holmstedt, and R. Ryhage, *Anal. Biochem.*, **25**, 530 (1968).

(8) B. Holmstedt and L. Palmer, *Adv. Biochem. Psychopharmacol.*, **7**, 1 (1973).

(9) H. C. Brown and K. Ichikawa, *J. Am. Chem. Soc.*, **84**, 373 (1962).

(10) W. Steglich and G. Hofle, *Angew. Chem. Int. Ed.*, **8**, 981 (1969).

(11) H. R. Sullivan, S. E. Smits, S. L. Due, R. E. Booher, and R. B. McMahon, *Life Sci.*, **11**, 1093 (1972).

(12) H. R. Sullivan, S. L. Due, and R. E. McMahon, *Res. Commun. Chem. Pathol. Pharmacol.*, **6**, 1072(1973).

(13) H. R. Sullivan, F. J. Marshall, R. E. McMahon, E. Anggard, L. M. Gunne, and J. H. Holmstrand, *Biomed. Mass Spectrom.*, **2**, 197 (1975).

(14) H. R. Sullivan, S. L. Due, and R. E. McMahon, *J. Am. Chem. Soc.*, **94**, 4050 (1972).

(15) A. Pohland, H. E. Boaz, and H. R. Sullivan, *J. Med. Chem.*, **14**, 194 (1971).

ACKNOWLEDGMENTS

Supported by Grant DA 00327 and by the Department of Mental Hygiene, State of New York, Office of Research.

The authors thank Sidney Bernstein for the illustrations.

Color Analysis of Dextrose Solutions Using a Color Difference Meter

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Received September 19, 1977, from *Pharmaceutical Product Development, McGaw Laboratories, Santa Ana, CA 92711.* Accepted for publication February 14, 1978.

Abstract□ A method for quantitating color measurements in dextrose solutions by using a color difference meter is described. This method was shown to correlate well with standard American Public Health Association (APHA) color measurements. A mathematical relationship was developed relating yellowness index values to APHA numbers as described in the USP for dextrose solutions. This relationship was tested by comparing the results from standard APHA color tests on laboratory samples of autoclaved dextrose solutions to APHA numbers calculated from yellowness index values for the same samples.

Keyphrases □ Dextrose solutions—color analysis, color difference meter compared to standard measurements □ Color—analysis, dextrose solutions, color difference meter compared to standard measurements

After sterilization, dextrose solutions may exhibit a brownish-yellow color as a result of dextrose degradation (1, 2). Currently, color measurement in many pharmaceutical solutions is performed by the American Public Health Association (APHA) method, which utilizes a concentration gradient of platinum–cobalt solutions in 100-ml Nessler tubes (3). The sample solution color can be measured by matching the color of the sample tube with one corresponding standard. Color is reported as parts per million of platinum–cobalt.

This study examined the correlation of yellowness index values, determined by a color difference meter[1], to the standard APHA colors. The practical use of the yellowness index for color evaluation of pharmaceutical dextrose solutions also was demonstrated. The advantage of this technique is that it allows an objective quantitation of color.

EXPERIMENTAL

A color difference meter, standardized using a calibrated white plate[2], was used for color measurement. Calibration values were derived by direct comparison to master standards traceable to measurements at the National Bureau of Standards.

A 6.4-cm optical cell[3] was the sample holder for each solution. The cell was filled with 80 ml of solution and placed over the 5.1-cm aperture of the detection head. A white reflective plate was placed over the cell; then a lightproof cover was placed over the detection head to exclude any ambient light. Light was transmitted through the bottom of the cell and reflected off the reflector plate into the detector head where an optical sensor transmitted a signal to the signal processor. The color meter then presented the color of solutions as four variables: L (brightness), a (green and red), b (blue and yellow), and YI (yellowness index) (4, 5). Color values were displayed by a digital readout to one decimal place.

Color values for a concentration gradient of platinum–cobalt solutions (0–80 ppm) were obtained using a color difference meter. Three readings were taken at each concentration level.

The practical application of the color difference meter was demonstrated through a comparison of observed APHA values for various autoclaved dextrose solutions to mathematically derived APHA values calculated from YI values. Solutions were made from various lots of dextrose[4] and were tested by USP methods (6). The particular solutions were chosen at random to represent various products with potential color variation.

The colors of five solutions of different dextrose concentrations were determined by six observers using the APHA method. The colors of these

[1] D25L-2, Hunter Associates Laboratory, Fairfax, Va.

[2] C2-6664, Hunter Associates Laboratory, Fairfax, Va.

[3] Agtron 13851210, Hunter Associates Laboratory, Fairfax, Va.

[4] Corn Products, Englewood Cliffs, NJ 07632.

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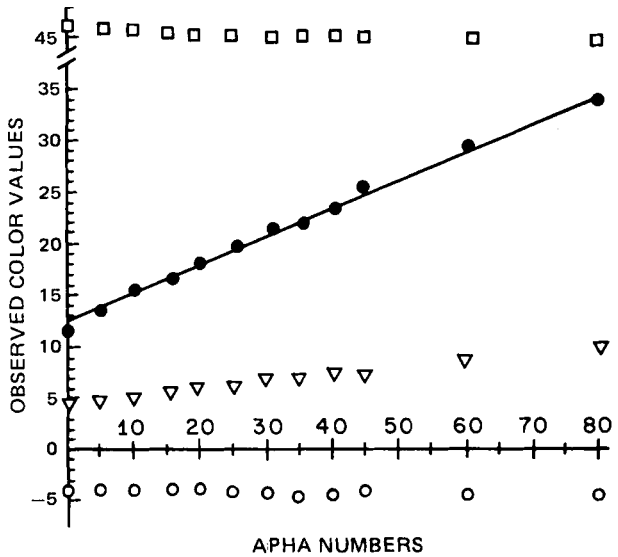

Figure 1—*Standard curve represents the relationship of L (□), a (○), b (▽), and YI (●) observed values to APHA numbers for platinum–cobalt solutions. The y intercept corresponds to the APHA number of the water standard (0 ppm platinum–cobalt). The slope of the YI line is 0.282, and the correlation coefficient is 0.9957.*

same five solutions were then determined using the color difference meter. The APHA values were calculated for these dextrose solutions and compared to the average observed APHA values.

RESULTS AND DISCUSSION

The L, a, b, and YI values were compared to the APHA numbers using regression analysis (Fig. 1). All color values had good correlation with the APHA colors (L, $r = 0.91$; a, $r = 0.77$; b, $r = 0.99$; and YI, $r = 0.99$). The variance of the points in L, a, and b values showed that these values were inappropriate for analytical use. The YI values, however, had a small individual point variance compared to differences between points. For this reason, the YI value, with the greatest correlation coefficient ($r = 0.99$), was selected for this study.

The relationship of YI to APHA color was linear over the entire range of the platinum–cobalt solutions studied. The following mathematical equation relating YI to APHA color was derived:

$$\text{APHA number} = \frac{[YI_s - YI_0]}{m} \qquad \text{(Eq. 1)}$$

Table I—Comparison of Calculated APHA Values to Observed APHA Numbers

Solution[a]	APHA Values Observed (Mean ± *SD*)[b]	Range of Individual Observations	APHA Values Determined by Yellowness Index	Range between Sample Readings[c]
5% Dextrose	3.0 ± 1.8	2–4	0.9	0.7–1.1
5% Dextrose in lactated Ringers	4.9 ± 1.5	2.5–7	4.0	3.9–4.1
30% Dextrose (diluted from 60%)	15.1 ± 2.3	12–18	12.9	Equal
25% Dextrose (diluted from 50%)	19.3 ± 2.3	17–23	20.7	Equal
60% Dextrose	32.1 ± 1.7	30–35	27.0	Equal
50% Dextrose	38.9 ± 2.1	37–42	40.0	38.4–41.7

[a] The solutions represent different lots of dextrose. [b] The average of six different observers. [c] Each solution was read twice at different times on the color difference meter.

where YI_s equals the YI value of the sample solution, YI_0 equals the YI value of a distilled water sample, and m corresponds to the slope of a line describing the relationship.

A comparison of APHA numbers calculated from the color difference meter and APHA numbers visually observed from various dextrose solutions is shown in Table I. The correlation of the observed APHA values with the calculated values indicated a 97% correlation ($r = 0.97$). The 50 and 60% dextrose solutions were diluted 1:1 to see if dilution of the solutions would result in a corresponding dilution of color and, as indicated in Table I, it did. Examination of the range of individual observations revealed that when six different observers graded the solutions using the APHA visual technique, the observed values differed considerably (approximately 5 ppm). Smaller differences were observed when the APHA values were determined from the yellowness index.

REFERENCES

(1) W. T. Wing, *J. Pharm. Pharmacol.*, **12**, 191T (1960).

(2) N. E. Webb, Jr., and G. J. Sperandio, *J. Am. Pharm. Assoc., Sci. Ed.*, **47**, 101 (1958).

(3) "Annual Book of ASTM Standards," parts 27 and 29, American Society for Testing Materials, Philadelphia, Pa., 1976, 01209-69.

(4) R. S. Hunter, "The Measurement of Appearance," Wiley, New York, N.Y., 1975, pp. 122, 123.

(5) "Annual Book of ASTM Standards," part 30, American Society for Testing Materials, Philadelphia, Pa., 1976, E450-75.

(6) "The United States Pharmacopeia," 19th rev., Mack Publishing Co., Easton, Pa., 1975, p. 765.