AAPS PharmSciTech **2003; 4 (4) Article 62 (http://www.aapspharmscitech.org).**

Physical Properties and Compact Analysis of Commonly Used Direct Compression Binders

Submitted: April 18, 2003; Accepted: October 9, 2003

Yeli Zhang,[1] Yuet Law,[1] and Sibu Chakrabarti[1]

[1]Health Care Department, National Starch and Chemical Company, 10 Finderne Avenue, Bridgewater, NJ 08807

ABSTRACT

This study investigated the basic physico-chemical property and binding functionality of commonly used commercial direct compression binders/fillers. The compressibility of these materials was also analyzed using compression parameters derived from the Heckel, Kawakita, and Cooper-Eaton equations. Five classes of excipients were evaluated, including microcrystalline cellulose (MCC), starch, lactose, dicalcium phosphate (DCP), and sugar. In general, the starch category exhibited the highest moisture content followed by MCC, DCP, lactose, and finally sugar; DCP displayed the highest density, followed by sugar, lactose, starch, and MCC; the material particle size is highly processing dependent. The data also demonstrated that MCC had moderate flowability, excellent compressibility, and extremely good compact hardness; with some exceptions, starch, lactose, and sugar generally exhibited moderate flowability, compressibility, and hardness; DCP had excellent flowability, but poor compressibility and hardness. This research additionally confirmed the binding mechanism that had been well documented: MCC performs as binder because of its plastic deformation under pressure; fragmentation is the predominant mechanism in the case of lactose and DCP; starch and sugar perform by both mechanisms.

KEYWORDS: direct compression, binder, tensile strength, Heckel analysis, Kawakita analysis, Cooper-Eaton analysis

Corresponding Author: Yeli Zhang, Health Care Department, National Starch and Chemical Company, 10 Finderne Avenue, Bridgewater, NJ 08807;
Tel: (908) 575-7234; Fax: (908) 707-3712;
Email: yeli.zhang@nstarch.com

INTRODUCTION

Tablet manufacturing by direct compression (DC) has increased steadily over the years. It offers advantages over other manufacturing processes, such as wet granulation, and provides high efficiency.

When formulating direct compression tablets, the choice of DC binder is extremely critical. It must fulfill certain requirements: good binding functionality and powder flowability are essential; a well-designed particle size distribution provides favorable mixing conditions; compatibility with other excipients or drugs is also essential, as is the ability to carry high amounts of active ingredient.[1] Currently, only a few materials meet the criteria to allow their classification as DC binders.[2-4] An understanding of the physico-chemical properties of these DC binders is critical for their proper use; therefore, one objective of this research was to study the basic physico-chemical properties of the commonly used DC binders.

The process of direct compression is a process of applying pressure (via an upper and a lower punch) to materials held in a die cavity. The events that occur in the process of compression are (1) transitional repacking, (2) deformation at point of contact, (3) fragmentation and/or deformation, (4) bonding, (5) deformation of the solid body, (6) decompression, and (7) ejection.[5] Therefore, another extremely important functionality of DC binders is their compressibility under pressure, which is predominantly determined by material properties such as surface energy and deformation. In the pharmaceutical industry, the measurement of porosity change as a function of compression pressure is widely used in describing the above powder compression process. The compressibility of a powder bed could be obtained from the relationship between porosity and applied pressure.[6] Therefore, another objective of this study was to evaluate the compressibility of commonly used binder-fillers by studying the porosity-pressure relationship in an attempt to understand, characterize, and compare the binding functionality of these materials.

Table 1. Common Commercial DC binder-fillers*

Excipient	Market/Trade Name	Manufacturer Supplier
Microcrystalline cellulose	Avicel PH101	FMC Corp
	Avicel PH102	FMC Corp
	SMCC 50	Penwest Pharmaceutical
	SMCC 90	Penwest Pharmaceutical
Pregelatinized starch	UNI-PURE DW	National Starch & Chemical Co
	UNI-PURE LD	National Starch & Chemical Co
	Starch 1500	Colorcon Inc
	Spress B820	Grain Processing Corp
Lactose	DC-Lactose	Quest International Inc
	Fast-Flo no. 316	Foremost Ingredients Group
Dibasic calcium phosphate	DI-TAB	Rhodia Inc
	A-TAB	Rhodia Inc
	Emcompress	Edward Mendell Co Inc
Sugar	Di-Pac	Domino Specialty Ingredients
	Sorbitol-Instant-Pharma	EM Industries
	ParTeck M300	EM Industries

*DC indicates direct compression.

MATERIALS AND METHODS

The excipients evaluated in this study were purchased from commercial suppliers and used as received. They are listed in **Table 1**.

Powder Evaluation

Moisture Content

The moisture content of the excipients was determined gravimetrically on a Sartorius MA-40 moisture balance (Sartorius, Goettingen, Germany). Approximately 5 g of sample was uniformly placed onto the sample pan, and then the heating cycle was started. The percentage of moisture content was calculated from the weight loss of the sample by heating. The instrument was allowed to cool between tests and a triplicate test was run for each sample.

Particle Size

The particle size and its distribution for all samples were measured by Malvern Mastersizer 2000 (Malvern Instruments Ltd, Worcestershire, UK). Approximately 5 mL of powder was used for each measurement. The air pressure was set at 2.0 bar, and the feed rate was set at 50%. The mass median diameter (particle size at which 50% by volume of the sample is smaller and 50% by volume is larger) and particle size distribution were recorded. Each sample was measured 3 times.

Density

The bulk and tap density of the excipients was determined according to the following method: a 50-mL glass cylinder was weighed and filled with 30 mL of powder and reweighed. The opening was secured with parafilm. The cylinder was gently reversed once, and the powder was carefully leveled without compacting. Bulk volume was determined after 1 mechanical tap on a tap density tester (model SWM 22, Erweka, Heusenstamm, Germany). Tap volume was measured after 2000 taps. Each analysis was repeated twice.

The true density of each material was determined by a helium pycnometer (AccuPyc 1330, Micrometitics Instrument Inc., Norcross, GA). The accuracy of the pycnometer was checked using a standard steel sphere before measurements on a series of samples. The experimental sample was accurately weighed and loaded into the sample cell. The sample volume was computed by measurements of the pressure observed by filling the sample chamber with ultra-high pure helium gas followed by discharging the gas into a second empty chamber. The measurements were repeated for 10 such cycles.

Flow Property

The flow behavior of each binder was measured using an automated powder flowability analyzer (API Aero-flow, Amherst Process Instruments Inc, Hadley, MA . Powder (50 mL) was placed in a transparent rotating drum, and the resultant avalanche was detected by the obscuration of photocells located behind the drum. The drum rotation speed was kept constant at 180 rpm, and the sampling rate was maintained at 5 Hz. The data were collected using the data acqui-

sition software, and the mean times for avalanche and scatter for 3 runs were recorded.

Compact Preparation and Evaluation

Compression

Compact compression was performed on a single-station manual tablet press (model MTCM-1, GlobePharma Inc, New Brunswick, NJ). Ten different compaction forces (from 2.2 kN to 22 kN) were used for each material. For each compact (n = 3), 600 mg of powder was weighed on an analytical balance, and then manually filled into the die. A flat-faced punch with a diameter of one-half inch was used.

Each compact was weighed accurately, and its dimensions (diameter and thickness) were measured with a digital slide caliper (Starett, The L. S. Starett Co, Athol, MA). This information was used for the calculation of relative density (Equation 1), porosity (Equation 2), and degree of volume reduction (Equation 3), which are essential parameters for Heckel, Kawakita, and Cooper-Eaten analysis.

$$D = \frac{\rho_A}{\rho_T} \tag{1}$$

$$\varepsilon = 1 - D \tag{2}$$

$$C = 1 - \frac{\rho_0}{\rho_A} \tag{3}$$

In each equation, D is the relative density of a powder compact at pressure P; ρ_A is the apparent density of a powder compact at pressure P; ρ_T is the true density of a powder; ε is the porosity; C is the degree of volume reduction of a powder compact at pressure P; and ρ_0 is the bulk density of a powder.

Hardness

Crushing strength of a compact was determined by compressing a compact diametrically on a Pharmatron tablet tester (model 6D, Dr Schleuniger Pharmatron Inc, Manchester, NH). The radial tensile strength of the compacts was calculated from the compact crushing strength and compact thickness in accordance with Fell and Newton's method,[7,8] in which the radial tensile strength σ_χ is given by

$$\sigma_x = \frac{2x}{\pi dt} \tag{4}$$

where σ_χ is the tensile strength (MPa); x is the force required to cause failure in tension (N); d is the diameter of the compact (mm); and t is the thickness of the compact (mm).

The use of tensile strength allows the dimensions of the compact to be taken into account, which is in contrast to the use of crushing strength. Only the force that led to sample failure in tension was used for the calculation of tensile strength.

Heckel Analysis

The Heckel equation is described as follows (Equation 5). It is based on the assumption that powder compression follows first-order kinetics, with the interparticulate pores as the reactant and the densification of the powder bed as the product.[9]

$$\ln \frac{1}{1 - D} = kP + A \tag{5}$$

where D is the relative density of a powder compact at pressure P. Constant k is a measure of the plasticity of a compressed material. Constant A is related to the die filling and particle rearrangement before deformation and bonding of the discrete particles.[6] Thus, a Heckel plot allows for the interpretation of the mechanism of bonding.

Kawakita Analysis

The Kawakita equation is described as follows (Equation 6). This equation describes the relationship between the degree of volume reduction of the powder column and the applied pressure.[10] The basis for the Kawakita equation for powder compression is that particles subjected to a compressive load in a confined space are viewed as a system in equilibrium at all stages of compression, so that the product of the pressure term and the volume term is a constant.

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \tag{6}$$

where C is the degree of volume reduction of a powder compact at pressure P. The constants (a and b) can be evaluated from a plot of P/C versus P. A value of a is indicative of the total volume reduction for the powder bed, and b is a constant that is inversely related to the yield strength of the particles. The data from this study were modeled via the Kawakita equation in an attempt to evaluate the relationship between the volume reduction and applied pressure for each studied DC binder.

Table 2. Particle Size, Moisture Content, and Density of Studied DC Binder-Fillers*

Sample	Particle Size (μm)	Moisture Content (%)	Density (g/mL)		
			Bulk	Tap	True
Avicel PH 101	56.3 ± 0.4	5.1 ± 0.2	0.34 ± 0.0	0.41 ± 0.00	1.64 ± 0.01
Avicel PH 102	113.8 ± 1.1	4.9 ± 0.3	0.36 ± 0.01	0.42 ± 0.01	1.62 ± 0.00
SMCC 50	59.8 ± 0.7	5.6 ± 0.4	0.32 ± 0.00	0.40 ± 0.00	1.62 ± 0.00
SMCC 90	126.4 ± 0.5	5.1 ± 0.2	0.47 ± 0.00	0.54 ± 0.01	1.64 ± 0.00
UNI-PURE DW	59.6 ± 0.8	7.3 ± 0.4	0.57 ± 0.00	0.67 ± 0.00	1.53 ± 0.00
UNI-PURE LD	32.9 ± 0.7	7.1 ± 0.3	0.14 ± 0.01	0.17 ± 0.01	1.41 ± 0.00
Starch 1500	78.2 ± 0.4	10.9 ± 0.2	0.61 ± 0.01	0.71 ± 0.01	1.52 ± 0.00
Spress B820	93.9 ± 0.1	9.8 ± 0.3	0.59 ± 0.01	0.70 ± 0.01	1.57 ± 0.01
DC-Lactose	136.0 ± 2.5	1.6 ± 0.2	0.53 ± 0.01	0.62 ± 0.00	1.60 ± 0.01
Fast-Flo no. 316	72.9 ± 0.7	4.9 ± 0.4	0.51 ± 0.01	0.60 ± 0.01	1.61 ± 0.01
DI TAB	196.1 ± 1.9	5.6 ± 0.2	0.87 ± 0.00	1.01 ± 0.00	2.32 ± 0.01
A-TAB	144.7 ± 1.2	1.3 ± 0.1	0.74 ± 0.00	0.85 ± 0.00	3.05 ± 0.02
Emcompress	189.1 ± 1.3	6.9 ± 0.4	0.94 ± 0.01	1.10 ± 0.01	2.35 ± 0.02
Di-Pac	255.4 ± 2.3	0.9 ± 0.1	0.67 ± 0.01	0.72 ± 0.01	1.64 ± 0.01
Sorbitol-Instant-Pharma	303.8 ± 1.2	0.7 ± 0.0	0.41 ± 0.00	0.50 ± 0.00	1.53 ± 0.00
ParTeck M300	112.3 ± 1.5	0.7 ± 0.1	0.43 ± 0.00	0.50 ± 0.00	1.52 ± 0.01

*DC indicates direct compression.

Cooper-Eaton Analysis

The Cooper-Eaton equation is described as follows (Equation 7). This equation considers that powder compaction occurs in 2 stages. The first stage is the filling of the voids in the powder-by-powder rearrangement. The second stage proceeds via elastic deformation, plastic flow, and/or fragmentation of the compressed particles.[6]

$$\frac{\left[\frac{1}{D_0}-\frac{1}{D}\right]}{\left[\frac{1}{D_0}-1\right]} = a_1 \exp\left(-\frac{k_1}{P}\right) + a_2 \exp\left(-\frac{k_2}{P}\right) \quad (7)$$

where D_0 is the relative density at zero pressure, and D is the relative density at pressure P. Cooper-Eaton constants a_1 and a_2 describe the theoretical maximum densification that could be achieved by filling voids of the same size (a_1) and of a smaller size (a_2) than the actual particles. The most probable pressures at which the respective densification processes would occur are described by k_1 and k_2. The data from this study were modeled via the Cooper-Eaton equation in an attempt to evaluate the stages of volume reduction.

RESULTS AND DISCUSSION

Powder Properties

Moisture Content

The moisture contents for the excipients are listed in **Table 2**. All excipients were within United States Pharmacopeia moisture content specifications. In general, the starch category exhibited the highest moisture content followed by MCC, DCP, lactose, and finally sugar.

Particle Size

The mass mean diameters for all samples are listed in **Table 2** and their particle size distribution curves are shown in **Figure 1**. UNI-PURE LD (National Starch & Chemical Co, Bridgewater, NJ) showed a bimodal particle size distribution curve because UNI-PURE LD is a coprocessed starch that contains 2 components. The particle size distribution curves for all other samples are unimodal. However, some unimodal distribution curves do have shoulders or are skewed. The difference in particle size and its distribution would affect the performance of the material as a DC binder.[1]

Density

The bulk, tap, and true densities for the excipients are listed in **Table 2**. DCP has the highest bulk and tap densities, followed by sugar, lactose, starch, and MCC. The exception is

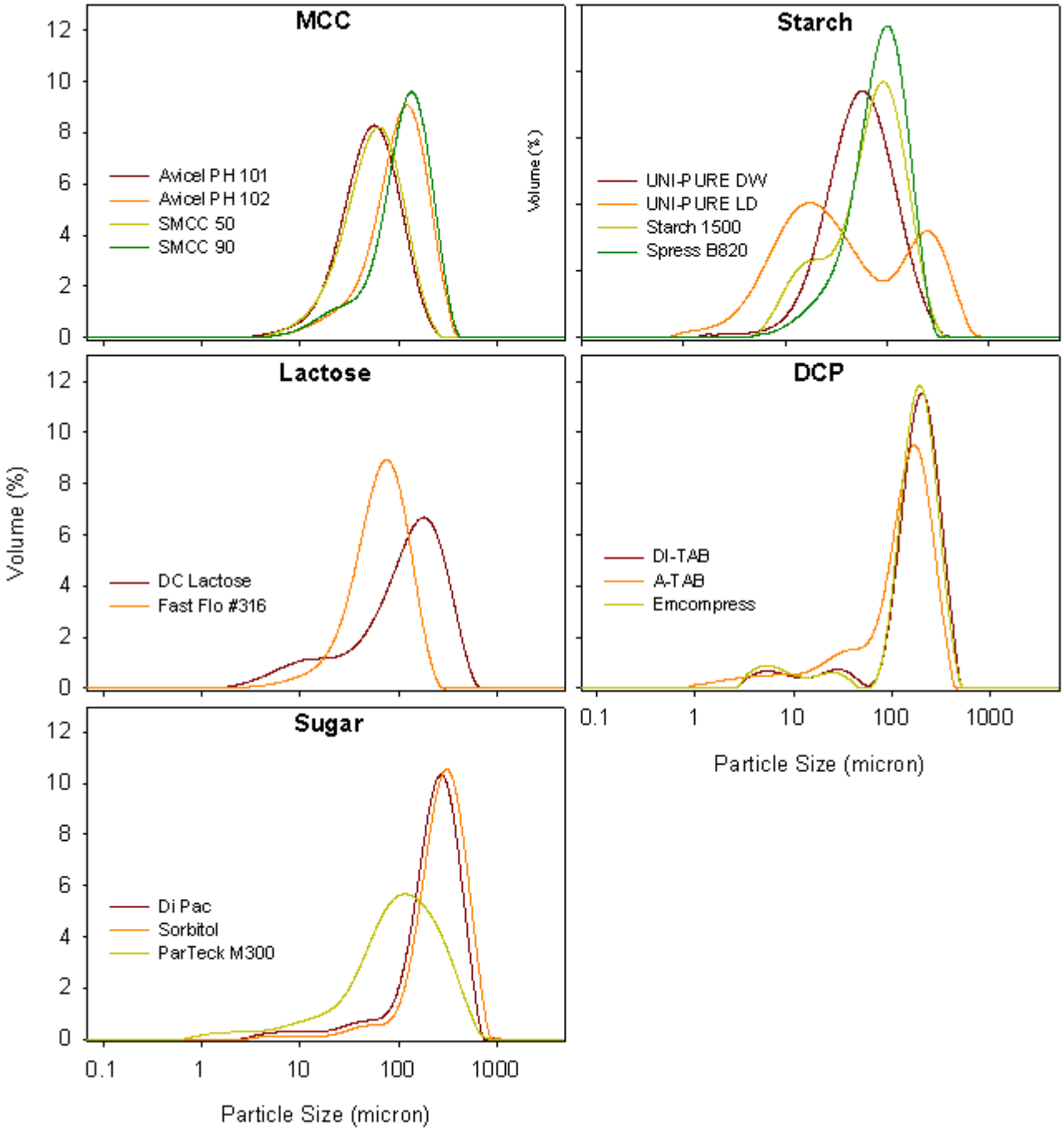

Figure 1. Particle size distributions of studied DC binder-fillers.

UNI-PURE LD in starch category, which is purposely designed to have very low density. Comparing true density to bulk and tap densities, the true density of these commercial binder-fillers is quite close to each other with the exception of DCP.

Flow Property

Dynamic powder flow characteristics were evaluated by powder avalanche and scatter in a rotating drum. Results from avalanching measurements are described as "strange attractor plots," and numerical values are sought to quantify the avalanching process. A strange attractor plot is constructed by joining points defined by the time between a set

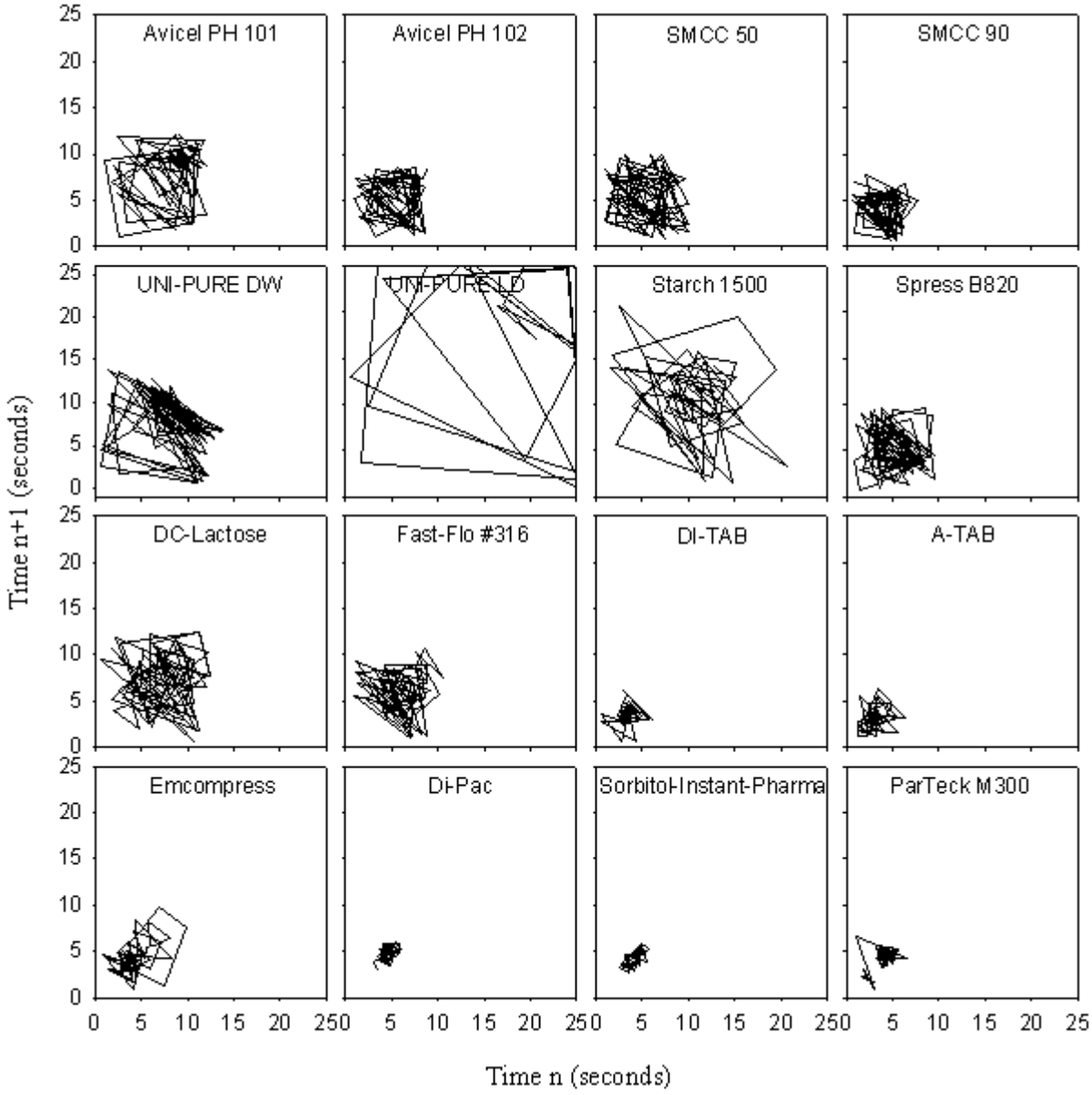

Figure 2. Flow behavior of studied DC binder-fillers.

of avalanches (t_n, t_{n+1}) and similar subsequent events (t_{n+2}, t_{n+3}). The centroid of this plot is called the mean time to avalanche (MTA). The expansion of the strange attractor plot in the X- and Y-directions reflects the time scatter of the avalanching process. MTA is the measure of the flowability of the powder, and the scatter value defines the regularity of the flow behavior. A powder with good flow properties will have an MTA close to zero and a low scatter value. The representative strange attractor plots for all studied materials are shown in **Figure 2**. The mean time for avalanche and scatter from 3 runs is summarized in **Table 3**.

The flowability is typically determined by powder properties such as density, surface area, moisture content, particle shape, particle size, and size distribution.[11] In general, DCP exhibited the best flow property (ie, the smallest MTA) among the studied excipients, followed by sugar, lactose, MCC, and starch.

Avicel PH 102 (FMC Corp, Newark, DE) showed better flow than Avicel PH 101(FMC Corp) because Avicel PH 102 has bigger particle size, and the particle shape is more spherical than Avicel PH 101 (rod-like particle).[1,12,13] Silicified microcrystalline cellulose (SMCC 50 and 90) (Penwest Pharmaceutical, Patterson, NY) improved the flow property

Table 3. Flow Behavior of Studied DC Binder-Fillers*

Excipients	Mean Time for Avalanche (Seconds)	Mean Time for Scatter (Seconds)
Avicel PH 101	8.60 ± 0.33	2.73 ± 0.20
Avicel PH 102	5.74 ± 0.12	2.35 ± 0.11
SMCC 50	5.42 ± 0.07	2.67 ± 0.07
SMCC 90	3.88 ± 0.27	1.79 ± 0.04
UNI PURE DW	7.84 ± 0.10	3.41 ± 0.22
UNI PURE LD	19.00 ± 1.29	8.76 ± 1.34
Starch 1500	10.27 ± 0.25	3.76 ± 0.43
Spress B820	4.73 ± 0.17	2.52 ± 0.09
DC-Lactose	7.21 ± 0.28	3.08 ± 0.27
Fast-Flo no. 316	5.88 ± 0.14	2.32 ± 0.14
DI-TAB	3.51 ± 0.04	0.81 ± 0.15
A-TAB	3.19 ± 0.08	0.75 ± 0.09
Emcompress	3.91 ± 0.25	1.47 ± 0.19
Di-Pac	4.62 ± 0.04	0.58 ± 0.05
Sorbitol-Instant-Pharma	4.14 ± 0.18	0.70 ± 0.03
ParTeck M300	4.35 ± 0.18	0.75 ± 0.08

*DC indicates direct compression. Data are given as mean ± SD (n = 3).

of regular microcrystalline cellulose (Avicel PH 101 and 102). SMCC 90 showed better flow than SMCC 50 because of bigger particle size and higher density. Although the bulk density of starch is generally higher than that of MCC, the poor flowability of these excipients when compared with MCC may be attributed to the high moisture content, which resulted in strong cohesion between particles. The very poor flowability of UNI-PURE LD comes from its extremely low bulk density and small particle size. The spherical particle shape of spray-dried DC-Lactose (Quest International Inc, Norwich, NY) and Fast-Flo no. 316 (Foremost Farms, Baraboo, WI) gave them moderate flow.[1,14] The sugar category generally showed good flow behavior. This may come from their large particle size, spherical particle shape, and low moisture content. The large particle size and high density of DCP are important factors for their excellent flow property.

Compact Properties

Hardness

The radial tensile strength results are shown in **Figure 3**. The crushing strength values for compacts made of UNI-PURE LD, Sorbitol-Instant-Pharma, and all MCC exceeded the instrument high limit, and hence only partial values have been reported. A linear relation between tensile strength and compression pressure was observed for all excipients under the condition of the test. Results demonstrated that as the compression force increases, tensile strength also increases. At the same compression force, MCC produced the hardest compacts, whereas DCP produced the softest compacts. The tensile strength of starch, lactose, and sugar compact fell in between. The exceptions were compacts made of UNI-PURE LD and Sorbitol-Instant-Pharma (EM Industries, Darmstadt, Germany), which exhibited similar tensile strength to MCC.

All studied MCC materials showed excellent compact hardness. According to Bolhuis,[1] Lee et al,[12] and Tsai et al,[13] hydrogen bonding played a big role in compact hardness. Hydrogen bonding is important because MCC undergoes significant plastic deformation during compression bringing an extremely large surface area into close contact and facilitating hydrogen bond formation between the plastically deformed, adjacent cellulose particles. In addition, the existence of moisture within the porous structure of MCC acts as an internal lubricant. This facilitates slippage and flow within the individual microcrystals during plastic deformation, which enforces the formation of hydrogen bond bridges and gives MCC a very good hardness.

Except for UNI-PURE LD, studied starch compacts generally have low hardness. It was reported that in comparison with other plastically deforming materials, such as MCC, the plastic deformation of starch during compression is too slow to produce adequate interparticle binding during rapid compression.[1] The slight difference of tensile strength among UNI-PURE DW (National Starch & Chemical Co, Bridgewater, NJ), Starch 1500 (Colorcon Inc, Indianapolis, IN), and Spress B820 (Grain Processing Corp, Muscatine, IA) may be attributed to their different degree of gelatinization, moisture content, particle size and distribution, and particle shape (data not shown). UNI-PURE LD powder

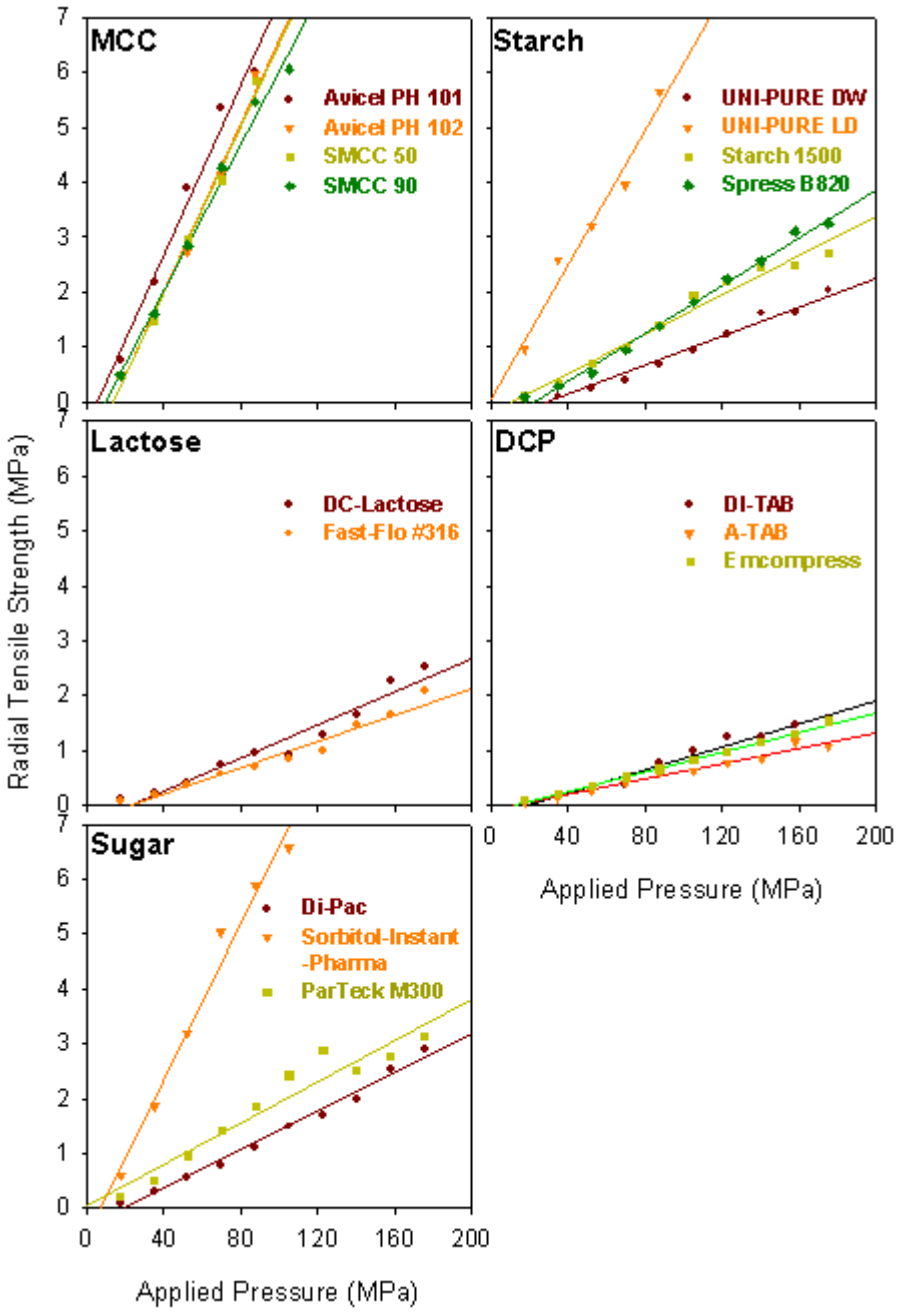

Figure 3. Radial tensile strength of studied DC binder-fillers.

consists of hollow spherical particles (scanning electron microscope data not shown), which contributed to its very low density. These unique characteristics of UNI-PURE LD give it excellent compressibility, binding functionality, and hardness.

Lactose produced soft compacts as shown in **Figure 3**. According to van der Voort Maarschalk and Bolhuis[15,16] and Cole et al,[17] lactose compacts are consolidated by both plastic deformation and fragmentation, but to a larger extent by fragmentation. Fragmentation creates a large number of small particles, thus the number of contact points that support the applied load is large, so that the stress on each contact point is relatively small. The strength of bonds formed in compacts will therefore be relatively low.

DCP exhibited poor binding properties. Because of the brittle nature of DCP, it undergoes considerable fragmentation during compression. Fracture creates a large number of interparticulate contact points, which imply that a compara-

Table 4. Heckel Plot Constants of Studied DC Binder-Fillers*

Excipient	k (1/MPa)	A	r^2
Avicel PH101	3.54×10^{-2}	0.726	0.96
Avicel PH102	3.77×10^{-2}	0.638	0.97
SMCC 50	3.74×10^{-2}	0.596	0.98
SMCC 90	3.27×10^{-2}	0.702	0.96
UNI-PURE DW	2.48×10^{-2}	0.640	0.99
UNI-PURE LD	4.10×10^{-2}	0.597	0.97
Starch 1500	2.93×10^{-2}	0.851	0.97
Spress B820	2.64×10^{-2}	0.758	0.98
DC-Lactose	2.23×10^{-2}	0.980	0.99
Fast-Flo no. 316	2.36×10^{-2}	0.932	0.96
DI-TAB	1.93×10^{-2}	0.958	0.89
A-TAB	0.87×10^{-2}	0.554	0.89
Emcompress	1.70×10^{-2}	1.011	0.94
Di-Pac	2.46×10^{-2}	1.017	0.96
Sorbitol-Instant-Pharma	4.60×10^{-2}	1.038	0.94
ParTeck M300	2.32×10^{-2}	0.918	0.97

*DC indicates direct compression.

tively weak type of bonding is involved.[1,15,16,18] Thus, the compact strength is low.

Di-Pac (Domino Specialty Ingredients, Baltimore, MD) behaved as an intermediate between plastic deformation and complete fragmentation, in which, particle fracture played a more dominant role than plastic deformation. Di-Pac compacts correspond to an intermediate hardness among the studied excipients.[1] Chemically, Sorbitol-Instant-Pharma is an isomer of ParTeck (EM Industries,Hawthorne, NY) M300. However, studies showed that their compact strength was strongly dependent on particle structure, particle size distribution, and density. Therefore, a different level of compact hardness was observed.[1,19]

Heckel Plots

The constants for the Heckel plots of the excipients evaluated in this study are displayed in **Table 4**. The slope of the Heckel plot (k) is indicative of the plastic behavior of the material.[6,9] A larger value for the slope is related to a greater amount of plasticity in the material. Generally, the plasticity decreases in the following order: MCC > lactose, sugar, starch > DCP. The exceptions are UNI-PURE LD and Sorbitol-Instant-Pharma, which exhibited a high plasticity similar to MCC.

Kawakita Equation

The Kawakita constants a and b for each of the excipients evaluated are listed in **Table 5**. In terms of a parameter, UNI-PURE LD exhibited the highest compressibility, followed by MCC and Sorbitol-Instant-Pharma. DCP, in general, showed the lowest compressibility. The compressibility of starch, lactose, and sugar fell in between. In terms of b parameter, generally, UNI-PURE LD showed the lowest yield strength, followed by MCC and the lactose category. The class of DCP and starch showed the highest yield strength. In the sugar category, Sorbitol-Instant-Pharma and ParTeck M300 demonstrated a lower yield strength, whereas Di-Pac exhibited a higher yield strength.

Cooper-Eaton Equation

The Cooper-Eaton constants for the excipients, profiled by the Cooper-Eaton equation, are listed in **Table 6**. If the sum $a_1 + a_2$ is greater than unity, a nonporous compact can be obtained at lower pressures.[6] For most of the studied binders, the sum $a_1 + a_2$ was closer or greater than unity, which indicated that a nonporous compact could be obtained with these binders at studied pressure.

It is worth mentioning that the compact hardness and compressibility results in this study were based on a manual tablet press. Because of its inherent problems, some of these results may not be consistent with values obtained from a compaction simulator.[1,10] However, the results from this study are a valuable complement to that from a compaction simulator.

CONCLUSION

This study confirmed the binding mechanism that already had been reported by others. For instance, MCC performs as binder because of its plastic deformation under pressure, whereas fragmentation is the predominant mechanism in

Table 5. Kawakita Constants of Studied DC Binder-Fillers*

Excipient	*a*	*b*	r^2
Avicel PH101	0.7839	0.1561	0.9999
Avicel PH102	0.7823	0.1197	0.9999
SMCC 50	0.8028	0.1297	0.9999
SMCC 90	0.7072	0.0834	0.9999
UNI-PURE DW	0.6112	0.0366	0.9953
UNI-PURE LD	0.9098	0.3415	0.9999
Starch 1500	0.5825	0.0573	0.9996
Spress B820	0.5975	0.0504	0.9994
DC-Lactose	0.6300	0.1266	0.9991
Fast-Flo no. 316	0.6435	0.1222	0.9994
DI-TAB	0.5628	0.0967	0.9988
A-TAB	0.6120	0.0980	0.9998
Emcompress	0.5298	0.0996	0.9996
Di-Pac	0.5530	0.0845	0.9995
Sorbitol-Instant-Pharma	0.7332	0.1973	0.9999
ParTeck M300	0.6804	0.1491	0.9997

*DC indicates direct compression.

Table 6. Cooper-Eaton Constants of Studied DC Binder-Fillers*

Excipient	a_1	a_2	k_1	k_2	r^2	a_1+a_2
Avicel PH101	0.5535	0.4418	0.2185	14.8818	0.9999	0.9953
Avicel PH102	0.7797	0.2227	4.0461	23.1731	0.9998	1.0024
SMCC 50	0.5519	0.4518	0.3268	17.5327	0.9990	1.0037
SMCC 90	0.3892	0.6026	0.0000	19.2785	0.9998	0.9918
UNI-PURE DW	0.5178	0.5432	2.2523	80.8271	0.9979	1.0610
UNI-PURE LD	0.9733	0.0409	1.6171	100.7765	0.9938	1.0142
Starch 1500	0.6887	0.3103	5.3200	60.4232	0.9992	0.9990
Spress B820	0.4599	0.5236	0.7261	42.3111	0.9992	0.9835
DC-Lactose	0.7968	0.2028	1.5997	98.1531	0.9933	0.9996
Fast-Flo no. 316	0.8954	0.2859	4.8115	342.0391	0.9966	1.1813
DI-TAB	0.5900	0.3489	0.0000	44.9345	0.9795	0.9389
A-TAB	0.4722	0.3490	0.0000	30.1026	0.9939	0.8212
Emcompress	0.8022	0.1420	5.2044	152.5689	0.9991	0.9442
Di-Pac	0.8232	0.1532	5.7795	106.0182	0.9973	0.9764
Sorbitol-Instant-Pharma	0.5842	0.4218	0.0000	13.3857	0.9975	1.0060
ParTeck M300	0.8340	0.1453	2.2077	75.3577	0.9983	0.9793

*DC indicates direct compression.

case of DCP and lactose. With some exceptions, starch and sugar generally perform by both mechanisms.

ACKNOWLEDGEMENTS

The National Starch and Chemical Company is greatly acknowledged for their financial support.

REFERENCES

1. Bolhuis GK. Materials for direct compaction. In: Alderborn G, Nyström C, eds. *Pharmaceutical Powder Compaction Technology*. New York, NY: Marcel Dekker Inc; 1996:419-478.

2. Wade A, Weller PJ. *Handbook of Pharmaceutical Excipients*. 2nd ed. Washington, DC: American Pharmaceutical Association; 1994.

3. Rudnic EM, Kottke MK. Tablet dosage forms. In: Banker GS, Rhodes CT, eds. *Modern Pharmaceutics*. New York, NY: Marcel Dekker Inc; 1996:333-391.4. Joshi V. Excipient choice in solid dosage forms. *Drug Deliv Technol*. 2002;2(6):36-40.

5. Parrott EL. Compression. In: Lieberman HA, Lachman L, Schwartz JB, eds. *Pharmaceutical Dosage Forms: Tablets*. Vol 2. New York, NY: Marcel Dekker Inc; 1990:153-182.

6. Paronen P, Iilla J. Porosity-pressure functions. In: Alderborn G, Nyström C, eds, *Pharmaceutical Powder Compaction Technology*. New York, NY: Marcel Dekker Inc; 1996:55-75.

7. Habib Y, Ausburger L, Reier G, Wheatley T, Shangraw R. Dilution potential: a new perspective. *Pharm Dev Technol*. 1996;1(2):205-212.

8. Fell JT, Newton JM. The tensile strength of lactose tablets. *J Pharm Pharmacol*. 1968;20(8):657-758.

9. Heckel RW. An analysis of powder compaction phenomena. *Trans AIME*. 1996;221:1001-1008.

10. Nicklasson F, Alderborn G. Analysis of the compression mechanics of pharmaceutical agglomerates of different porosity and composition using the Adams and Kawakita equations. *Pharm Res*. 2000;17(8):949-954.

11. Lavoie F, Cartilier L, Thibert R. New methods characterizing avalanche behavior to determine powder flow. *Pharm Res*. 2002;19(6):887-893.

12. Lee YSL, Poynter R, Podczeck F, Newton JM. Development of a dual approach to assess powder flow from avalanching behavior. *AAPS PharmSciTech*. 2000;1(3): Article 21.

13. Tsai T, Wu JS, Ho HO, Sheu MT. Modification of physical characteristics of microcrystalline cellulose by codrying with β-cyclodextrins. *J Pharm Sci*. 1998;87(1):117-122.

14. Taylor MK, Ginsburg J, Hickey AJ, Gheyas F. Composite method to quantify powder flow as a screening method in early tablet or capsule formulation development. *AAPS PharmSciTech*. 2000;1(3): Article 18.

15. van der Voort Maarschalk K, Bolhuis GK. Improving properties of materials for direct compression. *Pharm Technol Europe*. 1998;10(9):30-35.

16. van der Voort Maarschalk K, Bolhuis GK. Improving properties of materials for direct compression. *Pharm Technol Europe*. 1998; 10(10):28-36.

17. Cole ET, Rees JE, Hersey JA. Relations between compaction data for some crystalline pharmaceutical materials. *Pharm Acta Helv*. 1975;50(1-2):28-32.

18. Roberts RJ, Rowe RC. The young's modulus of pharmaceutical materials. *Int J Pharm*. 1987;37:15-18.

19. Olsson H, Nyström C. Assessing tablet bond types from structural features that affect tablet tensile strength. *Pharm Res*. 2001;18(2);203-210.