

Adsorption of Sorbic Acid by Plastic Cellulose Acetates

By WITOLD SASKI

The adsorption of sorbic acid from aqueous solutions by plastic cellulose acetate and cellulose triacetate was studied. Adsorption isotherms at $25 \pm 0.2^\circ$ were determined and Langmuir constants were calculated. The method presented is recommended as satisfactory for use in comparative studies of adsorption of drugs, fungistatic and bacteriostatic agents by plastic materials. Adsorption of sorbic acid as a function of pH was studied and was shown to decline to zero in the vicinity of the point of maximum ionization of sorbic acid.

PLASTICS have been rapidly replacing the conventional materials for the manufacture of containers and various devices used in pharmaceutical and medical practice. The common belief that plastics are inert and, therefore, safe for any use is unjustified. It has been demonstrated that they may cause a tissue sensitivity or toxic response when used as surgical implants. A constituent may be released from the plastic to the solution which is to be injected into the patient when plastic devices such as syringes and tubings are used. A plastic device or container may bind or adsorb a significant quantity of the drug, bacteriostatic or fungistatic agent present in the formulation and affect the potency and perhaps even the stability of the product. A review of the literature on the subject was published by Autian (1).

Plastics, by definition (2), are a large and varied group of materials which consist of, or contain as an essential ingredient, a substance of high molecular weight which while solid in the finished state, at some stage in its manufacture is soft enough to be formed into various shapes, usually through the application, either singly or together, of heat and pressure. The thermosets are plastics which harden and form a permanent shape upon heating. On reheating and cooling, these thermosets will no longer have the same characteristics they originally had. In contrast to the thermosets, the thermoplastics can be reheated and cooled a number of times without materially altering their original characteristics. Fluorocarbons, polyethylenes, vinyls, nylons, styrenes, acrylics, and cellulotics are examples of thermoplastics.

To attain the desirable properties of plastic materials, various additives are needed. They may consist of plasticizers, fillers, and stabilizers.

In cellulose plastics (3), the plasticizers most frequently used are the phthalates—diethyl, dibutyl, dioctyl, and methoxyethyl phthalate. Although triphenyl phosphate is a relatively poor plasticizer when compared with the phthalates, it is frequently used in order to produce a more rigid sheet or to reduce the flammability of the product. The proportions of the above plasticizers used may vary widely, frequently running from as low as 8 to as high as 40 parts per 100 parts of cellulose ester, depending upon the physical properties desired in the finished sheet. In addition to plasticizers, coloring agents, ultraviolet light absorbers, and various types of surface coatings to improve slip characteristics may also be employed (4).

The present study set out to determine the extent of possible adsorption of the fungistatic agent, 2,4-hexadienoic (sorbic) acid, by plastic cellulose acetates, and to develop a method suitable for comparative evaluation of the adsorptive capacities of different plastic materials.

EXPERIMENTAL

Apparatus and Materials.—The following apparatus was used: Beckman DU spectrophotometer, Photovolt model 110 electronic pH meter, Christian Becker analytical balance, constant temperature water bath, and the Burrell wrist-action model DD shaker. The following materials were used: plastic cellulose acetate sheets, 0.01 in. thick;¹ plastic cellulose triacetate sheets, 0.01 in. thick;² sorbic acid;³ alcohol U.S.P.; 1 N hydrochloric acid, and 1 N sodium hydroxide.

Methods of Analysis.—Sorbic acid was recrystallized and the melting point determined according to standard procedures. The quantitative determinations of sorbic acid in solutions were performed using standard spectrophotometric techniques. A 256 m μ wavelength of maximum absorption was used (5). In all instances, the solutions to be assayed were adjusted to contain 3 mcg. or less of sorbic acid per ml.

Adsorption as a Function of Time.—Strips of

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¹ Marketed as Kodacel A29, by Eastman Kodak Co.

² Marketed as Kodapak IV, Type F 401, by Eastman Kodak Co.

³ Marketed as Sorbistat by Chas. Pfizer & Co., Inc.

plastic cellulose acetate sheet, 0.01 in. thick and approximately 1 in. \times 7 in. in size, were weighed on the analytical balance and placed into glass-stoppered cylinders containing exactly 100 ml. of a 0.150% (w/v) sorbic acid solution in distilled water. Seven cylinders were used: six with plastic strips, and one as a control and to check on possible sorbic acid degradation. The cylinders were placed in the constant temperature bath adjusted to $25 \pm 0.2^\circ$ and subjected to constant and uniform shaking by means of the Burrell wrist-action model DD shaker set in position 1.

The procedure developed in this investigation was as follows. One-milliliter portions of the solution were withdrawn from each cylinder and diluted to 500 ml. in a volumetric flask to obtain the desired sorbic acid concentration. The adsorbance of the samples was then determined, using quartz 1-cm. cells in the Beckman DU spectrophotometer. The results are shown in Table I and Fig. 1. It became apparent that the equilibrium concentration of

sorbic acid in aqueous solution in the presence of plastic cellulose acetate is reached within 14 days. This finding has been utilized in the subsequent experiments.

Adsorption as a Function of Concentration.—Following the procedure described, strips of cellulose acetate were placed into cylinders containing 100 ml. of aqueous solutions of sorbic acid. Triplicate samples of each of five concentrations, 0.050, 0.075, 0.100, 0.125, and 0.150% (w/v), were used. This experiment was carried out as before in the constant temperature water bath at $25 \pm 0.2^\circ$ and with the shaker set at the same speed. Since the previous experiment determined that the equilibrium concentration of sorbic acid was reached within 14 days, no samples were tested until this time had elapsed. Following the identical procedure, strips of plastic cellulose triacetate were subjected to the same treatment. The results are reported in Table II. Figure 2 shows the adsorption iso-

TABLE I.—ADSORPTION OF SORBIC ACID BY PLASTIC CELLULOSE ACETATE AS A FUNCTION OF TIME^a

No. Days Elapsed	Mg. Acid per Gm. Plastic
3	16.00
5	26.15
7	32.70
9	36.34
10	38.00
12	39.50
14	40.00
16	40.00
20	39.60

^a Concentration of the aqueous solution: 0.150% (w/v); temperature: $25 \pm 0.2^\circ$.

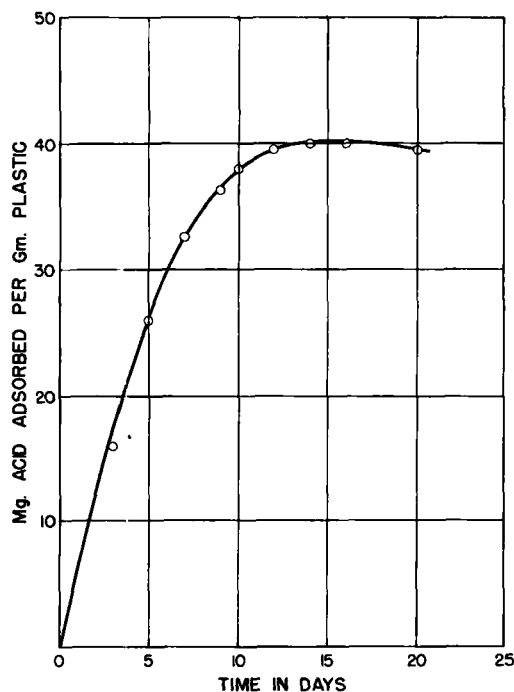


Fig. 1.—Adsorption of sorbic acid by plastic cellulose acetate as a function of time.

TABLE II.—ADSORPTION OF SORBIC ACID AS A FUNCTION OF CONCENTRATION^{a, b}

	Acid Concn., %	x/m	c	$\frac{c}{x/m}$
Cellulose acetate	0.050	16.05	26.50	1.65
	0.075	27.50	52.25	1.90
	0.100	30.34	64.54	2.15
	0.125	38.00	87.40	2.30
	0.150	39.51	95.63	2.45
Cellulose triacetate	0.050	9.56	37.76	3.95
	0.075	11.30	60.00	5.31
	0.100	13.20	85.50	6.47
	0.125	14.16	104.16	7.35
	0.150	15.34	129.30	8.43

^a Temperature $25 \pm 0.2^\circ$. ^b x/m = mg. of sorbic acid adsorbed per Gm. of plastic; c = equilibrium concentration in mg. sorbic acid per 100 ml.

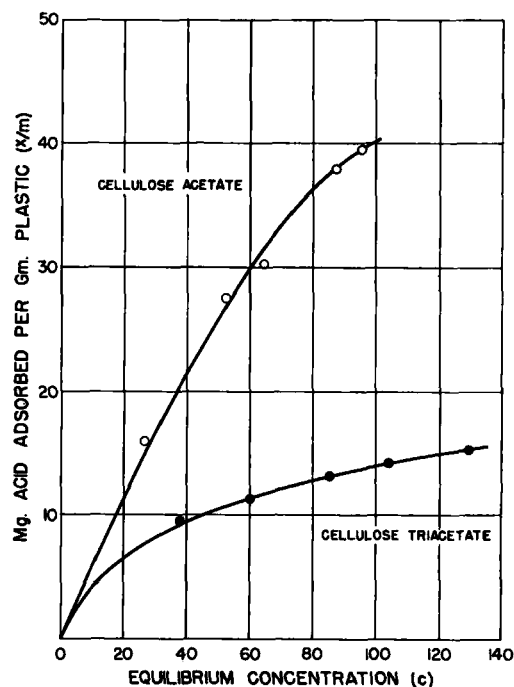


Fig. 2.—Langmuir adsorption isotherms for plastic cellulose acetate and cellulose triacetate.

therms for both plastic materials. Figure 3 shows the linear form of the Langmuir adsorption isotherms for both plastics.

Adsorption as a Function of pH.—Following essentially the same procedure, strips of plastic cellulose acetate were placed into glass cylinders containing 100 ml. of a 0.150% (w/v) sorbic acid aqueous solution adjusted to various pH levels by the addition of 1 *N* solution of hydrochloric acid or 1 *N* solution of sodium hydroxide, all in triplicate. The solutions were not buffered, in order to avoid the possibility of interference with adsorption by the buffer salts. The pH of each solution was determined with the Photovolt model 110 electronic pH meter, both at the outset of the experiment and at the end of the apparent equilibration period of 14 days. The results are reported in Table III and graphically presented in Fig. 4, which represents the pH data obtained after contact with the plastic. Sorbic acid percentage ionization values were calculated and shown in Table III.

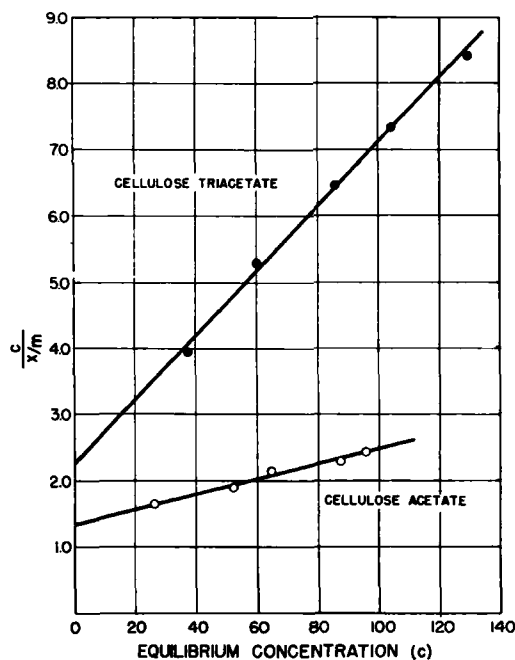


Fig. 3.—Linear form of the Langmuir adsorption isotherms for plastic cellulose acetate and cellulose triacetate.

Adsorption as a Function of Solvent System.—The effect of ethyl alcohol concentration on sorbic acid adsorption by plastic cellulose acetate was determined. The concentration of sorbic acid in all samples was 0.150% (w/v) and the concentrations of the alcohol were 0, 9.5, 19.0, 38.0, and 76.0 (v/v), respectively, with triplicate samples of each concentration being tested, together with an appropriate number of controls. The procedure followed was that previously described. The results are graphically presented in Fig. 5.

RESULTS AND DISCUSSION

After having determined the time necessary to attain equilibrium, the effect of sorbic acid concentration on adsorption by plastic cellulose acetate and cellulose triacetate was studied. This is presented in two ways. First, by plotting the equilibrium concentration of sorbic acid in mg. per 100 ml. of solution (*c*) as abscissa against the number of mg. of sorbic acid adsorbed by one Gm. of plastic, as shown in Fig. 2.

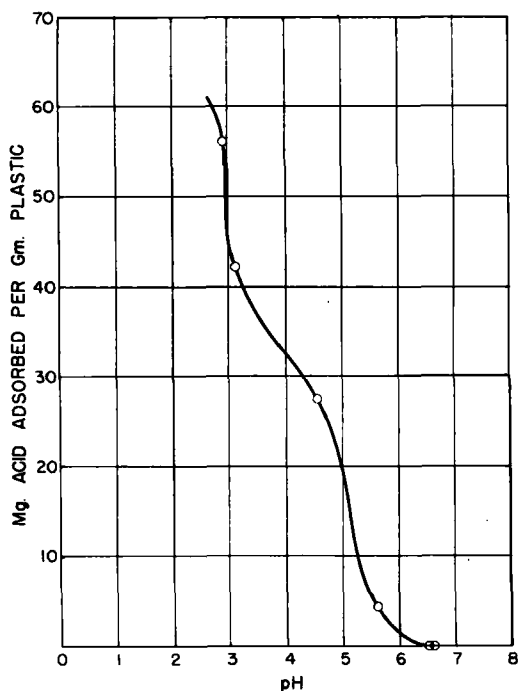


Fig. 4.—Adsorption of sorbic acid by plastic cellulose acetate at various pH levels.

TABLE III.—ADSORPTION OF SORBIC ACID BY PLASTIC CELLULOSE ACETATE AT VARIOUS pH LEVELS^a

Av. Wt. of Plastic in Gm.	pH		Calculated Percentage Ionization ^b	Sorbic Acid	
	Before Contact with Plastic	After Contact with Plastic		Mg. Adsorbed	Mg. Adsorbed per Gm. Plastic
1.1140	2.60	2.90	1.36	62.5	56.10
1.1854	3.30	3.10	2.14	50.0	42.18
1.1763	4.50	4.55	38.16	32.5	27.63
1.1294	5.52	5.60	87.25	5.1	4.51
1.2755	7.30	6.50	98.21	0	0
1.2095	10.80	6.60	98.57	0	0

^a From a 0.150% (w/v) solution. Temperature 25 ± 0.2°. ^b Calculated from the equation (8):

$$\text{Percentage ionization} = \frac{100}{1 + \text{Antilog}(pK_a - \text{pH})}; \quad pK_a \text{ of sorbic acid is } 4.76.$$

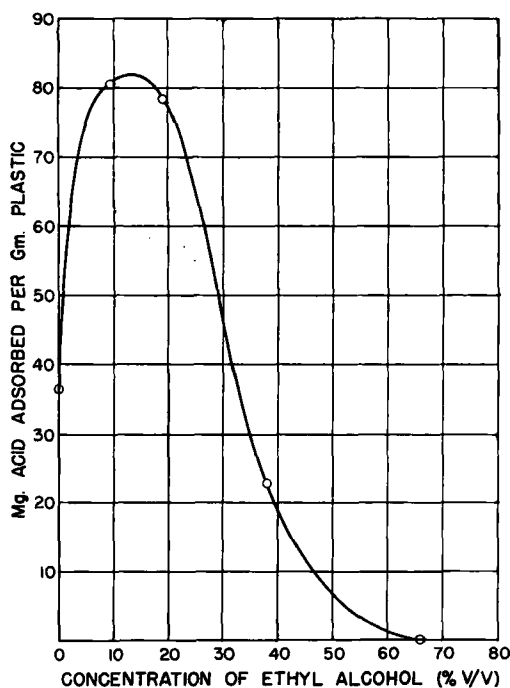


Fig. 5.—Effect of ethyl alcohol on the adsorption of sorbic acid (0.150% w/v) by plastic cellulose acetate.

The second method of presenting these data is by plotting the equilibrium concentration against the ratio of the equilibrium concentration to the number of mg. of sorbic acid adsorbed by one Gm. of plastic, as shown in Fig. 3. This type of graph, which represents the linear form of the Langmuir equation (7), is particularly useful. Derived from the equation

$$\frac{x}{m} = \frac{abc}{1 + a c}$$

where x/m = mg. of sorbic acid adsorbed per Gm. of plastic, c = equilibrium concentration in mg. sorbic acid per 100 ml., and a and b are constants, the linear form of the Langmuir equation is

$$\frac{c}{x/m} = \frac{1}{b} c + \frac{1}{a b}$$

In this form, the slope is $1/b$ and the intercept is $1/ab$. By plotting $\frac{c}{x/m}$ against c , linear curves are obtained from which may be found the slopes and intercepts. The closer the line is to paralleling c , the greater adsorptive power of the plastic. The slope of the line may be determined, as well as the values of the constants, a and b .

The described procedure provides a satisfactory quantitative method for the evaluation of different plastic materials with respect to their relative adsorptive capacities in contact with various drugs and bacteriostatic and fungistatic agents. Langmuir adsorption isotherms have been employed by Barr, *et al.*, in adsorption studies on clays (8, 9).

The adsorptive avidity of plastic cellulose acetate has been compared with that manifested by plastic

cellulose triacetate. As Fig. 3 shows, such avidity with respect to sorbic acid is much higher in case of cellulose acetate. The slopes of the two linear curves for the two respective plastics were calculated and so were the constants a and b . They are shown in Table IV.

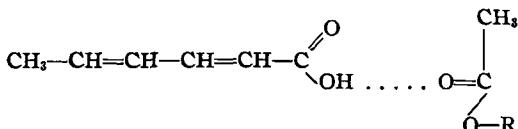
TABLE IV.—CONSTANTS OF LANGMUIR EQUATION FOR SORBIC ACID

Plastic	a	b
Cellulose acetate	0.0085	87.0
Cellulose triacetate	0.0218	20.4

It can be seen that the b value for plastic cellulose acetate is more than four times as high as for cellulose triacetate.

The anhydroglucose units of cellulose each contain three hydroxyl groups, one primary alcohol group and two secondary alcohol groups, which can be acetylated. Study of the distribution of the acetyl groups along the cellulose chain indicates that the esterification is fairly uniform, so that most of the anhydroglucose units will contain at least two acetyl groups. Acetylation obviously alters the surface characteristics of cellulose. The extent of acetylation of cellulose apparently influences the adsorption of weak acidic substances. Vickerstaff suggested that as a consequence of the alteration of the cellulose structure by acetylation, the negative surface potential of cellulose acetate in water is much higher than that of cellulose, and this will assist the repulsion of anionic dyes (10). This theory should extend to cellulose triacetate and sorbic acid. Cellulose triacetate results from the replacement of all or most of the hydroxyl units on the cellulose chain with acetyl groups (11). The much lesser adsorptive capacity of plastic cellulose triacetate as compared with cellulose acetate is in agreement with Vickerstaff's theory.

As has been demonstrated in the experiment with sorbic acid at different pH levels, upon approaching neutrality from the acid side, and nearly complete ionization of the acid, adsorption becomes reduced to zero. The undissociated sorbic acid may be adsorbed on the ester groupings by the formation of the hydrogen bond



The decrease of adsorption upon the increase of the percentage of ionization is not surprising since it seems to have been generally found that ionization of an adsorptive decreases its surface activity. It has been suggested (12) that this may be so because the ion, with its envelope of solvent, is much more soluble than the undissociated molecule, and so shows less tendency to escape from the solution. As is shown in Table III, considerable change in pH occurred at the higher pH values at the end of the experiment. Assays of the controls revealed that no decomposition of the sorbic acid at these high pH levels had occurred. This would indicate that possibly a plasticizer was the cause

of the decrease in pH. The term "apparent equilibration" with reference to the pH data is used advisedly since the data clearly show that the true equilibrium with the original plastic will never be reached. Since the plastic is leaching one or more constituents into the solution, the material is continually being altered and it is improbable that a true equilibrium is attained.

Although the adsorption of acids and bases has been found in some cases to be proportional to the concentration of undissociated molecules, many highly ionized surface-active substances are known so that the extent of ionization itself cannot be a sole controlling factor. As a matter of fact, the experiments conducted with hydroalcoholic solvents have demonstrated the maximum sorbic acid adsorption from the solution containing about 10% (v/v) of ethyl alcohol. This finding had not been anticipated. Autian and Shaikh, in their study on adsorption of sorbic acid by nylon (13), noted that as the water is replaced with a less polar solvent, the binding of sorbic acid decreased. The experiments described, which were carried out three times, show that plastic cellulose acetate behaves differently with respect to sorbic acid. No explanation can be given by this author for the reason or reasons why the adsorption increases and then sharply decreases with increase in alcohol concentration.

The effect of temperature has not been studied because of the instability of sorbic acid at somewhat elevated temperatures (14).

SUMMARY AND CONCLUSIONS

The adsorption of sorbic acid by plastic cellulose acetate and cellulose triacetate has been

studied and a method for its determination has been developed. Langmuir adsorption isotherms were determined and the constants calculated. The main significance of this paper is that the applicability of the Langmuir equation to the comparative study of different plastic materials with respect to adsorption has been demonstrated. The method suggested is just one parameter which may be helpful in studying drug-plastic interactions but many other tests and procedures might be necessary to establish useful standards for a particular plastic.

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Multiple Dose Excretion Kinetics

By R. G. WIEGAND, J. D. BUDDENHAGEN, and C. J. ENDICOTT

General mathematical equations describing expected blood and urine drug concentrations were derived to analyze riboflavin excretion data after a single large oral dose followed by multiple smaller but equal doses at equal time intervals. The urinary excretion equation was applied to the riboflavin data to obtain the least squares fit using the IBM digital computer, and by this means the absorption and excretion rates were determined. Such calculations can be applied to find the optimum dosage regimen of other drugs for which the kinetic constants are known. The general expressions reduce to all simpler cases already reported in the literature.

THE FITTING of equations to experimental data on blood and urine concentrations of drug has found wide application in determining the kinetics of the processes involved and in measuring the rates of these processes. Considering absorption and elimination of drug to

be apparent first order processes, equations describing blood drug levels (1-4) and urine levels (2, 5) after a single oral dose of drug have been reported. The general equation for blood levels after multiple oral administration of drug at equal doses and time intervals was derived by Dost (4). Boxer, *et al.* (6), had earlier used a simplified form of this equation to obtain the expected maximum and minimum blood levels

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