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TECHNICAL NOTE

Effect of Colloidal Silicon Dioxide on Flowing and Tableting Properties of an Experimental, Crosslinked Polyalkylammonium Polymer

Rong-Kun Chang,* Michael Leonzio, and Munir A. Hussain

DuPont Pharmaceuticals Company, Experimental Station, Wilmington, Delaware 19880-0400

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INTRODUCTION

Glidants are usually incorporated in solid formulations to improve the flow properties of granules or powders. The possible mechanisms for enhancing flowability by glidants include reducing surface roughness, reducing friction between particles, reducing attractive forces by physically separating the host particles, reducing electrostatic forces, and acting as moisture scavengers. The bonding properties of excipients may also be affected by colloidal silicon dioxide. Nurnberg (1) reported an increased mechanical strength of lactose tablets on addition of 1% colloidal silica. Lerk et al. (2) reported that the addition of Aerosil 200 to magnesium stearate can suppress the negative effect of magnesium stearate on the crushing strength of tablets. Van Aerde et al. (3) also observed an increased tensile strength of piracetam tablets. However, Chowhan et al. (4) showed that powder mixtures containing up to 1% colloidal silica generally resulted in a decrease in the tensile strength and an increase in flow rate. Tasic et al. (5) also observed that colloidal silica did not affect compactability of acetaminophen tablet formulation. In addition, the effect of colloidal silica on flowability and compactability of powders may be sensitive to the concentration of colloidal silica in the system. In other words, there may be an optimum concentration of colloidal silica for optimum flowability and compactability. Addition of colloidal silica above the precise concentration range results in a decreased flow and a loss of cohesion in the tablet (6).

DMP 504 is an experimental crosslinked polyakylammonium polymer, synthesized from hexamethylene diamine and 1,10-dibromodecane. The polymer contains randomly distributed primary, secondary, tertiary, and quaternary amine groups in their hydrochloride salt form (7). The alkylammonium groups that comprise this polymer form a random network containing a high level of branching and a low level of crosslinking. DMP 504 complexes with bile acids and is intended for oral use as a nonsystemic cholesterol lowering agent. Development of a tablet dosage form for DMP 504 is important for improvement of patient compliance.

This report evaluates the effect of colloidal silicon dioxide on flowing and tableting properties of DMP 504.

MATERIALS AND METHODS

Materials

DMP 504 was prepared by the Chemical Processing Division of the DuPont Merck Pharmaceutical Company, and was used as received. The physicochemical proper-

Address correspondence to M. A. Hussain, DuPont Pharmaceuticals Company, Bldg. 400, Rm. 1269, Wilmington, DE 19880-0400. Fax: (302) 695-7592.
*Present address: Shire Laboratories Inc., 1550 East Gude Drive, Rockville, MD 20850.

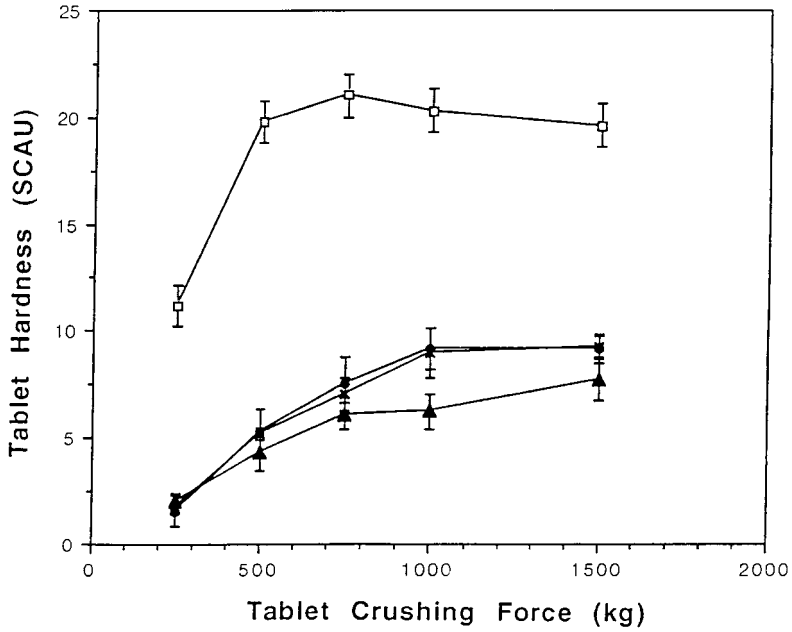

Figure 1. Compressional force–tablet hardness relationships for powder blends containing 0 (□), 0.5 (●), 1 (×), and 2% (▲) magnesium stearate.

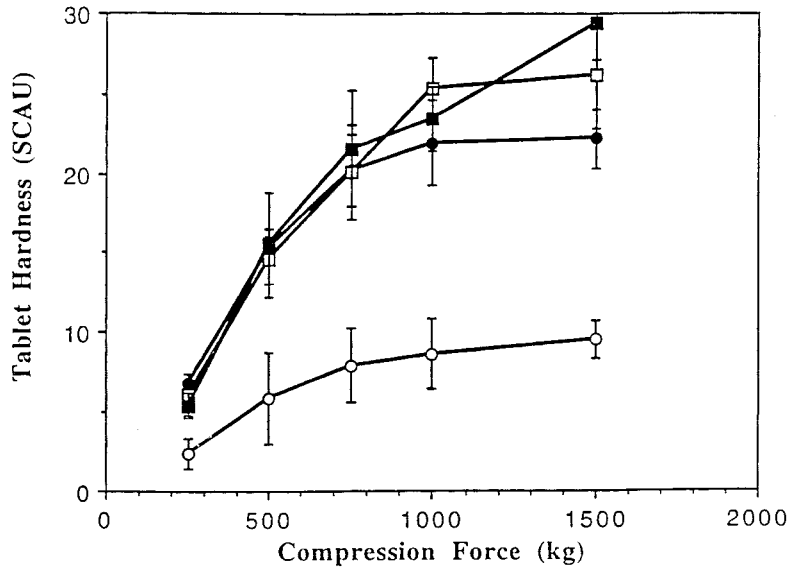

Figure 2. Compressional force-tablet hardness relationships for powder blends containing 0 (○), 0.5 (●), 1 (□), and 2% (■) colloidal silicon dioxide.

ties of DMP 504 were reported previously (7). The 10, 50, and 90 percentiles of particle size were 32, 77, and 142 μm, respectively. The surface area measured by using nitrogen adsorption of the DMP 504 powder was 2.5 m^2/g. The true density of the polymer was 1.06 g/cm^3. The bulk and tapped densities were 0.36 and 0.5 g/cm^3, respectively. Colloidal silicon dioxide was received from Cabot Corp. (Naperville, IL) (Cab-O-Sil M-5). Magnesium stearate was obtained from Mallinckrodt Speciality Chemicals Co. (St. Louis, MO).

Methods

Different levels of colloidal silicon dioxide (0.5, 1.0, and 2.0%) were mixed with DMP 504 powder in a Turbula mixer (Glenmills, Inc., Clifton, NJ) at 30 rpm for 3 min. The powder blends were screened through a U.S. 20 mesh screen and the screened powder blends were lubricated with 1% magnesium stearate (prescreened through a 30-mesh screen) in a Turbula mixer at 30 rpm for 3 min. In the absence of colloidal silicon dioxide in the formulations, DMP 504 powder was screened through U.S. 20 mesh screen and the screened powder was lubricated with either 0, 0.5, 1, or 2% magnesium stearate (prescreened through a 30-mesh screen) in a Turbula mixer at 30 rpm for 3 min. Tablets (250 mg tablet weight) were compressed on an instrumented Manesty model F-3 single-punch tablet press (Thomas Engineering, Hoffman Estate, IL) with 11/32-in. standard concave punches at five compression forces (250, 500, 750, 1000, and 1500 kg). The batch size for all of the experiments was 500 g. Tablet weights of 20 randomly selected tablets were measured by using an AC 100 analytical balance (Mettler, Hightstown, NJ). Tablet thickness was determined with a micrometer ($n = 10$) and tablet hardness was measured with a TBH-28 hardness tester (Erweka, Milford, CT) ($n = 10$).

RESULTS AND DISCUSSION

Previous data generated in this laboratory demonstrated that the consolidation of different particle size fractions of DMP 504 powder exhibited a type A Heckle plot, indicating that the plastic deformation is the primary consolidation mechanism for DMP 504 (8). A multicompression cycle approach revealed that DMP 504 powder has similar compression cycle profiles for the first and subsequent compression cycles, further indicating that DMP 504 is a plastic material under the experimental conditions (8,9). The presence of lubricants and glidants in the formulation will generally produce weakened bonding because of the formation of a barrier between host particles by these excipients. However, in some

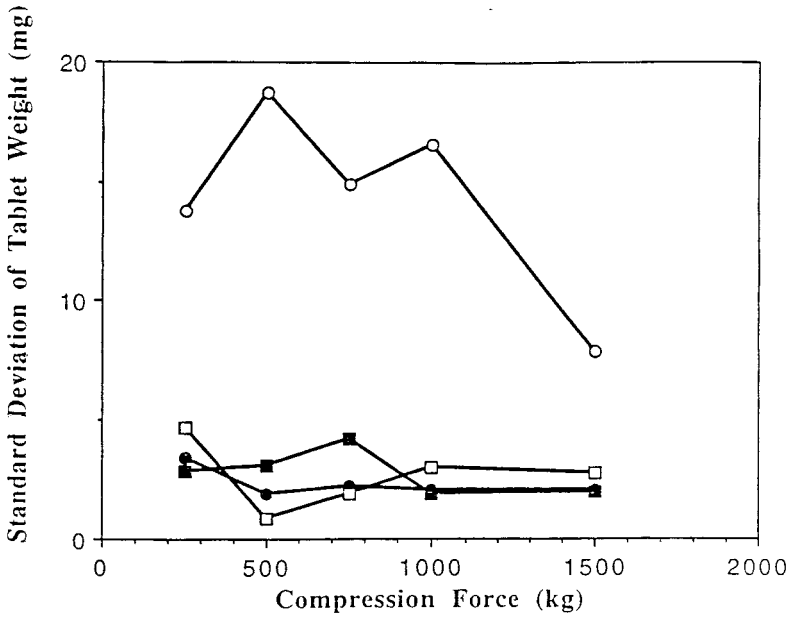

Figure 3. Effect of 0 (○), 0.5 (●), 1 (□), and 2% (■) colloidal silicon dioxide on weight variation of DMP 504 tablets.

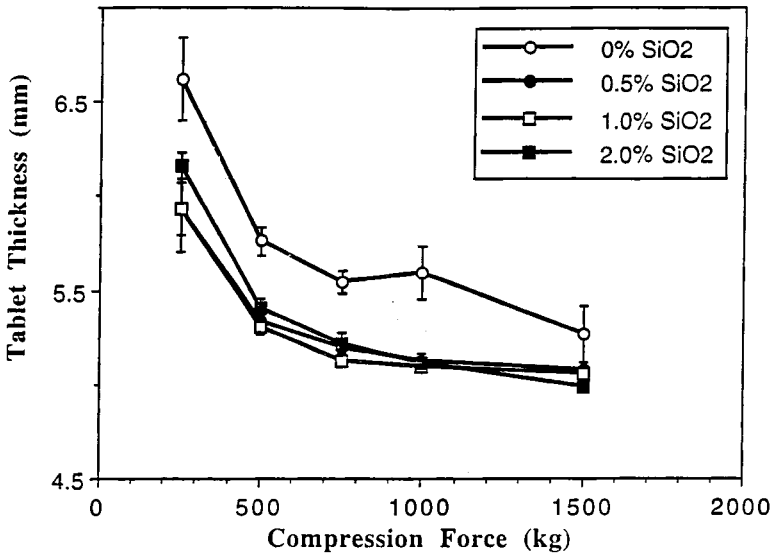

Figure 4. Compressional force-tablet thickness relationships for powder blends containing 0 (○), 0.5 (●), 1 (□), and 2% (■) colloidal silicon dioxide.

cases, addition of lubricant and glidant in the formulation may allow reduced particulate friction and increased densification to take place, which leads to an increased tablet crushing strength (10).

Figure 1 shows the effect of magnesium stearate on the tablet crushing strength. The susceptibility of DMP 504 to magnesium stearate lubrication was noted and further substantiated the plastic nature of DMP 504 powder. When a small amount of colloidal silicon dioxide was added in the formulation, a dramatic enhancement of the crushing strength of the tablets at all compression forces was observed (Fig. 2). The possible reasons for this increase of tablet hardness by the addition of colloidal silicon dioxide are (*a*) reducing the negative bonding effect of lubricant by stripping off magnesium stearate from the surface of the host particles, and (*b*) facilitating densification of the powder mixture because of the glidant action. Because the crushing strengths for tablets with 0.5 and 1% magnesium stearate at five compression forces are identical, increase in tablet hardness most likely is due to the facilitated densification via the glidant effect of colloidal silicon dioxide.

Particulate flow has a direct effect on tablet weight uniformity. Therefore, the flow properties of the powder mixture were evaluated by using the standard deviation of tablet weight. Figure 3 clearly demonstrates that colloidal silicon dioxide was an effective glidant. This study also showed that no increase in glidant activity was observed with concentrations higher than 0.5% by weight in the formulation. Figure 4 shows the plot of the thickness of tablets containing different levels of colloidal silicon dioxide versus five compression forces. A small amount of colloidal silicon dioxide in the formulation significantly reduced the tablet thickness. The improved flow properties and reduced tablet thickness by the addition of colloidal silicon dioxide in the tablet formulation provide the evidence for the increased tablet hardness through the facilitated densification.

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