The Effect of Swelling Characteristics of Superdisintegrants on the Aqueous Coating Solution Penetration into the Tablet Matrix During the Film Coating Process

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The mechanism and the extent of sorption of water molecules by tablets containing superdisintegrants and microcrystalline cellulose, following the aqueous film coating of formulated tablets, were investigated. The penetration of water from the coating solution into the tablet matrix resulted in significant changes in physical properties of the coated tablet cores, such as residual moisture content, tensile strength, and pore-size distribution. The swelling and the morphological characteristics of each individual disintegrant compound and microcrystalline cellulose were found to have important implications on the extent of penetration of water from the aqueous film coating solution. A hypothesis concerning the interaction between microcrystalline cellulose and the superdisintegrant particles present in the tablet matrix is proposed.

KEY WORDS: aqueous film coating; coating solution penetration; superdisintegrants; microcrystalline cellulose; swelling.

INTRODUCTION

The use of aqueous-based coating systems has alleviated problems associated with environmental pollution and recovery of organic solvents while, at the same time, causing concern about the stability of sensitive tablet cores being exposed to an aqueous environment and elevated temperatures (1,2). Although new approaches, such as the use of coating equipment with increased drying efficiency and optimized processes (3–5), have tended to minimize such concerns, the question of moisture penetration from the applied polymer solution into the tablet core has remained speculative and undetermined.

Based on the results of a previous study (6), it was established that following the aqueous film coating of formulated tablets containing superdisintegrants (Ac-Di-sol, Primojel, and Polyplasdone-XL, at 5, 10, and 20%, w/w) penetration of the polymer coating solution into the tablet core had occurred and was not restricted to the tablet surface. The findings indicated that the extent of moisture sorption by tablet cores, coated under normal operating conditions, was sufficient to result in significant changes in tablet physical characteristics such as residual moisture content, the glass transition temperature of the tablet matrix, tensile strength, and the tablet pore–volume distribution.

The main purpose of the present study was to gain further understanding into the mode of penetration of the coating solution into the tablet substrates containing superdisintegrants during the aqueous film coating process. The significance of the swelling characteristics of each individual disintegrant compound and its interaction with microcrystalline cellulose present in the tablet matrix was investigated.

MATERIALS AND METHODS

The formulated tablets consisted of the following components: dibasic calcium phosphate, dihydrate, USP (Di-Tab) from Rhone-Poulenc (Westport, Connecticut); microcrystalline cellulose, NF (Avicel PH 101), and croscarmellose sodium, type A, NF (Ac-Di-Sol), from FMC Corporation (Philadelphia, Pennsylvania); sodium starch glycolate, NF (Primojel), from Generichem Corporation (Little Falls, New Jersey); crospovidone, NF (Polyplasdone-XL), from ISP Chemicals Corporation (Wayne, New Jersey); and magnesium stearate and cobalt chloride hexahydrate from Mallinckrodt Inc. (Paris, Kentucky). The aqueous film coating solution consisted of hydroxypropyl methylcellulose 2910, USP (Methocel E-5) from Dow Chemical Company (Midland, Michigan); polyethylene glycol 3350 NF from Ruger Chemical Company (Irvington, New Jersey); and polyethylene glycol 8000 from Union Carbide Corporation (Danbury, Connecticut). All excipients were used as received from the suppliers, with the exception of Avicel PH 101 and cobalt chloride hexahydrate, which were pre-dried for 21 hr at 80°C.

The material properties of each excipient were evaluated as follows. (a) The percentage loss on drying based on the initial sample weight was obtained as follows:

$$\% \text{ loss on drying} = \frac{\text{loss in weight}}{\text{initial sample weight}} \times 100 \quad (1)$$

(b) The bulk powder percent porosity was determined from

$$\% \text{ void space} = 1 - \frac{\rho_b}{\rho_T} \times 100 \quad (2)$$

where ρ_b is the packed bulk density (g/mL) and ρ_T is the powder density (g/mL) determined by measuring the weight of a displaced liquid (ethyl acetate AR) by a powder sample contained within a pycnometer. (c) The specific surface area (m^2/g) was determined from the single point nitrogen adsorption-desorption isotherm, using a Micromeritics Flow Sorb II 2300 surface-area instrument (Norcross, Georgia). (d) The hydration capacity of a 4% aqueous dispersion each superdisintegrant was determined from

$$\text{hydration capacity} = \frac{\text{final hydrated volume} - \text{dry sample volume}}{\text{dry sample volume}} \times 100 \quad (3)$$

Tablet Formulation and Preparation

Table I shows the percentage of excipients used in the

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Table I. Tablet Formulation Composition

Tablet ingredient	Formulation code (%, w/w)										
	A_I[a]	A_{II}	A_{III}	P_I[b]	P_{II}	P_{III}	CP_I[c]	CP_{II}	CP_{III}	AC	C
Ac-Di-Sol	5	10	20								
Primojel				5	10	20					
Polyplasdone-XL							5	10	20		
Cobalt chloride	1	1	1	1	1	1	1	1	1	1	1
Magnesium stearate	1	1	1	1	1	1	1	1	1	1	1
Without Avicel											
Di-Tab	93	88	78	93	88	78	93	88	78	—	98
With Avicel											
Avicel PH 101	20	20	20	20	20	20	20	20	20	20	—
Di-Tab	73	68	58	73	68	58	73	68	53	78	—

[a] A_I, A_{II}, and A_{III}—Ac-Di-Sol at 5, 10, and 20% (w/w), respectively.
[b] P_I, P_{II}, and P_{III}—Primojel at 5, 10, and 20% (w/w), respectively.
[c] CP_I, CP_{II}, and CP_{III}—Polyplasdone-XL at 5, 10, and 20% (w/w), respectively.

manufacture of the various tablet formulations, each denoted by an appropriate code name. Tablets were prepared by using a standardized blending procedure as previously described (6). Five hundred-milligram samples of the mixed powder ingredients were weighed and directly placed in a 12.7-mm flat-faced punch and die set and compressed at a compression load of 6000 lb (211 MPa) at a constant rate of loading using a standard hydraulic laboratory press (Carver press, Menomonee Falls, Wisconsin).

Coating Solution Composition

The polymer coating solution consisted of the following ingredients: (a) Methocel E-5 (6%, w/w), (b) polyethylene glycol 3350 (1%, w/w), (c) polyethylene glycol 8000 (1%, w/w), and (d) distilled water (q.s. 100%, w/w).

Coating Procedure

The coating process was performed using a 24-in. Accela-Cota (Thomas Engineering, Hoffman Estates, Illinois). The formulated tablets, both with and without Avicel PH 101 (i.e., A_I through CP_{III}, AC, and C, given in Table I), were mixed with 2.0 kg of standard convex, red-colored, lactose tablets precoated with hydroxypropyl methyl cellulose. The tablet mixtures were placed in the coating pan and coating was performed under the conditions stated in Table II. An ultrasonic spray nozzle system was used in this study. The Sonicore spray nozzle system, Model 052H (Parsippany, New Jersey), was used to deliver the coating solution onto the table bed.

Evaluation of Physical and Chemical Properties of Formulated Tablets Before and After the Aqueous Film Coating Operation

Prior to all testing procedures and evaluations, the polymer film layer was carefully peeled from the edges and surfaces of each coated tablet, with the aid of a sharp razor blade.

Measurement of Tablet Weight and Physical Dimension

Marked formulated tablets were individually measured for their weight and dimensions (i.e., thickness and diameter using a standard micrometer). The change in tablet volume due to exposure to the aqueous film coating environment was expressed as the percentage increase in tablet core thickness. This was calculated from the difference in mean thickness values (average of 20 readings) of uncoated and coated tablet cores (film layer removed) and is expressed as a percentage of uncoated tablet thickness.

Measurement of the Rate of Liquid Penetration into Tablets

Water uptake rate profiles were generated for the uncoated and coated tablet formulations with Avicel PH 101 (Table I), using a laboratory apparatus similar to that described by several investigators to measure the rate of penetration of liquid into tablets (7–11). The apparatus consisted of a buchner funnel (15 mL) fitted with a sintered glass filter, connected to a 1-mL pipette (0.01-mL divisions) via a piece of tygon tubing (70 cm × ⅜- in. O.D., ¼-in. I.D.), both of which were clamped vertically in place. The apparatus was filled with a continuous column of distilled water and adjusted to zero reading on the pipette prior to determination. The tablet was placed inside a glass holder (4 cm × 1.5-cm O.D.; 1.3-cm I.D.) so that its lower surface was flush

Table II. Process Parameters and Levels for the 24-in. Accela-Cota

Tablet load	2.1 kg
Inlet air temperature	60°C
Exhaust air temperature	50°C
Exhaust air flow rate	423 ft^3/min
Pan rotational speed	10 rpm
Air pressure to the spray nozzle	35 psig
Solution spray rate[a]	73 g/min
Tablet bed warming	15 min (jugging)
Total coating time	53 min
Tablet weight gain	7.41% (w/w)

[a] Intermittent spraying with 0.67 min of spraying/min.

with the bottom of the glass tube and was placed on top of the sintered glass disk. Liquid was drawn into the tablet through the moist glass filter and liquid uptake was recorded as the change in the level of liquid in the pipette. The glass tube holder improved the reproducibility of the measurements by providing a better contact area between the tablet surface and the sintered glass disk. It also prevented the tablet from falling apart.

Five replicate measurements were carried out for each formulated tablet. In each measurement, the timing was started as soon as the tablet surface touched the moist glass filter and the volumetric liquid uptake was recorded as a function of time until saturation was reached. The water uptake rate profiles were generated by plotting the volume of liquid penetrated into the tablet matrix versus time.

Scanning Electron Microscopy

Fracture surface morphology and microstructure of uncoated and aqueous film-coated tablets A_{II}, P_{II}, and CP_{II} (containing Avicel PH 101) were examined using a Jeol, Model JSM-6300 scanning electron microscope (Tokyo, Japan) and scanning electron photomicrographs were taken.

Mercury Intrusion Porosimetry

A microprocessor-controlled Micromeritics Autopore II, Model 9220 (Norcross, Georgia), mercury intrusion instrument was used to measure tablet pore–volume and pore volume–size distribution.

RESULTS AND DISCUSSION

Evaluation of Excipient Material Properties

Superdisintegrants were classified as very hygroscopic according to Callahan *et al.* (12). That is, the moisture content of such powders may increase at relative humidities as low as 40 to 50% and the increase in moisture content after storage for one week above 90% relative humidity may exceed 30%.

Table III summarizes the results of the physical properties of the excipients used in this study. Ac-Di-Sol possessed the highest initial moisture content, at 10% (w/w), and Polyplasdone-XL powder contained the least amount of sorbed water, at 4.97% (w/w).

The low tap density, high bed porosity, and large specific surface area of Polyplasdone-XL were indicative of the presence of a loosely packed and porous powder, providing for an internal hydrophilic capillary network. The lower initial moisture content of Polyplasdone-XL of 4.97%, compared to 10% (w/w) for Ac-Di-Sol, was postulated to be due to its amphiphilic character (i.e., fewer polar groups to which water is attached) and the capillary condensation of moisture into micropores. This moisture may be inaccessible to removal by normal drying conditions.

The results of the measurements of the hydration capacities of superdisintegrants showed that Primojel powder had the largest hydrated settled volume compared to both Ac-Di-Sol and Polyplasdone-XL powders. All three materials exhibited swelling in distilled water but the extent and the nature of the swollen materials varied greatly. Polyplasdone-XL, due to its very high molecular weight and highly cross-linked nature, showed a relatively low degree of swelling (an opaque sediment of 26 mL) and exhibited no tendency toward gel formation because of its insolubility in water. Primojel and Ac-Di-Sol formed translucent layers of much greater height (100 and 44 mL, respectively), which was highly gelatinous in the case of Primojel. The dissolution and gelation of the amylose component of Primojel particles and the accumulation of grains swelled in water accounted for the formation of a jelly (15). Ac-Di-Sol particles, which are cylindrical in shape, increase in radius but show little change in length when exposed to water (15). This asymmetry in swelling, together with a greater degree of cross-linkage and entanglement of fibrous strands, may have accounted for the lower hydration capacity of Ac-Di-Sol as compared to Primojel.

Tablet Morphology and Measurement of Physical Dimension

Tablets showed expansion in their thickness following the coating operation. Figure 1 shows the results of the percentage increase in core thickness for formulated tablets with Avicel PH 101 (see Table II). Tablets containing superdisintegrants showed significantly greater increases in thickness compared with the two control tablet formulations composed of Di-Tab alone and a combination of Di-Tab and Avicel PH 101. At the 5% (w/w) disintegrant concentration level, the percentage increase in core thickness was relatively small for all tablet formulation types and ranged from 2.03% for P_I to 2.97 and 3.45% for CP_I and A_I, respectively.

Table III. Derived Bulk Powder Physical Properties

	Material characteristics					
Excipient	Loss on drying (%, w/w)	True density (g/mL)	Tap density (g/mL)	Void volume (%)	Surface area (m^2/g)	Hydration capacity (%)
Ac-Di-Sol	10	1.565	0.721	53.91	0.45	646
Primogel	5.56	1.499	0.943	37.08	0.22	1983
Polyplasdone-XL	4.97	1.155	0.459	60.27	1.35	100
Avicel PH 101	4.95	1.618	0.455	71.91	0.21[a]	
Di-Tab	8.0	2.257	0.909	59.73	2.7	
Magnesium stearate	4.0	1.08[b]	0.202	81.30	—	

[a] Data from Nakai *et al.* (13).
[b] Data from *Handbook of Pharmaceutical Excipients* (14).

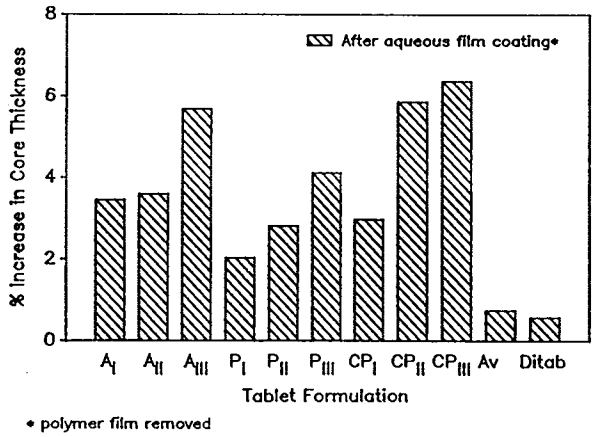

Fig. 1. Percentage increase in tablet core thickness for tablet formulations containing Avicel, pH 101, after the aqueous film coating process.

At the 10% (w/w) level, the percentage increase in tablet core thickness was significantly greater for CP_{II}, at 5.85%, compared to the values for both A_{II} and P_{II}. At the 20% (w/w) concentration level, the value for percentage increase in core thickness for CP_{III} was significantly greater than that for P_{III} but only marginally higher than the corresponding value for tablet A_{III}.

From these results it was concluded that the increase in tablet thickness, and hence volume, was caused by the hydration and swelling of the disintegrant particles within the tablet matrix as a result of contact with water in the aqueous film coating solution. A number of possible mechanisms may account for the observed differences in tablet thickness data. These include (a) the mode and the extent of penetration of the coating solution into the tablet substrate, (b) the swelling characteristics and the particle morphology of disintegrants within the tablet matrix, and (c) the wicking action attributed to microcrystalline cellulose alone and its interaction with the disintegrant particles present in the tablets.

Scanning electron microscopy (SEM) photomicrographs of the compressed and fracture surfaces of the coated tablets revealed a disrupted and cracked appearance. Figure 2 shows the fibrous nature of Ac-Di-Sol, which had protruded outward from the flat plane of the tablet edge and surface. The close proximity of adjacent fibrous strands of Ac-Di-Sol and that of microcrystalline cellulose may have promoted the potential for interparticulate bonding and network formation through the formation of interhydroxyl hydrogen bonds in and between these modified cellulose structures. The elastic relaxation of modified cellulose fibers may have been responsible for the disrupted and flaky appearance of Ac-Di-Sol containing coated tablet cores.

Figure 3 shows the spherical shape of Primojel particles. These modified starch grains appeared as a continuum of many discrete particles within the tablet matrix. Due to its spherical shape, upon exposure to moisture, these particles expanded equiaxially and the resulting changes in coated tablet dimension were accompanied by an increase in tablet diameter as well as thickness. This may account for the fact that Primojel-containing tablets exhibited the lowest overall percentage increase in core thickness following the coating operation.

Tablets containing Polyplasdone-XL showed the highest overall increase in tablet core thickness following the coating operation, which presumably resulted from the formation of a hydrophilic capillary network within the tablet matrix, enabling water from the coating solution to be drawn into the tablet by capillary suction (see Fig. 4).

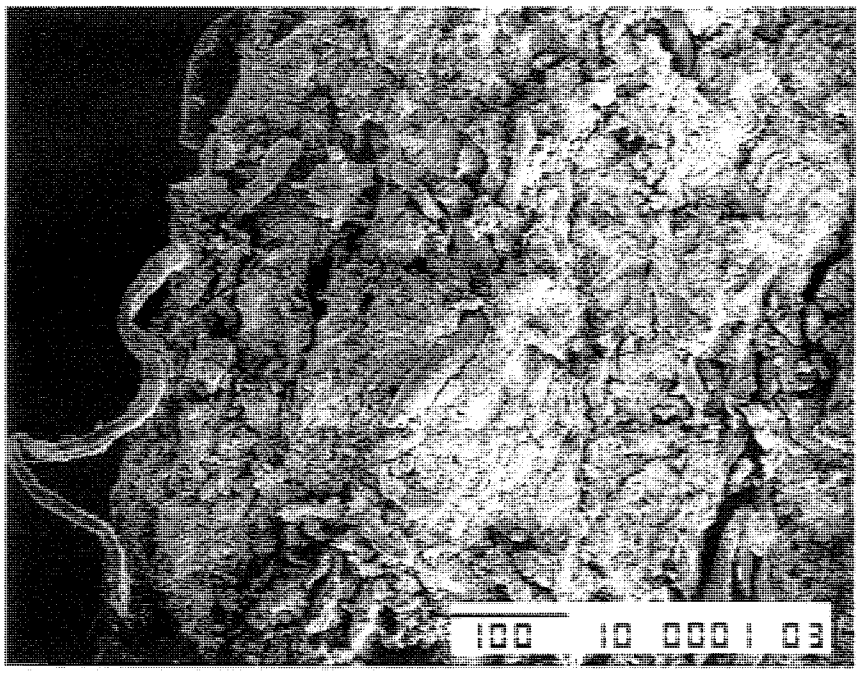

Fig. 2. SEM photomicrograph of the coated tablet fracture surfaces A_{II}, containing 10% (w/w) Ac-Di-Sol and 20% (w/w) Avicel, pH 101. ×150.

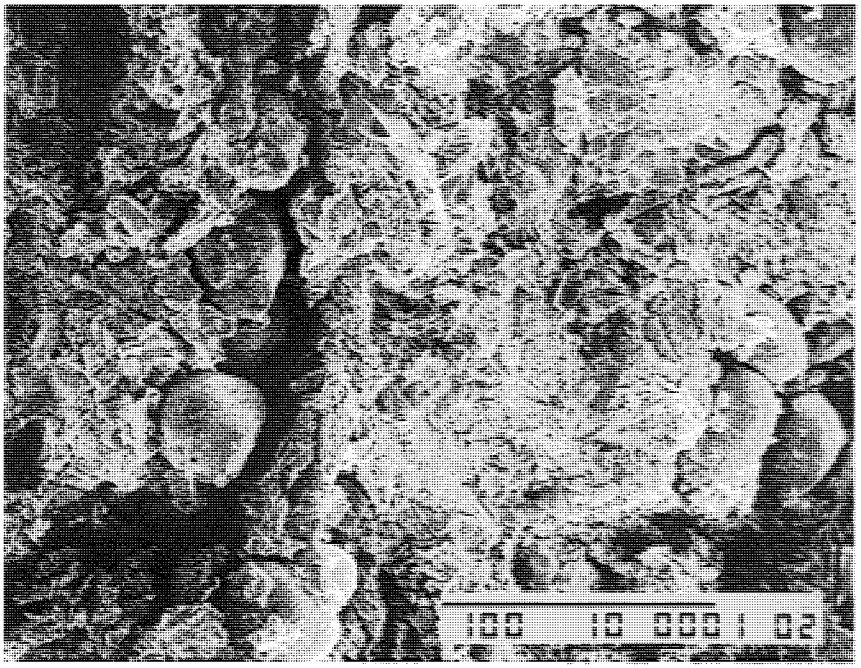

Fig. 3. SEM photomicrograph of the coated tablet fracture surfaces P_{II}, containing 10% (w/w) Primojel and 20% (w/w) Avicel, pH 101. ×350.

The results of percentage increases in core thickness for tablet formulations which contained the same percentages of the superdisintegrants, without microcrystalline cellulose, indicated changes that were only due to the action of superdisintegrants. A similar pattern but a lesser increase in tablet core dimensional changes was observed. Tablets containing Polyplasdone-XL showed the greatest percentage increase in core thickness following the aqueous film coating operation. This occurred at all disintegrant concentration levels (5, 10, and 20%, w/w).

Tablet thickness data were plotted to illustrate the percentage difference in core thickness between each coated tablet formulation pair (i.e., one that contained 0% Avicel PH 101 and one that contained 20%, w/w, of the Avicel). These values represented the contribution of microcrystalline cellulose to the extent of tablet swelling. From Fig. 5 it

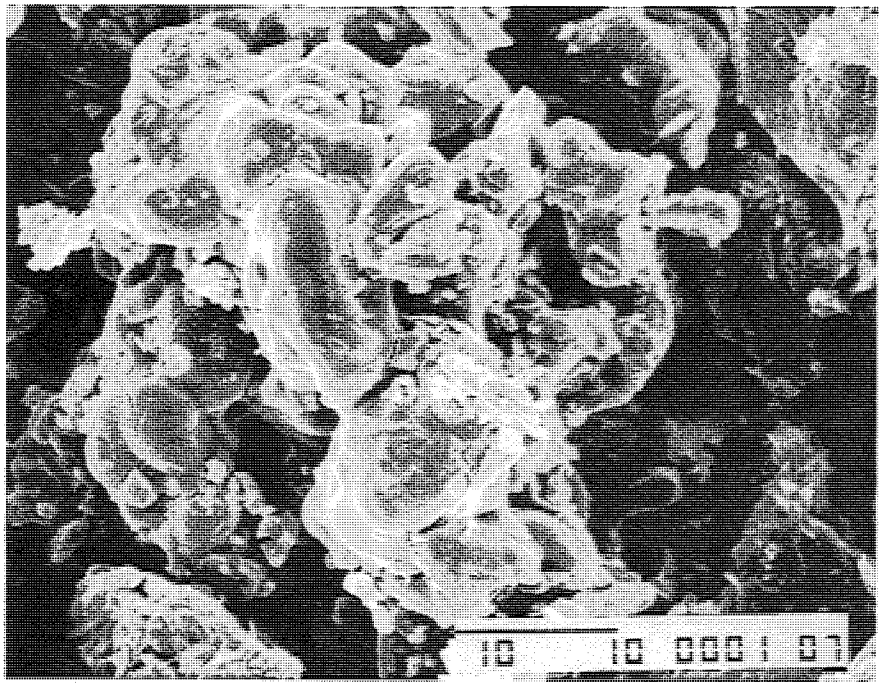

Fig. 4. SEM photomicrograph of the coated tablet fracture surfaces CP_{II}, containing 10% (w/w) Polyplasdone-XL and 20% (w/w) Avicel, pH 101. ×2000.

was observed that the percentage increase in coated tablet core thickness attributed to the inclusion of microcrystalline cellulose in the tablet matrix was dependent on the type and the concentration of disintegrant present in the tablet. The greatest percentage increase in coated tablet core thickness was observed when microcrystalline cellulose was combined with Polyplasdone-Xl. This occurred at all disintegrant concentration levels. On the other hand, the smallest increases were obtained for the combination of microcrystalline cellulose and Ac-Di-Sol (at 10 and 20%, w/w) and intermediate values were obtained for its combination with Primojel particles. These results indicated that microcrystalline cellulose acted synergistically to the greatest degree with Polyplasdone-XL and to a lesser extent with Ac-Di-Sol particles, resulting in enhanced tablet swelling and expansion after exposure to an aqueous film coating process.

Determination of Volumetric Water Uptake Rate Profiles

In general, it was observed that an increase in disintegrant concentration from 5 to 20% (w/w) resulted in an increase in the total volume of water taken up by the tablets, as well as faster rates of water uptake. The concentration dependent effect of the disintegrant within the tablet matrix was particularly obvious for Primojel as shown in Fig. 6. Primojel containing coated tablet cores exhibited the fastest rate of water uptake and the highest final saturation volume as compared with coated tablets containing 10 and 20% (w/w) of either Ac-Di-Sol or Polyplasdone-XL. The high swelling and water absorptive capacity of Primojel tablets were in accordance with the behavior of the loose disintegrant powder (shown in Table III). Coated tablet cores containing Polyplasdone-XL exhibited the slowest rate of water uptake and the lowest saturation volume at the 10% (w/w) level but showed profiles similar to those of Ac-Di-Sol tablets at 5 and 20% (w/w) levels.

Figures 7 and 8 show the water penetration rate profiles for uncoated and coated tablet formulations containing 10 and 20% (w/w) of each disintegrant compound, respectively. Both the rate and the extent of water uptake were reduced for coated as compared to uncoated tablets containing each

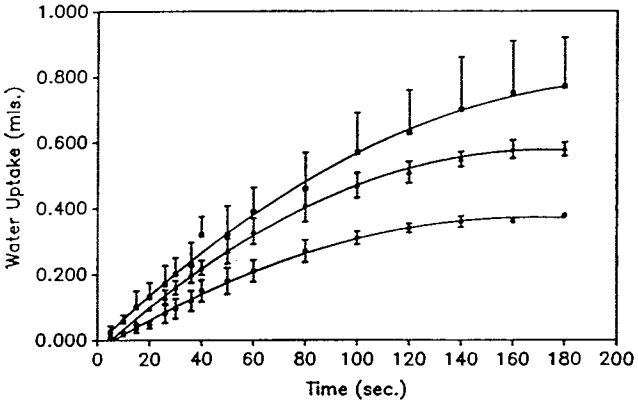

Fig. 6. Volumetric water uptake profiles for aqueous film-coated tablet cores containing Primojel at 5, 10, and 20% (w/w) concentration levels. (●) P_I, Primojel, 5% (w/w); (▲) P_{II}, Primojel, 105% (w/w); (■) P_{III}, Primojel, 20% (w/w).

of the disintegrant compounds at 10% (w/w). At the 20% (w/w) level this difference was seen only for Ac-Di-Sol containing coated tablet cores. The reduced water absorptive capacity of coated tablet formulations, as compared to uncoated tablets, was attributed to the penetration of water from the applied polymer solution into tablets during the coating process, so that as the disintegrant particles sorbed moisture, their capacity for water uptake was reduced over time. At the 20% (w/w) disintegrant concentration, the capacity to take up water was still very high. This minimized the effect due to the hydration of disintegrant particles already hydrated during the coating process. The reduced water uptake capacity of coated Ac-Di-Sol tablets at the 20% (w/w) level was postulated to be due to the elastic relaxation of the modified cellulose fibers as a result of exposure to water and an increase in tablet void volume, thus leading to a low final saturation volume.

Evaluation of Tablet Pore System Characteristics

The mean pore diameters of all coated tablets were previously shown to be significantly greater than the values for

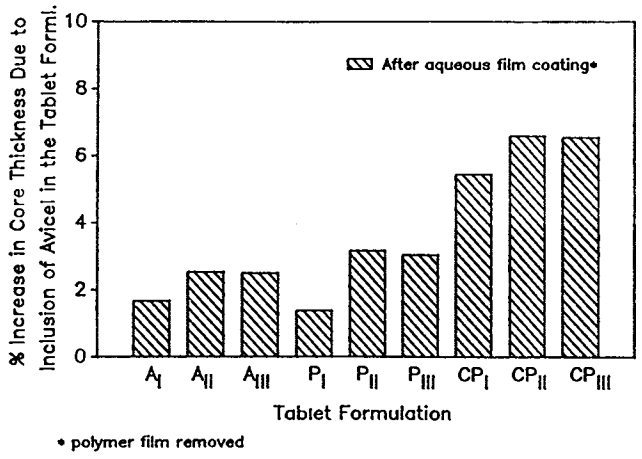

Fig. 5. Percentage difference in core thickness between each coated tablet formulation type containing zero or 20% (w/w) Avicel, pH 101.

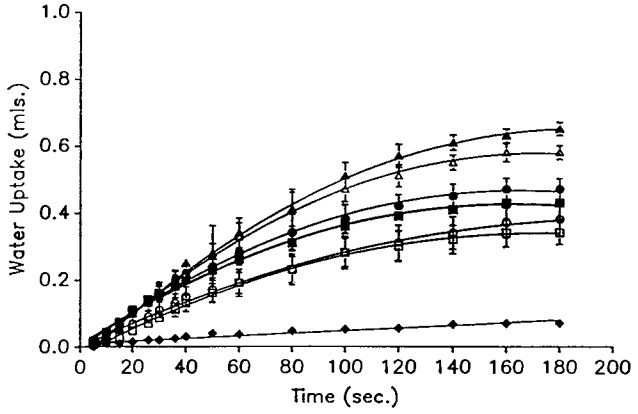

Fig. 7. Volumetric water uptake rate profiles for tablet cores containing each superdisintegrant at a 10% (w/w) concentration level before and after the aqueous film coating process (●, ○) Ac-Di-Sol; (▲, △) Primojel; (■, □) Polyplasdone-XL; (♦) control. Filled symbols, uncoated tablets; open symbols, aqueous film coated.

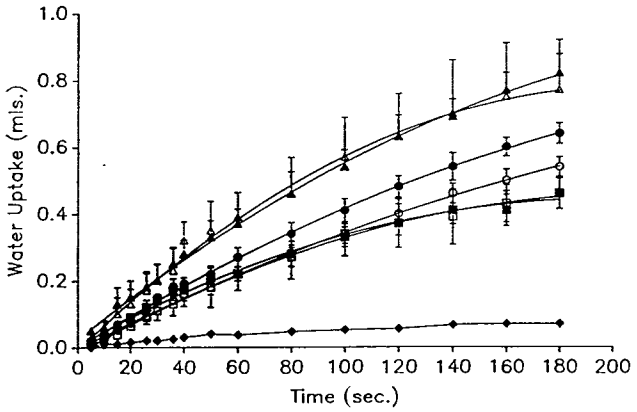

Fig. 8. Volumetric water uptake rate profiles for tablet cores containing each superdisintegrant at a 20% (w/w) concentration level before and after the aqueous film coating process (●, ○) Ac-Di-Sol; (▲, △) Primojel; (■, □) Polyplasdone-XL; (♦) control. Filled symbols, uncoated tablets; open symbols, aqueous film coated.

the corresponding uncoated tablets (6). The examination of uncoated tablet mean pore diameters indicated that there was little or no difference between the mean pore diameter of tablet formulations containing 5 and 10% (w/w) of each disintegrant compound, but at the 20% (w/w) level, Polyplasdone-XL possessed the largest value for the mean pore diameter. Figure 9 shows the same comparison for coated tablet formulations. The mean pore diameter for both CP_{II} and CP_{III} tablets (with Avicel PH 101, given in Table I) was significantly larger than that for Ac-Di-Sol and Primojel-containing coated tablets. In addition, the percentage porosity for coated and uncoated Polyplasdone-Xl tablets showed that following the coating operation, the total tablet void volume was increased (6). These results indicated that the penetration of water from the applied coating solution into the tablet had resulted in swelling and expansion of disintegrant particles, which then enlarged the tablet internal pore structure.

Hypothesis of Superdisintegrant Interaction with Microcrystalline Cellulose

A hypothesis concerning the interaction between microcrystalline cellulose and the superdisintegrants present in the tablet matrices was proposed and was based on the data obtained from the measurements of uncoated and coated tablet dimensional changes, water uptake rate profiles, hydration capacities of the bulk disintegrant powders, and scanning microscopical examination of the tablets.

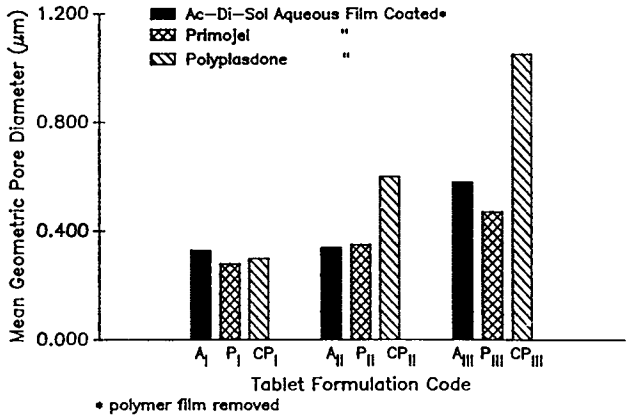

Fig. 9. Mean geometric pore diameter for aqueous film-coated tablet cores containing Avicel, pH 101, and each superdisintegrant at 5, 10, and 20% (w/w), determined by mercury intrusion.

Ac-Di-Sol is an internally cross-linked form of sodium carboxymethyl cellulose (16). The presence of hydroxyl groups on the cellulose backbone of Ac-Di-Sol and microcrystalline cellulose strands may have provided ample sites for both intraparticle and interparticle hydrogen bonding. The potential for network formation between Ac-Di-Sol and microcrystalline cellulose polymer strands was enhanced due to their fibrous nature and through interaction by hydrogen bonding, ion–dipole, and dipole–dipole interactions. This accounted for the binding between these particles. In the aqueous film coating process, upon penetration of water molecules into the tablet matrix, the interhydroxyl hydrogen bonds were broken and were replaced by hydroxyl–water hydrogen bonds. The association and hydrogen bonding both within and between neighboring fibrous strands of Ac-Di-Sol and microcrystalline cellulose, however, meant that some of the hydroxyl groups of the modified cellulose strands of Ac-Di-Sol molecules that otherwise would be free and available for hydration and hydrogen bond formation with penetrating water molecules were tied up by hydrogen bonding with microcrystalline cellulose molecules. In the presence of limited amounts of moisture (both in the liquid and vapor state), such as in an aqueous film coating environment, the decreased availability of some of the hydroxyl groups may have significant implications. In such a circumstance a competition between Ac-Di-Sol and microcrystalline cellulose polymer chains for hydration and hydrogen bonding with water molecules may have resulted in effectively reducing both the access and the availability of free hydrogen bonding sites required for the hydration of Ac-Di-Sol particles.

Furthermore, polymers including cellulosic materials possess glassy as well as amorphous regions. Water sorption usually takes place in the amorphous regions of the polymer, where there is greater chain mobility (17,18). Glassy or crystalline regions of polymers are those regions in which hydrogen bonding occurs with regularity and order. Amorphous regions are those regions in which hydrogen bonding is not regular. If it is the case that interaction through hydrogen bonding between neighboring Ac-Di-Sol and microcrystalline cellulose fibers increases the order or alignment of such polymer strands, this may also effectively reduce amorphous or rubbery regions and act to reduce water sorption into the tablet core. The glass transition temperatures (T_g) of pure disintegrant powders and powder samples from crushed tablet were previously determined (Pourkavoos and Peck, Ref. 6). T_g was equal to 275%C for Ac-Di-Sol powder and 305°C for uncoated tablet A_{II} (containing 10%, w/w, Ac-Di-Sol and 20%, w/w, microcrystalline cellulose). It, therefore, appears that the combined polymer chain mobilities of the amorphous polymer components of the tablet matrix A_{II} were less than the polymer chain mobility of pure Ac-Di-Sol powder.

Since Ac-Di-Sol has a far greater swelling capacity than microcrystalline cellulose, the interaction between these two

components may have resulted in diminution of the full extent of synergism between microcrystalline cellulose and Ac-Di-Sol fibrous strands. This in turn may have resulted in smaller increases in tablet core thickness following the aqueous film coating operation. Figure 5 showed that, indeed, microcrystalline cellulose acted synergistically to the least extent with tablet formulations containing Ac-Di-Sol to increase tablet swelling following the coating operation.

Primojel is a low substituted derivative of potato starch obtained by cross-linking and carboxymethylation (approximately 25 carboxymethyl groups per 100 glucose units) (19). Primojel and microcrystalline cellulose particles may have participated in hydrogen bond formation due to the presence of hydroxyl groups in the amylose (straight chain) and amylopectin (branched chain) components of the modified starch grains and the microcrystalline cellulose fibers. However, due to the differing particle morphologies, there was less chance of close association, alignment, or network formation between the neighboring microcrystalline cellulose and Primojel particles. This may have accounted for the slightly greater synergistic effect that was observed for the combination of microcrystalline cellulose and Primojel as compared to Ac-Di-Sol.

An increase in viscosity due to the swollen Primojel grains was evident upon hydration of the pure disintegrant powder, which formed a translucent and gelatinous mass. In addition, the effect of applied compression force has been reported to split open some sodium carboxymethyl starch grains and cause the release of their soluble contents (15). The latter was attributed to the amylopectin fraction, which is the soluble component inside each modified starch grain and makes up 70–80% of its content. Because of the spherical nature of Primojel particles, the swollen grains were reported to increase in diameter as well as thickness (15,20). In this study, the dimensional changes of coated tablet cores containing Primojel showed an increase in tablet diameter as well as thickness. In addition, the wicking action and water sorptive properties of microcrystalline cellulose fibers may have contributed to the viscosity producing effects of the swollen Primojel grains.

Polyplasdone-XL is an insoluble form of highly cross-linked polyvinylpyrrolidone. It is commercially prepared by popcorn polymerization (proliferous polymerization) of vinylpyrrolidone (21–23). The resulting cross-linked polymer was reported to posses no extensive chemical cross-linkage but was largely cross-linked by polymer chain entanglement (24). Carli *et al.* (25) demonstrated that popcorn povidones were amphiphilic, whereas the chemically cross-linked povidones exhibited a higher polarity.

Upon hydration of the cross-linked polyvinylpyrrolidone, the amide group in the polymer monomer unit provided the only site available for hydrogen bonding with water molecules, and in this regard it acted as a hydrogen bond acceptor. For these reasons, it was postulated that there was less or no intermolecular and intramolecular hydrogen bonding between Polyplasdone-XL polymer strands compared to Ac-Di-Sol and Primojel. In addition, due to its high molecular weight and highly cross-linked nature, Polyplasdone-Xl showed virtually no tendency toward gel formation and exhibited a relatively low degree of swelling upon hydration of the bulk powder.

Polyplasdone-XL powder agglomerates and microcrystalline cellulose fibers did not interact via network formation or through hydrogen bonding to any great extent. This was attributed to both particle morphology and structural features (26). The limited interaction between the highly hydrophilic microcrystalline cellulose and the amphiphilic Polyplasdone-XL would indicate that each component was free to exert its full water sorption capacity. Thus, the high capillary activity of Polyplasdone-XL particles was enhanced by the wicking and the water sorptive properties of microcrystalline cellulose. Microcrystalline cellulose acted synergistically to the greatest extent with Polyplasdone-XL, as indicated by the degree of tablet swelling and increase in tablet volume, compared to systems combined with Ac-Di-Sol or Primojel.

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