

Adsorption of Certified Dyes by Starch

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The adsorption of five anionic certified dyes, FD&C Red No. 3, FD&C Blue No. 2, FD&C Green No. 1, FD&C Yellow No. 5, and Ext. D&C Red No. 15, by rice starch, wheat starch, and three varieties of cornstarch, was measured. Adsorption was found to fit the Langmuir equation in all cases. The extent of adsorption by the various cornstarches is related to the ratio of amylopectin to amylose, an increase in adsorption occurring with an increase in the amylopectin content. No dye adsorption was observed when potato starch was used. This is believed to be because of the presence of phosphate ester groups not present in the other starches.

ONE OF THE most troublesome applications of dyes in pharmaceutical products is the coloring of compressed tablets. It is generally found that the wet mass is uniform in color, but that the large granules, after drying, have a high concentration of dye at the surface and a low concentration beneath the surface. Thus, dye migrates toward the outside during drying and compression of this mixture, causing spotted tablets. At the present time, although pigments have been reported to yield evenly colored tablets (1, 2), there is no general means for predicting the facility of migration or preventing the migration of water-soluble dyes during tablet manufacture.

It was felt that studies concerned with dye affinity for solids would be of value to those concerned with this problem since an improvement of dye-solid affinity should reduce migration. This report is concerned with the affinity of selected water-soluble anionic, certified dyes for various natural starches. Starch was chosen since it is widely used in tableting, is available from a variety of different natural sources, and is insoluble in water at moderate temperatures.

EXPERIMENTAL

General Procedure for Measurement of Adsorption.—Adsorption studies were conducted using Kimax, heavy duty, screw-capped centrifuge tubes (Kimble Glass Co.) which have a capacity of about 40 ml. Tin-lined screw caps (Arthur H. Thomas) were used since they were found not to adsorb dye.

A rubber ring was placed around the neck of the tube to prevent leakage. To maintain constant temperature and thorough mixing, the tubes were placed on a rotating wheel in a water bath at $30 \pm 0.1^\circ$ and were continuously rotated at 32 r.p.m. Approximately 1 Gm. of starch, accurately weighed, and 20 ml. of dye solution were placed into the tubes. These were placed in the bath and removed after 48 hours, since this was previously determined to be the time required to ensure equilibrium. The tubes were centrifuged at 2500 r.p.m. for 5 minutes, and a 10-ml. aliquot of dye solution was removed. Controls containing only dye solution were treated in the same manner and more than one sample for each dye concentration was used.

Dyes Investigated.—Since there are a large number of water-soluble certified dyes, those chosen for study are representative of the chemical groups into which most of these dyes fall. Ext. D&C Red No.

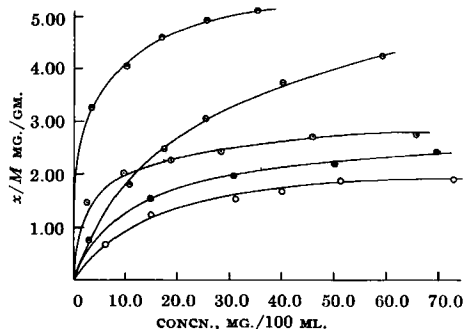


Fig. 1.—Plots of milligrams of dye adsorbed per gram of cornstarch, (x/M), vs. milligrams of dye per 100 ml. of solution at equilibrium for FD&C Red No. 3 (●), FD&C Blue No. 2 (⊖), Ext. D&C Red No. 15 (⊙), FD&C Yellow No. 5 (⊕), and FD&C Green No. 1 (⊖).

15 (formerly FD&C Red No. 1) was chosen as an azo dye, FD&C Green No. 1 as a triphenylmethane dye, FD&C Yellow No. 5 as a pyrazalone dye, FD&C Blue No. 2 as an indigo dye, and FD&C Red No. 3 as a xanthine dye. All dyes were obtained from the Calco Chemical Division, American Cyanamid Co., and were used as received.

The concentration of dye in solution was measured spectrophotometrically using a Beckman model DU spectrophotometer. Absorbance measurements were made at 504 $m\mu$ for Ext. D&C Red No. 15, 527 $m\mu$ for FD&C Red No. 3, 426 $m\mu$ for FD&C Yellow No. 5, 620 $m\mu$ for FD&C Blue No. 2, and 428 $m\mu$ for FD&C Green No. 1. The final dilution of all dyes, except FD&C Red No. 3, was made into a phosphate-citrate buffer at a pH 5.00, while the final dilution of FD&C Red No. 3 was made into a borate buffer at pH 9.20. The pH values were measured using a Beckman model G pH meter.

Starches Investigated.—Starches utilized in this investigation included those from potato, rice, wheat, and three varieties of corn. The cornstarches included U.S.P. cornstarch containing about 72% amylopectin and 28% amylose, waxy maize starch commercially available with the brand name, Amioca,¹ and containing 100% amylopectin, and Amylon,¹ a cornstarch containing about 60% amylose and 40% amylopectin.

RESULTS

From the difference in dye concentration before and after contact with starch, the number of milligrams of dye adsorbed per gram of starch, x/M , was calculated for each concentration of dye used.

¹ Obtained from National Starch and Chemical Corp., New York, N. Y.

Received January 18, 1963, from the College of Pharmacy, University of Michigan, Ann Arbor.

Accepted for publication March 15, 1963.

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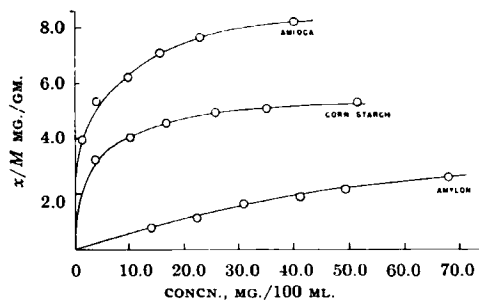


Fig. 2.—Plots of milligrams of FD&C Red No. 3 adsorbed per gram of starch, (x/M) , vs. milligrams of dye per 100 ml. of solution at equilibrium for three varieties of cornstarch.

Adsorption of all dyes occurred on all starch samples except potato starch, which did not adsorb these dyes. Figure 1 shows a typical plot of x/M versus C , the concentration of dye in solution at equilibrium, for all five dyes on cornstarch. Figure 2 shows the marked differences in adsorption for a particular dye on the three cornstarches. The data obtained were found to fit the Langmuir adsorption equation

$$x/M = \frac{k_1 k_2 C}{1 + k_1 C} \quad (\text{Eq. 1})$$

where k_1 and k_2 are constants. This is shown in Fig. 3 by the fit of the data to the linear form of this equation

$$C/(x/M) = \frac{C}{k_2} + \frac{1}{k_1 k_2} \quad (\text{Eq. 2})$$

From plots of $C/(x/M)$ versus C the constants, k_1 and k_2 , were evaluated as shown in Table I. The constant, k_2 , expressed in milligrams adsorbed per unit mass of adsorbent, is the maximum value for x/M at a given temperature. This can be seen by applying the Langmuir equation at high concentrations, where the value of $k_1 C$ becomes much greater than 1, and

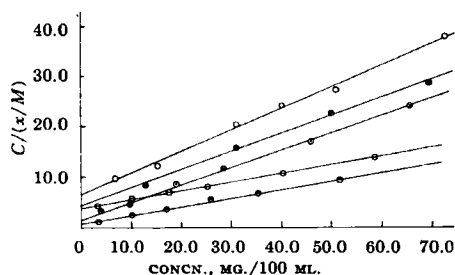


Fig. 3.—Langmuir plots for the adsorption of dyes on cornstarch; FD&C Red No. 3 (\ominus), FD&C Blue No. 2 (\circ), Ext. D&C Red No. 15 (\square), FD&C Yellow No. 5 (\triangle), and FD&C Green No. 1 (\circ).

$$x/M = k_2 \quad (\text{Eq. 3})$$

The constant, k_1 , expressed in 100 ml./mg.^{-1} indicates the fraction of maximum adsorption per unit concentration. This is apparent at low concentrations where C may be considered to be much less than 1 and

$$\frac{x/M}{k_2} = k_1 C \quad (\text{Eq. 4})$$

DISCUSSION

A comparison of the constants, k_1 and k_2 , indicates that there is little difference in adsorption of a particular dye on corn, rice, and wheat starches, although the particle sizes are quite different (3). Calculation of the maximum number of dye molecules adsorbed, utilizing k_2 values, indicates more adsorption than is accountable for on the basis of surface adsorption on the starch grains. This, plus the fact that 48 hours is required to reach equilibrium, suggests that penetration of the various dyes into the starch grain is occurring. As has been shown with cellulose (4), the adsorption probably occurs at the hydroxyl groups of the starch granule. Whether the anionic or the nonionic polar group of the dye is responsible for this interaction has not been definitely determined. Hydrogen bonding between nonionic polar groups of a dye

TABLE I.—LANGMUIR CONSTANTS^a FOR ADSORPTION OF DYES ON VARIOUS STARCHES^b

Starch	FD&C Blue No. 2	Ext. D&C Red No. 15	FD&C Yellow No. 5	FD&C Red No. 3	FD&C Green No. 1
Rice					
k_1^c	0.118	0.146	0.100	0.226	0.0318
k_2^d	3.55	3.18	2.71	6.64	1.03
Wheat					
k_1	0.155	0.158	0.123	0.223	0.0808
k_2	3.15	3.02	2.47	6.20	1.73
Corn					
k_1	0.0438	0.195	0.0916	0.284	0.0644
k_2	5.85	2.94	2.75	5.67	2.30
Amylon					
k_1	0.231	0.223	...
k_2	2.62	2.57	...
Amioca					
k_1	0.0241	0.231	0.195	0.337	0.0419
k_2	11.6	4.19	3.27	8.86	4.65

^a On the basis of the dry weight of the starches. ^b Blank spaces indicate little or no adsorption. ^c Units of 100 ml./mg. ^d Units of mg./Gm.

and cellulose hydroxyl groups has been proposed (4).

A comparison of the adsorption by the three varieties of cornstarch indicates that Amioca adsorbed all dyes to the greatest extent, U.S.P. cornstarch next, and then Amylon. This trend is related to the amylopectin content. Recent studies concerned with anionic dye binding of soluble starches have shown the opposite results (5): the less interaction occurring, the higher the proportion of amylopectin. This is attributed to the greater rigidity of the branched portions of starch in solution compared to the more flexible linear amylose chains. One would not necessarily expect interactions involving the intact starch grain to be the same as that in solution. The results presented here confirm this.

The lack of anionic dye adsorption on potato starch is apparently because of the presence of phosphate esters (6) which impart a negative charge to the potato starch grain, but which are absent in the other starches. Schoch and Maywald (7) have shown that potato starch and carboxylated starches adsorb cationic dyes strongly but do not adsorb anionic dyes. Adsorption of anionic dyes on potato starch has been observed when neutral electrolytes are added (8). These would be expected to reduce the repulsive forces between the dye and starch by breaking down the electric double layer.

In view of the observed affinity of anionic certified dyes for starch it would appear that the addition of starch to a tablet granulation before the addition of the dye solution should aid in preventing color migration. A recent communication

(9) has indicated that starch does enhance color distribution and prevent migration when added to tablet granulations.

In general, it is proposed that adsorption isotherm data can be used to study color migration problems. These isotherms indicate the amount of dye adsorbed as a function of that amount remaining in solution. Since it is the dye in solution which migrates upon drying, the objective should be to minimize this concentration while increasing the amount adsorbed. For systems described by the Langmuir equation the constants, k_1 and k_2 can be considered as a measure of the extent of adsorption for a given dye concentration and the maximum amount of adsorption, respectively. Therefore, by measuring adsorption as a function of such factors as temperature, solvent, electrolyte concentration, and the presence of tablet components, it should be possible to pick systems giving maximum dye adsorption with a minimum of dissolved dye, resulting in maximum color distribution.

Further studies are being conducted and will be reported in a future communication.

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Reduction of 1,2,3-Trimercaptopropane Content of Dimercaprol

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A multiple batch extraction procedure is described which can serve to reduce the trithiol content of dimercaprol to levels conforming to the U.S.P. XVI monograph.

PREVIOUS REPORTS (1, 2) indicate the presence of the trithiol, 1,2,3-trimercaptopropane, in many laboratory, pilot plant, and commercial lots of dimercaprol (BAL). The toxicity of BAL is substantially increased by this impurity and the revised monograph on dimercaprol appearing in the first U.S.P. XVI supplement contains limits on the concentration in which it may be present. Many lots of BAL, presently available for drug use, contain far more than the established 1.5% limit of the trithiol. Since BAL is not currently manufactured in this country, a purification process is needed.

This report presents the results of a study of the removal of 1,2,3-trimercaptopropane from BAL by a

liquid-liquid extraction procedure, using petroleum ether as the extracting solvent. This method may be used with a variety of solvents under various experimental conditions, e.g., BAL saturated with water to increase the partitioning of the trithiol into the organic solvent phase to obtain basic information of value for the development of a commercial process for the purification of BAL containing excessive quantities of the trithiol impurity.

EXPERIMENTAL

Materials.—BAL purified by passage through a partition chromatographic column, followed by distillation at low pressure; 1,2,3-trimercaptopropane, hereinafter designated as TSH; petroleum ether, shaken with concentrated sulfuric acid over a period of several days and distilled between 35–50° were employed.

Procedure.—Known concentrations of TSH in BAL were equilibrated with petroleum ether. The volume of the BAL was chosen sufficiently large so that it was not significantly changed by the extraction. The petroleum ether phase was analyzed for sulfhydryl content, and the resultant data utilized in calculations of extraction efficiency.

Received April 9, 1963, from the U. S. Army Chemical Research Development Laboratories, Edgewood Arsenal, Edgewood, Md.

Accepted for publication April 19, 1963.

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