

The authors thank Mr. S. J. Lomax of the Visual Aids Unit, Beechams Pharmaceuticals, for valuable assistance in the preparation of the figures. They also thank Portsmouth School of Pharmacy and Beechams Pharmaceuticals for use of some of the technical

facilities.

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Water-Sorption Properties of Tablet Disintegrants

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Abstract □ The water-sorption properties of four tablet disintegrants, starch, sodium carboxymethylcellulose, sodium starch glycolate, and a cation-exchange resin, were examined in the form of powders and in compressed tablets prepared from calcium phosphate dibasic dihydrate. Dissolution properties of the tablets compare well to the water-sorption properties. The effect of storage in the presence of water vapor upon tablets containing the various disintegrants was evaluated in terms of tablet hardness and disintegration time. Differences in the effects produced in the various tablet formulations can be related to the differing mechanisms whereby the disintegrants effect tablet rupture. Photomicrographic data support the conclusions drawn from the water-sorption, disintegration, and dissolution studies. Sodium starch glycolate and the cation-exchange resin merit careful consideration by formulators using calcium phosphate dibasic dihydrate or similar direct compression matrixes.

Keyphrases □ Water sorption of tablet disintegrants (starch, sodium carboxymethylcellulose, sodium starch glycolate, cation-exchange resin)—disintegration and dissolution, powders and calcium phosphate dibasic dihydrate tablets □ Tablet disintegrants (starch, sodium carboxymethylcellulose, sodium starch glycolate, cation-exchange resin)—water sorption of powders and calcium phosphate dibasic dihydrate tablets, disintegration, dissolution

Previously, the disintegration and dissolution properties of tablets containing sodium starch glycolate and a cation-exchange resin were reported (1, 2). The results of these evaluations clearly showed that both the cation-exchange resin and sodium starch glycolate are extremely efficient disintegrants in a variety of tablet systems. The objective of the present study was to examine the water-sorption properties of these disintegrants in an attempt to evaluate the basic factors controlling their disintegrant action. Starch and sodium carboxymethylcellulose were included for comparative purposes.

EXPERIMENTAL

Materials—The following were used: calcium phosphate dibasic dihydrate¹ (unmilled), corn starch² BP, sodium salicylate², amaranth² BPC, a cation-exchange resin³, sodium starch glycolate⁴, sodium carboxymethylcellulose⁵, and magnesium stearate⁶.

Dried Disintegrant Powders—The dried disintegrants were

Table I—Effect of Humidity on Disintegration Properties of Calcium Phosphate Dibasic Dihydrate Tablets, Containing Several Disintegrants, Stored at 100% Relative Humidity at 37° [Punch Size 1.1 cm (7/16 in.) Flat]

Disintegrants, 10% (w/v)	Disintegration Time, min					
	Initial	2 hr	4 hr	8 hr	22 hr	30 hr
Starch	15 ^a	15 ^a	15 ^a	15 ^a	15 ^a	15 ^a
Sodium carboxymethylcellulose	43	50	50	55	55	60
Sodium starch glycolate	0.6	2.8	7.0	13.0	15	15
Cation-exchange resin	0.83	2.0	7.0	8.0	60	60

^a Particles remaining.

exposed to 100% relative humidity at 37°. Two replicate readings of water uptake, always in good agreement, were obtained at various times over 25 hr. Figure 1 shows the water sorption by the disintegrant as a function of time.

Tablet Containing 10% Disintegrant—Calcium phosphate dibasic dihydrate was chosen as the excipient because of its very low equilibrium moisture content (2.5%). Furthermore, tablets made from the material were easier to handle after having absorbed moisture than were other tablets, such as those prepared from lactose.

The tablets containing 10% disintegrant were made using 1.1-cm (7/16-in.) flat punches on a single-punch tablet press⁷. All tablets were made under the same conditions of pressure and die fill settings. Fifty tablets of each formulation were used for the water-sorption study. Five lots of 10 tablets of each formulation (one lot for each time interval of 5, 10, 15, 20, and 25 hr) were weighed and labeled individually; their thickness and diameter measurements were taken, using a micrometer, before and after exposure to 100% relative humidity.

Figure 2 shows the water uptake by these tablets as a function of time. The results of expansion and thickness changes accompanying water sorption are presented in Figs. 3 and 4. (Changes in density reflect overall structural changes, whereas individual measurement of thickness and diameter changes allows observation of whether expansion occurs preferentially in, or at right angles to, the plane of compression.) These tablets were also tested for disintegration time⁸ using the BP method and for hardness⁹. The effect of storage on disintegration time and hardness of tablets prepared from calcium phosphate dibasic dihydrate is shown in Tables I and II.

To express the relative affinities for water of these disintegrants, the term "absorption efficiency" was used; it is calculated in a similar way as dissolution efficiency (3). Figures 5 and 6 show the absorption efficiencies of pure disintegrants and of the disintegrants

¹ Albright and Wilson, Oldbury, England.

² J. M. Loveridge, Southampton, England.

³ Amberlite IRP88, Lenning, London, England.

⁴ Primojel, Slater, Winsford, England.

⁵ Courlose P20, British Celanese, Coventry, England.

⁶ British Drug Houses, Poole, England.

⁷ Manesty F3.

⁸ Manesty disintegration tester.

⁹ Erweka hardness tester.

Table II—Effect of Humidity on Hardness of Calcium Phosphate Dibasic Dihydrate Tablets Stored at 100% Relative Humidity at 37°

Disintegrants, 10% (w/w)	Hardness, Erweka Units					
	Initial	2 hr	4 hr	8 hr	22 hr	30 hr
Starch	5.6	5.5	5.0	5.5	5.0	4.0
Sodium carboxymethylcellulose	5.2	3.2	2.0	2.2	2.0	2.0
Sodium starch glycolate	4.0	3.5	3.0	3.0	2.0	—
Cation-exchange resin	3.0	—	—	—	—	—

incorporated into tablets after 5 and 25 hr. Dissolution efficiencies of tablets prepared from calcium phosphate dibasic dihydrate containing 1% amaranth are shown in Fig. 7.

Surface Structure of Disintegrant Compacts after Absorbing Moisture—To obtain further information about the mechanism of action of the disintegrants evaluated in this study, compacts of disintegrants were photographed after being exposed to moisture. The disintegrant (250 mg) was compressed at 76.1 MNm⁻², using a hydraulic press and 13-mm flat punches. The compacts were exposed to an atmosphere of 100% relative humidity at 37°. Photomicrographs of the compacts were taken before and after 2 and 4 hr of exposure to humid conditions.

The surface structure of compacts prepared from sodium starch glycolate is shown in Figs. 8–10, and that of cation-exchange resin compacts is shown in Figs. 11–13. The structure of starch and its compacts has been extensively studied using a scanning electron microscope (4); therefore, the photomicrographs were not included in this report. Also, since the structure of sodium carboxymethylcellulose on absorbing moisture was quite similar to that of the resin compacts, only the resin compacts are shown here.

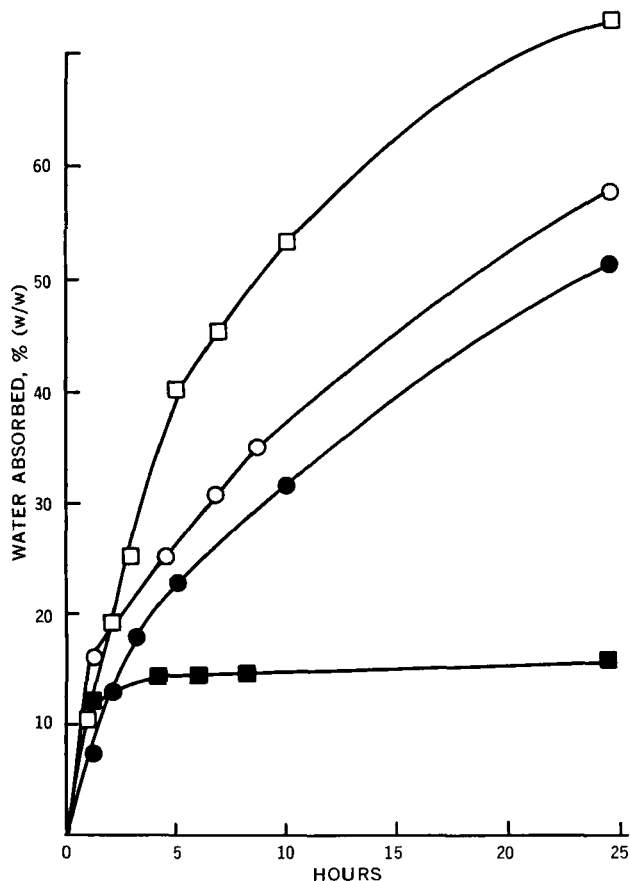


Figure 1—Water absorption by dried disintegrant powders. Key: □, cation-exchange resin; ○, sodium starch glycolate; ●, sodium carboxymethylcellulose; and ■, starch.

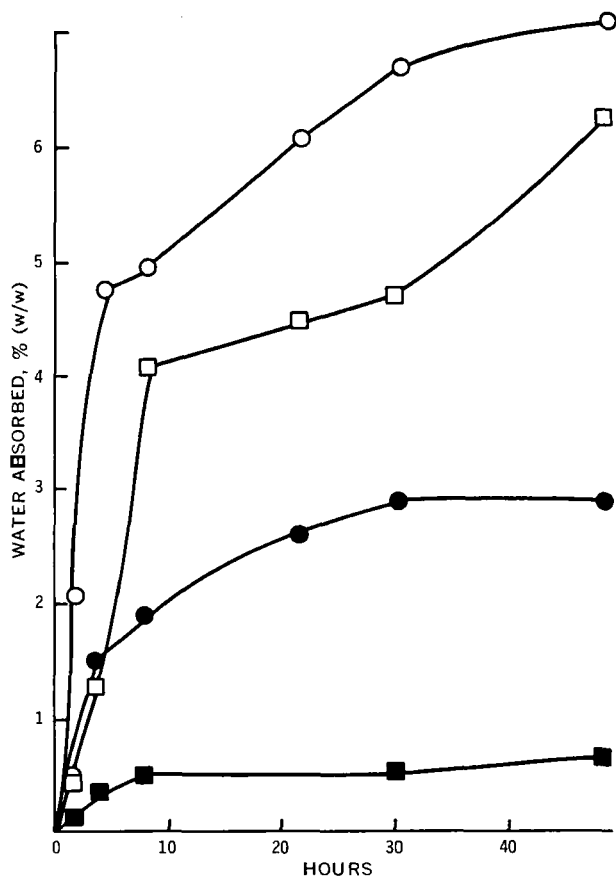


Figure 2—Water sorption of calcium phosphate dibasic dihydrate tablets containing 10% (w/w) disintegrant. Key: ○, cation-exchange resin; □, sodium starch glycolate; ●, sodium carboxymethylcellulose; and ■, starch.

RESULTS AND DISCUSSION

The water sorption by these disintegrants as a function of time in powder form and when incorporated in tablets is shown in Figs. 1 and 2. The cation-exchange resin exhibited the highest water uptake followed by sodium starch glycolate, sodium carboxymethylcellulose, and starch. Figure 3 shows the expansion of calcium phosphate dibasic dihydrate tablets containing 10% (w/w) disintegrant, when exposed to 100% relative humidity, as a function of time. Tablets containing 10% (w/w) cation-exchange resin showed the highest decrease in apparent density followed by tablets containing sodium starch glycolate, sodium carboxymethylcellulose, and starch. An interesting observation was made in the case of calcium phosphate dibasic dihydrate containing 10% (w/w) sodium carboxymethylcellulose; when tablets were exposed to 100% relative humidity at 37°, they showed considerably more expansion in their thickness than in their diameter (Fig. 4). It is possible that the expansion in the axis in which compression was applied is due to the elastic behavior of sodium carboxymethylcellulose after absorbing moisture. The other tablets showed more even expansion in both directions.

The results of these water-sorption studies, as evidenced by absorption efficiencies (Figs. 5 and 6), clearly demonstrate that the disintegrants with the highest water uptake are generally the most effective in most tablet systems (Fig. 7 and Refs. 1 and 2). Although no attempt is made to define fully the complete mechanism of action of these disintegrants, it appears that the main reasons for the effectiveness of sodium starch glycolate and the cation-exchange resin are their high uptake of water (Fig. 1), the relatively rapid absorption of water by tablets containing these disintegrants (Fig. 2), and their marked swelling and expansion properties (Figs. 3 and 4). It is, of course, fully expected that there may be difficulties in comparing water sorption, in hours, and tablet dissolution, in minutes.

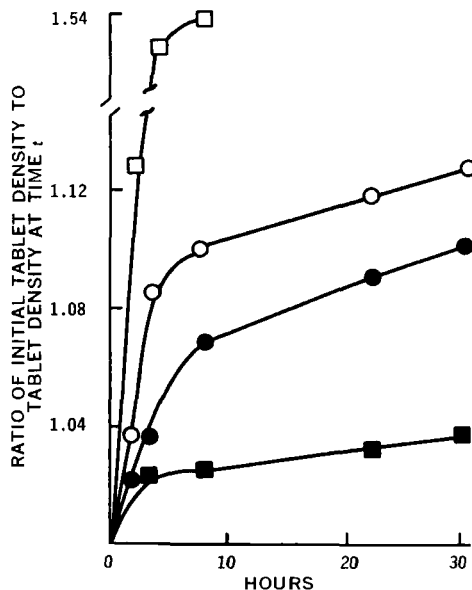


Figure 3—Change of apparent tablet density of calcium phosphate dibasic dihydrate tablets containing 10% (w/w) disintegrant on exposure to 100% relative humidity at 37°. Key: □, cation-exchange resin; ○, sodium starch glycolate; ●, sodium carboxymethylcellulose; and ■, starch.

The effect of storage (100% relative humidity) on disintegration time and hardness of tablets prepared from calcium phosphate dibasic dihydrate containing disintegrants is shown in Tables I and II. Generally, tablet hardness decreased and disintegration time increased under humid conditions. Although very little information is available on the effect of storage on calcium phosphate dibasic dihydrate tablets containing disintegrants, these results are in general agreement with those obtained with tablets prepared from lactose (7). The results presented in Tables I and II also show that the tablets containing effective disintegrants, which possess higher affinity for water, were most affected. The tablets contain-

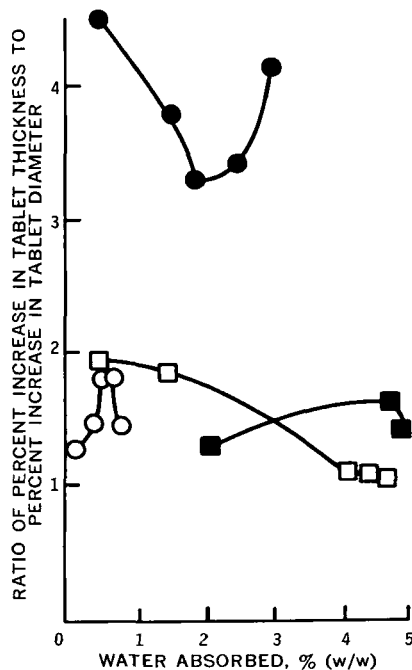


Figure 4—Change of tablet diameter and thickness of calcium phosphate dibasic dihydrate tablets containing 10% (w/w) disintegrant when exposed to 100% relative humidity at 37°. Key: □, cation-exchange resin; ○, sodium starch glycolate; ●, sodium carboxymethylcellulose; and ■, starch.

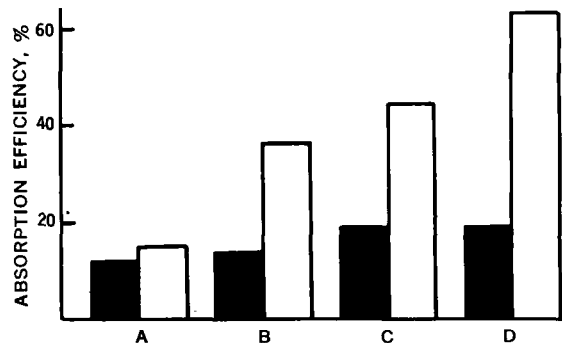


Figure 5—Absorption efficiencies of disintegrant powders on exposure to 100% relative humidity at 37°. Dark bars represent 5 hr, and open bars represent 25 hr. Key: A, starch; B, sodium carboxymethylcellulose; C, sodium starch glycolate; and D, cation-exchange resin.

ing cation-exchange resin and sodium starch glycolate showed a considerable increase in their disintegration time and a marked reduction in their strength after storage.

Tablets containing a disintegrant break up rapidly in water because of the sudden and immediate application of stress. However, when a tablet containing such a disintegrant is exposed to water vapor, stress is built up slowly and the tablet absorbs some of the strain. Because the disintegrants within these tablets have lost some of their absorption and swelling ability, the disintegration time tends to increase. It can be seen that tablets containing disintegrants in which swelling is an important mechanism of action were most affected, *i.e.*, cation-exchange resin and sodium starch glycolate. Because swelling is not thought to be an important mechanism in the action of starch, the properties of tablets containing this disintegrant were not greatly affected on exposure to 100% relative humidity. The reduction in the strength of tablets can be explained by the absorption of moisture by the disintegrant, thus causing swelling and bond disruption. Because moisture has an especially deleterious effect on the disintegration time and hardness of tablets containing the most effective disintegrants (with high affinity for moisture), suitable packaging is of supreme importance when such a disintegrant is used in tablets.

A complete picture of the mechanism of action of sodium starch

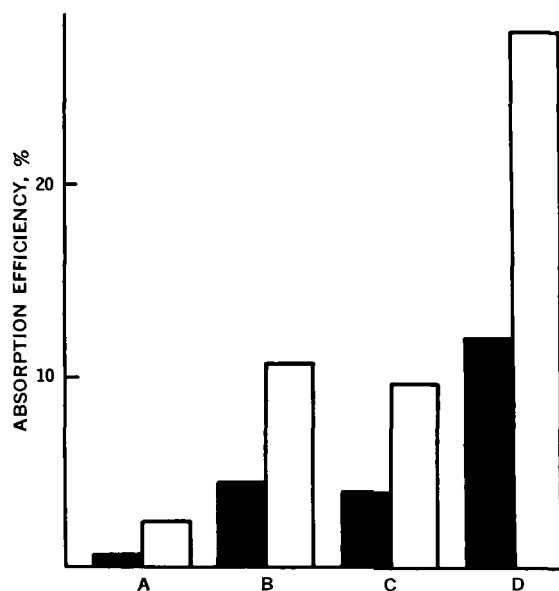


Figure 6—Absorption efficiencies of calcium phosphate dibasic dihydrate tablets containing 10% (w/w) disintegrant on exposure to 100% relative humidity at 37°. Dark bars represent 5 hr, and open bars represent 25 hr. Key: A, starch; B, sodium carboxymethylcellulose; C, sodium starch glycolate; and D, cation-exchange resin.

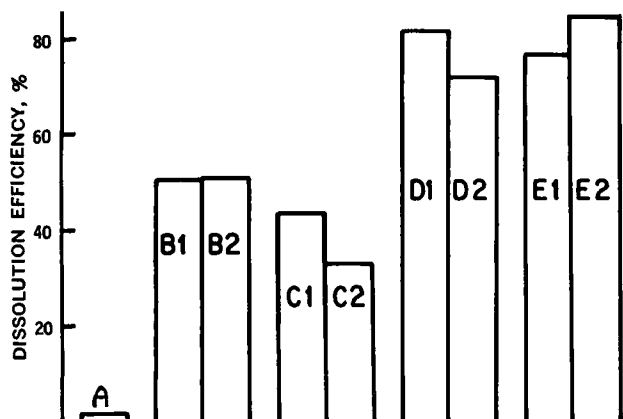


Figure 7—Dissolution efficiencies of tablets prepared from calcium phosphate dibasic dihydrate containing 1% (w/w) amaranth as tracer. Key: A, without disintegrant; B1, starch, 5%; B2, starch, 10%; C1, sodium carboxymethylcellulose, 5%; C2, sodium carboxymethylcellulose, 10%; D1, sodium starch glycolate, 5%; D2, sodium starch glycolate, 10%; E1, cation-exchange resin, 5%; and E2, cation-exchange resin, 10%.

glycolate emerges from the results presented in Figs. 8–10. On absorbing moisture, the sodium starch glycolate grains show considerable structural changes. Initially, the grains swell and become distorted, followed by the dissolution of disintegrant particles. The mechanism of action of sodium starch glycolate is probably similar to that of starch, as described by Lowenthal and Wood (4). Sodium starch glycolate possesses the additional advantages of being soluble and readily dispersible in water. Its spherical particles, dispersed in a tablet system, offer a larger surface, thus improving “wicking” (if this mechanism is operative) and allowing rapid penetration of water into the tablet interior (Fig. 4). The main reasons for the efficiency of this disintegrant probably are its high rate of water uptake (Fig. 1) and its marked swelling properties (Figs. 4 and 5); these factors cause pressure to be exerted within the tablet, thus breaking up interparticle bonding. This is then followed by the dissolution of sodium starch glycolate particles, which results in the crumbling and disintegration of the entire tablet structure.

Figures 11–13 show the surface structure of cation-exchange resin compacts before and after absorbing moisture (the absorbed moisture may be seen on the surface of compacts in Figs. 12 and 13). These photographs confirm previous findings that the resin possesses a very high rate of water uptake (Figs. 1–3). Kun and Kunin (5) described hydration of the cation-exchange resin as a two-step process: (a) the hydration of the gel phase or the microreticular phase, and (b) the filling of macropores with

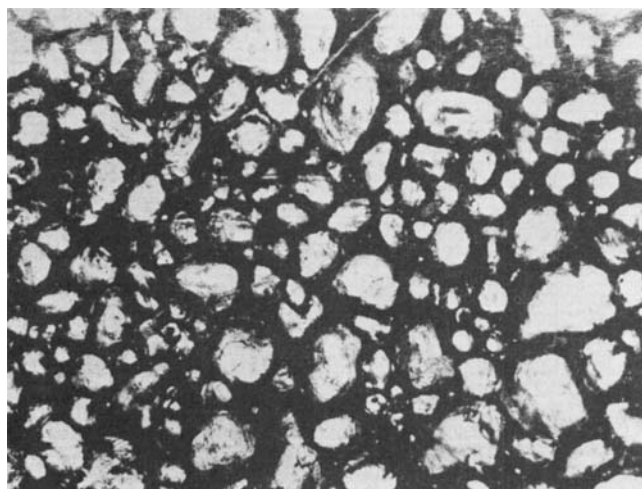


Figure 8—Photomicrograph of sodium starch glycolate compact before exposure to humidity.



Figure 9—Photomicrograph of sodium starch glycolate compact after 2 hr of exposure to 100% relative humidity at 37°.

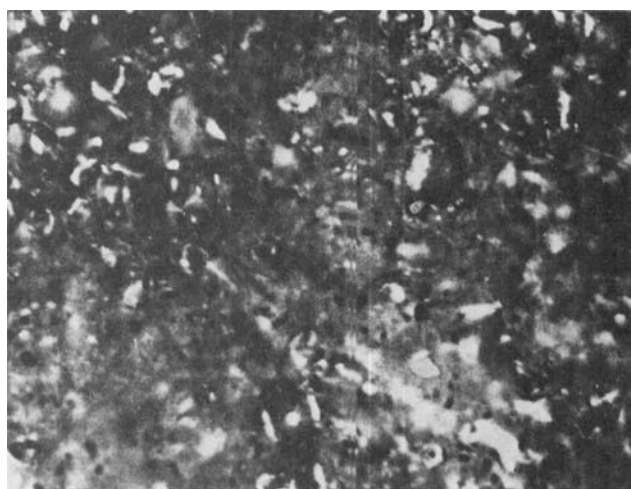


Figure 10—Photomicrograph of sodium starch glycolate compact after 4 hr of exposure to 100% relative humidity at 37°.

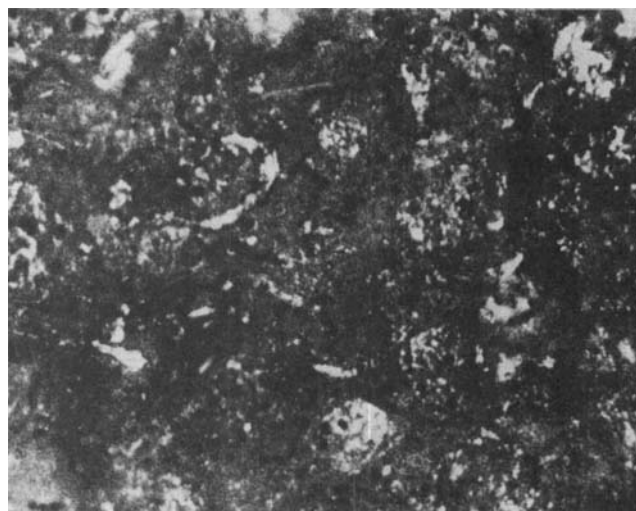


Figure 11—Photomicrograph of cation-exchange resin compact before exposure to humidity.

water, either by capillary condensation or hydraulically. From the results of the study of water sorption by the cation-exchange resin (Figs. 1, 2, and 11–13), it becomes clear that the disintegration of tablets containing the cation-exchange resin is probably caused by

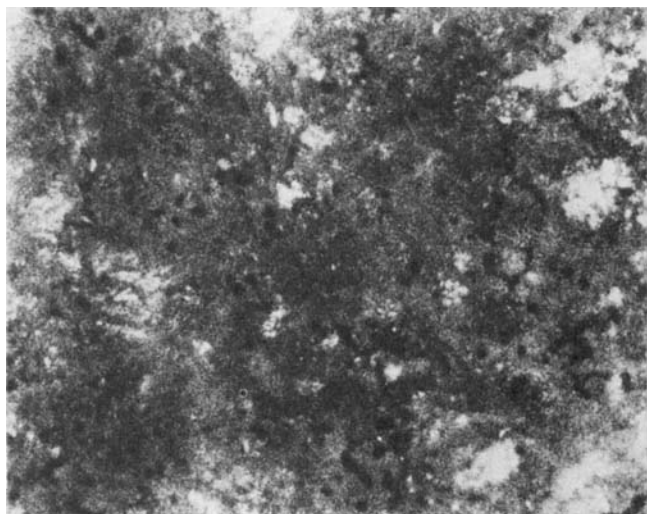


Figure 12—Photomicrograph of cation-exchange resin compact after 2 hr of exposure to 100% relative humidity at 37°.

the rapid penetration of water into the tablet interior and the crumbling of the tablet is brought about by the extensive swelling of resin particles. The nonadhesiveness of the cation-exchange resin in the hydrated state is also a useful property.

There is a similarity between starch and the cation-exchange resin in that both require a minimum effective concentration (1, 2). For starch it is said that a certain concentration is required to form an effective capillary system that will draw the water into the tablet interior (6, 7). Lowenthal and Wood (4), however, disagreed with this explanation and proposed that water hydrates the hydroxy group of starch molecules, causing them to move apart. The slight swelling that occurs is due to the rapid hydration step and a slower sorption of water step. These authors believed that the degree of breakup depends upon the number and size of starch grain agglomerates (total starch concentration in the tablet). The greater the number and size of agglomerate, the greater is the disruption. Similarly, a certain critical amount of cation-exchange resin would be necessary to produce sufficient swelling to rupture the tablet. Although sodium carboxymethylcellulose has a very high affinity for water, it is well known that its adhesiveness in the hydrated state is responsible for the poor disintegration properties (1, 2) of this material.

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Figure 13—Photomicrograph of cation-exchange resin compact after 4 hr of exposure to 100% relative humidity at 37°.

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ACKNOWLEDGMENTS AND ADDRESSES

Received June 13, 1974, from the *Department of Pharmaceutics, State University of New York at Buffalo, Buffalo, NY 14207*

Accepted for publication September 30, 1974.

Presented to the Industrial Pharmaceutical Technology Section, APhA Academy of Pharmaceutical Sciences, Chicago meeting, August 1974.

The authors thank Portsmouth Polytechnic and Beechams Pharmaceuticals for use of technical facilities.

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