Mechanism of Action of Starch as a Tablet Disintegrant II
Effect of Pepsin and Surfactants on Swelling of Starch Grains at 37°

By JAMES T. INGRAM and WERNER LOWENTHAL

The study of the effects of the individual components of simulated gastric fluid USP on starch grain swelling is completed. There is no statistically significant swelling demonstrated by pepsin in the submersion medium when compared to simulated gastric fluid and distilled water. Surfactants demonstrated no significant effect on starch grain swelling over that of distilled water. Apparent effectiveness of surfactants in improving tablet disintegration in some cases is postulated as being due to an increase in the rate of wetting. In the same experiment, the significant differences observed between corn and amioca starches and the moisture contents of these two starches are postulated as being due to the initial size differences of the grains being maintained during the experiment.

It does not seem probable that untreated or unmodified starch will swell sufficiently at 37° to cause tablet disintegration. If swelling is the primary mechanism whereby starch exerts its disintegrant effect, then this property must be imparted to the starch by the environmental conditions. The minimal effects of acid and salts in the submersion medium were demonstrated previously (1). Changes in pH had little effect on swelling; however, evidence was obtained to show that starch grains may swell more at a pH of 5.3 than in lower pH media. Salts did effect increased swelling, and the results indicated that salts of polyvalent cations produced more swelling than the salts of monovalent cations. Ionic concentration did not show an effect on swelling.

In order to complete the study of the effects of the individual components of simulated gastric fluid USP (SGF) on starch swelling, pepsin is included as a submersion medium in the present study.

Since surfactants have been shown to be effective in certain cases in improving tablet disintegration (2, 3), an experiment is included to determine their effect on starch swelling. Surfactants, when sprayed onto granulations containing starch, were shown by Cooper and Brecht (2) to be generally effective in improving tablet disintegration. A total of 21 surfactants, representing anionic, cationic, and nonionic classifications as well as a wide range of chemical and physical properties, were incorporated into calcium lactate tablets containing starch. Disintegration tests on these tablets revealed that the four surfactants that were most efficient in improving disintegration time were anionic in ionization, waxy solids, and structurally related to sulfosuccinic acid.

Aradi (3) also studied the influence of surfactants on disintegration and found a positive relationship between surfactants and improvement of disintegration time.

Gray and Schoch (4) studied the effect of various surfactants on the swelling behavior of several typical starches. Viscosity measurements on aqueous solutions of the starches heated above the pasting range were used as a measure of swelling. It was reasoned that if the surfactant complexes strongly with the linear fraction of the starch, it should restrict swelling. If no such complex is formed or if a waxy starch is used, the surfactant should act as a wetting agent and assist hydration of the starch molecules with subsequent swelling of the starch grains. Results of the study show that polar surfactants which complex strongly with the linear fraction restricted the swelling and solubilization of corn, potato, and even waxy sorghum starches. Cationic quaternary ammonium surfactants anomalously increased the hydration of corn and waxy sorghum starches, but drastically reduced the swelling and solubilization of potato starch.

EXPERIMENTAL

The study was planned to determine the effect of pepsin and surfactants on starch grain swelling. The swelling of starch grains was determined microscopically by measurement of the individual grain diameters using the procedure described previously (1). Two full factorial experimental designs were used and analyses of variance were calculated to determine the effects of pepsin and surfactants with various starches. Two types of starches at two moisture contents were used to determine if the type of starch and moisture content would have any effect on swelling in the submersion media used and to give more sensitive experimental design.

Commercial grades of corn and amioca (waxy corn) starches were chosen for the investigation. For the high moisture content, the commercially available starches[1] were used. For the low moisture content cornstarch, a commercial redried cornstarch[2] (P825) containing 1.5% maximum moisture was used. For the low moisture content amioca starch, the commercially available amioca starch was dried at 93° to a constant moisture content of 2.88% w/w.

RESULTS AND DISCUSSION

To investigate the effect of pepsin on swelling of starch grains, a 2 × 2 × 3 full factorial experimental design was used. A 0.32% w/w aqueous solution of pepsin, distilled water, and SGF were used as submersion media. It was previously shown that there is no significant difference between distilled

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[1] Melojel (MJ) and amioca starch marketed by National Starch and Chemical Corp.
[2] Marketed as Purity 825 by National Starch and Chemical Corp.

TABLE I—COMPARISON OF MEAN GRAIN SIZES OF STARCHES AFTER SUBMERSION FOR 5 min. IN PEPSIN SOLUTION, SGF, AND DISTILLED WATER

Moisture Content	Medium: Distilled Water	SGF	Pepsin
	Corn		
High (MJ)	6.129[a]	6.408	6.133
Low (P825)	5.919	5.805	6.665
	Amioca		
High	6.157	6.388	6.571
Low	5.672	6.320	6.197

[a] Mean grain sizes in scale divisions; one scale division = 1.8 μ.

TABLE II—EFFECT OF SURFACTANTS IN SUBMERSION MEDIUM ON MEAN GRAIN SIZES OF STARCHES

Moisture	Medium	Time, min.: 0[a]	5
	Corn		
High (MJ)	Distilled water	6.133[b]	6.129
	P80	6.133	4.846
	BzC	6.133	5.867
	NaLS	6.133	6.181
Low (P825)	Distilled water	5.676	5.919
	P80	5.676	5.664
	BzC	5.676	5.422
	NaLS	5.676	5.052
	Amioca		
High	Distilled water	5.482	6.157
	P80	5.482	5.740
	BzC	5.482	5.728
	NaLS	5.482	5.319
Low	Distilled water	5.063	5.672
	P80	5.063	4.949
	BzC	5.063	4.897
	NaLS	5.063	5.796

[a] Unsubmerged. [b] Mean grain sizes in scale divisions; one scale division = 1.8 μ.

water and SGF as submersion media, and that the significance of the time effect was due to the difference in grain diameters between unsubmerged starch (0 time) and submerged starch (1). For these reasons, the time effect was not investigated. Distilled water and SGF were included as a basis of comparison.

The starches were slurried in the submersion media at 37° and the mean grain diameters were determined after submersion for 5 min. Table I shows the mean grain sizes and the variables investigated. In the analysis of variance, interactions were not significant and were combined with the error term. There was no significant difference demonstrated among any of the variables investigated.

The effectiveness of surfactants in improving tablet disintegration may be due to the fact that surfactants increase the rate of starch grain wetting. Nogami, Nagai, and Uchida (5) state that immersional wetting might be a controlling factor in disintegration of tablets made under low compressional force. In order to investigate the possibility that surfactants improve tablet disintegration by increasing the swelling capability of the starch grains, a 4 × 2 × 2 × 2 factorial experimental design was used.

Table II shows the variables studied and the mean grain sizes. Polysorbate 80 (P80), benzalkonium chloride (BzC), and sodium lauryl sulfate (NaLS) were selected as the surfactants because they represent each of the ionic classifications—nonionic, cationic, and anionic, respectively. Aqueous solutions containing 1% surfactant were used as submersion media and distilled water was included as a control. Due to the high mobility of the starch grains in the surfactant solutions, measurement of the grain diameters was almost impossible when the slides were prepared directly from the surfactant slurry. To overcome this difficulty, the sample removed from each slurry was mixed with glycerin, which does not affect the swelling of starch grains (6). This increased the viscosity sufficiently to fix the grains and allow measurement of the diameters. In the analysis of variance, the three-factor interactions were not significant and were combined with the error term. The type of starch × time interaction was significant. Type of starch and moisture content were significant at the 0.5% level. These differences are probably due to maintenance of the initial grains size difference for the duration of the experiment. Significant differences among the surfactants and distilled water were not demonstrated.

SUMMARY AND CONCLUSIONS

Previous work on the effect of environmental conditions on starch grain swelling is reviewed and determination of the effects of the individual components of simulated gastric fluid USP was completed. There was no statistically significant swelling demonstrated by pepsin in the submersion medium when compared to simulated gastric fluid and distilled water.

Surfactants did not significantly affect starch swelling when compared to distilled water. Surfactant effectiveness in occasionally improving tablet disintegration is apparently not due to any effect on starch grain swelling, but is more likely due to an increase in the wetting rate of the tablet resulting from the decrease in surface tension.

The study of the effects of tableting procedure on starch grain swelling and tablet disintegration is being completed.

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Keyphrases

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