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RESEARCH PAPER

Changes in Volume and Compression Energy upon Compression of Calcium Silicate Tablets

Tomoaki Asano,[1] Satoru Tsubuku,[1] Shinya Sugawara,[1] Masaharu Miyajima,[1] Hiroshi Sato,[1] Hiroshi Yuasa,[2] and Yoshio Kanaya[2]

[1]*Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., 2512-1, Oshikiri, Kohnan, Saitama 360-01, Japan*
[2]*Laboratory of Medical & Pharmaceutical Technology, School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1, Horinouchi, Hachioji, Tokyo 192-03, Japan*

ABSTRACT

The compression mechanism of calcium silicate (Florite® RE, FLR) was evaluated by determining the physicochemical properties such as compression energy, volume reduction percentage during the compression process, and elastic recovery of FLR tablets. The results obtained were compared with those of microcrystalline cellulose (MCC), anhydrous dibasic calcium phosphate (ADCP), cornstarch (CS), and lactose (LAC). FLR is found to have higher plasticity in the compression process and lower elastic recovery in a wide range of tablet hardnesses compared with the other 4 excipients. The results also indicate that a large part of compression energy was consumed for plastic deformation and fragmentation of particles. These characteristics are attributable to FLR's porous structure and are responsible for FLR tablets' high hardness, an important property in tablet formulation. As a consequence, it was suggested that FLR would be a useful excipient for the formation of tablets in the pharmaceutical industry.

INTRODUCTION

Florite® RE (FLR) is a calcium silicate with a characteristic porous structure, and has come into use recently as a medicinal additive. Due to its porous structure, FLR was used for the solid preparation of an oily medicine such as tocopheryl nicotiate (1,2), and for the preparation of ground mixture to improve the dissolution and compression characteristics of acetaminophen (3). Kano et al. (4) have reported that the use of FLR is quite effective in preventing interaction among components in tablets. FLR tablets have also been found to have high mechanical strength even under low compression pressure (5). However, there has been no study on why FLR possesses such good compactibility. The mechanical strength of tablets generally described as hardness and friability is affected not only by the physical properties of the constituent powder, but also by the compression mechanism of the powder during compression (6). Therefore, it is important to clarify the compression mechanism of FLR to elucidate why it has good compactibility.

In the present study, the compression energy and volume change of FLR powder during the compression process, and the mechanical strength and the elastic recovery of FLR tablets were investigated in order to describe the compression behavior of FLR. The results obtained were compared with those of other additives (microcrystalline cellulose, anhydrous dibasic calcium phosphate, cornstarch, and lactose) used as excipients for tablets.

MATERIALS AND METHODS

Materials

Calcium silicate (Florite RE, FLR, Eisai Co., Ltd.), microcrystalline cellulose (Avicel® PH-101, MCC, Asahi Kasei Kogyo Co., Ltd.), anhydrous dibasic calcium phosphate (ADCP, Kyowa Kagaku Kogyo Co., Ltd.), cornstarch (CS, Nihon Shokuhin Kakou Co., Ltd.), and lactose (LAC, Pharmatose® 200Mesh, DMV Co., Ltd.) were used after sieving through a 200-mesh sieve.

Measurement of the Property of Excipients (7,8)

The specific surface area of each excipient was measured by the air permeability method (Shimadzu Corporation, Type SS-100), and calculated by Kozeny Carman's equation, Eq. (1):

$$S_W = \frac{14}{\rho}\sqrt{\frac{\Delta P A t}{\eta L Q}\cdot\frac{\varepsilon^3}{(1-\varepsilon)^2}} \tag{1}$$

$$\varepsilon = 1 - \frac{W}{\rho A L} \tag{2}$$

where S_W is the specific surface area, ρ is the density of the powder, ΔP is the difference in pressure between upper and lower parts of powder column, A is the cross-sectional area of the powder column, t is the time for air flow through powder column, η is the viscosity of air, L is the length of the powder column, Q is the volume of air flowing through the powder column, ε is the porosity of the powder column, and W is the sample weight. Particle diameter (D) was determined by the following equation:

$$D = \frac{6}{\rho S_W} \tag{3}$$

Density was measured using an air comparison pycnometer (Beckman Co. Ltd., Model 930). Bulk density was determined by the volume and weight of powder when powder passed through a 24-mesh sieve was poured into a 100-ml cup using a powder tester (Hosokawa Micron Corporation, type PT-D). The results are shown in Table 1.

Observation of Particles of Excipients

The particles of various excipients were observed and photographed with a scanning electron microscope (SEM, JEOL Ltd., JST-T200).

Apparatus and Procedures

Tableting Machine

A single-punch tableting machine (Okada Seiko Co., Ltd., N-30E) with flat-face punches (cross-sectional area = 1 cm^2) was used at speed of 9.4 strokes per minute. A pair of load cells (NEC San-ei Instruments, Ltd., 9E08-D4-20) was attached at lower and upper punches.

Measurement of Punch Distance

Displacement transducers (NEC San-ei Instruments, Ltd., 9E08-D4-20) were fixed on both sides of lower and upper punches. The displacement outputs of punches, as well as the compression stress output from a load cell positioned above the upper punch, were

Table 1

Particle Diameters, Densities, and Angle of Repose of Used Powder

	Particle Diameter[a] (μm)	True Density[b] ($\times 10^3$ kg^{-3} m^{-3})	Bulk Density[c] ($\times 10^3$ kg^{-3} m^{-3})	Angle of Repose[a] (degree)
Florite® RE	0.54 ± 0.01	2.65 ± 0.30	0.08 ± 0.00	48.4 ± 1.1
Microcrystalline cellulose	9.04 ± 0.12	1.55 ± 0.01	0.29 ± 0.00	36.0 ± 2.9
Anhydrous dibasic calcium phosphate	7.97 ± 0.04	2.87 ± 0.01	0.81 ± 0.01	39.4 ± 0.9
Cornstarch	12.77 ± 0.15	1.46 ± 0.00	0.39 ± 0.01	43.8 ± 2.5
Lactose	11.01 ± 0.05	1.56 ± 0.00	0.37 ± 0.01	44.8 ± 2.4

Data represent mean ± *SD*. [a]$n = 5$, [b]$n = 4$, [c]$n = 3$.

converted to voltage change with a strain amplifier (NEC San-ei Instruments, Ltd., AS2102) and recorded with a digital recorder (NEC San-ei Instruments, Ltd., 8M37). Data was taken every 10 msec. The volume of the powder column during compression was calculated from the displacement of punches and the diameter of the die.

Tableting Procedures

After lubricating punches and die with magnesium stearate powder, sample powder (400 mg) was tapped into the die by hand and tableted by the direct compression method.

Measurement of Mechanical Energy

The plots of the compression stress against the thickness of the powder column gave the hysteresis loop shown in Fig. 1(a). As the sample was compressed, stress appeared at point *A*, and reached maximum *B* at point *C*, where the thickness of the powder column was minimum. Then, by decompression, stress became zero at point *D*. The area of the hysteresis loop (area *ABD*, S_{PE}), the area of the decompression process (area *BCD*, S_{EE}), and the total area of compression ($S_{PE} + S_{EE}$) correspond to plastic energy (*PE*), elastic energy (*EE*), and compression energy, (*CE*), respectively (8). Figure 1(b) shows the hysteresis loop obtained in compression of FLR. *PE/CE* ratio was also determined as an indication of the compactibility of an excipient.

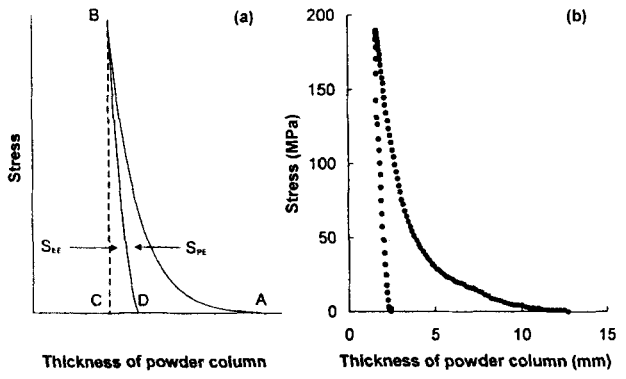

Figure 1. Plot of the compression stress against thickness of powder column: (a) schematic illustration; (b) the hysteresis loop on compression of FLR.

Tablet Hardness

Tablet hardness was obtained as diametrical compression pressure when tablets were fractured with the tableting machine described above.

Tablet Volume

Volume reduction percentage of a tablet was calculated from both volumes of powder column at point *A* (V_A) and at point *B* (V_B) in Fig. 1(a) by the following equation:

$$\text{Volume reduction percentage} = \left(1 - \frac{V_B}{V_A}\right) \times 100 \quad (4)$$

The tablet volume (V_{24h}) was determined from the diameter and thickness of tablet after 24 hr of the compression. Elastic recovery (*ER*) was obtained from V_B and V_{24h} by Eq. (5):

$$ER = \frac{V_{24h}}{V_B} \times 100\ (\%) \quad (5)$$

RESULTS AND DISCUSSION

Microscopic Observation

Scanning electron micrographs of 5 excipients are shown in Fig. 2. These excipients appear quite distinct: FLR and ADCP are particles with a rough surface, MCC seems to be fibrous structure, and LAC shows crystalline particles with a relatively smooth surface. CS is the smallest particle and has a smooth surface. However, the average diameter (summarized in Table 1) of FLR is significantly smaller than that of the other excipients. Further, the average diameter of CS is almost the same as that of LAC. It is noticed that an average diameter obtained is strongly dependent upon the measuring method. In the present study, specific surface area (S_W) determined by the air permeability method decides the result of this measurement. FLR is reported to have more pores compared with the other excipients (9); therefore, S_W of FLR contains surface area inside of the pore, so S_W of FLR is large. As a result, the average diameter is small. These morphological and physical properties of excipients are thought to be closely related to compactibility.

Mechanical Energy, Compactibility, and Hardness of Each Excipient

It is well known that energy is consumed during compression (10). De Blaey et al. (11) classified the energy consumed into the following 5 steps:

a. For arriving at the closest possible proximity of the particles of the granulate
b. By friction between the particles
c. By friction with the die wall
d. By plastic deformation
e. By elastic deformation

These steps are schematically illustrated by Carstensen (12). Steps a and b, which can be regarded as particle rearrangement and interparticulate friction, can be ignored because each powder was input into the die with tapping before the compression and, as pointed out by Blaey et al. (11), the stress was increased after the upper punch had penetrated 2–3 mm into the die. Further, step c can be also ignored since the die wall and the surface of punches are lubricated by magnesium stearate powder. Thus, the energy is assumed to be mainly consumed by steps d and e in this study.

A plot of the compression energy (*CE*) against the stress is found to be linear, as shown in Fig. 3. In this figure, the stress obtained for FLR is clearly lower than that for the other excipients over the experimental compression energy, and the increase rate of the stress observed as a slope of linear relationship is evidently small for FLR. An occurrence of little stress by use of large *CE* means that *CE* is relaxed; that is, stress relaxation occurs in FLR tablets. The results obtained agree well with those of Yuasa et al. (9), that the stress relaxation is considered to be caused rapidly by the plastic deformation and brittleness fracture of FLR particles. This result also suggests that large plastic deformation occurs

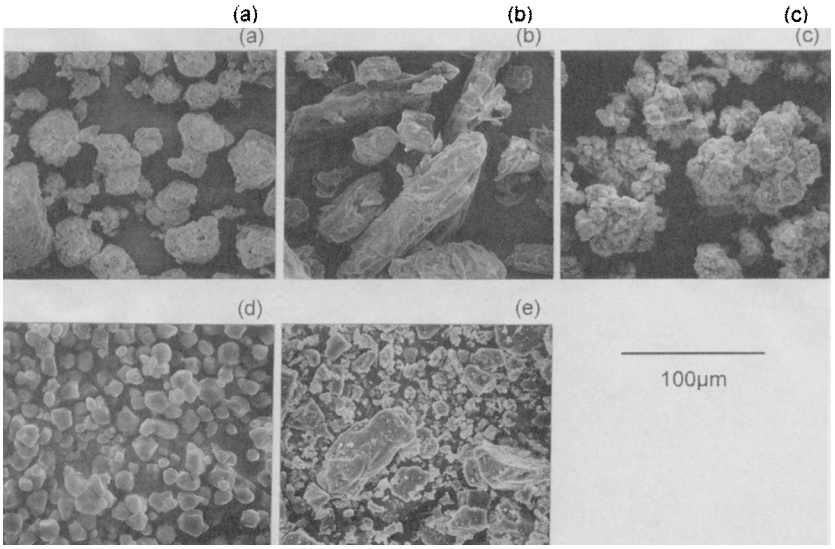

Figure 2. Scanning electron micrographs of particles of various excipients. (a) FLR, (b) MCC, (c) ADCP, (d) CS, (e) LAC.

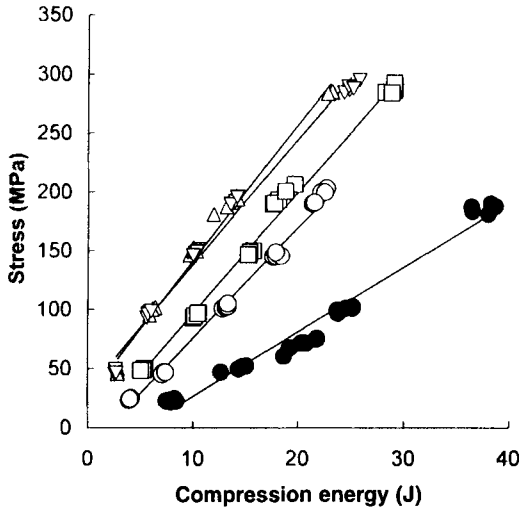

Figure 3. Relationship between compression energy and stress. ●, FLR; ○, MCC; Δ, ADCP; □, CS; ▽, LAC.

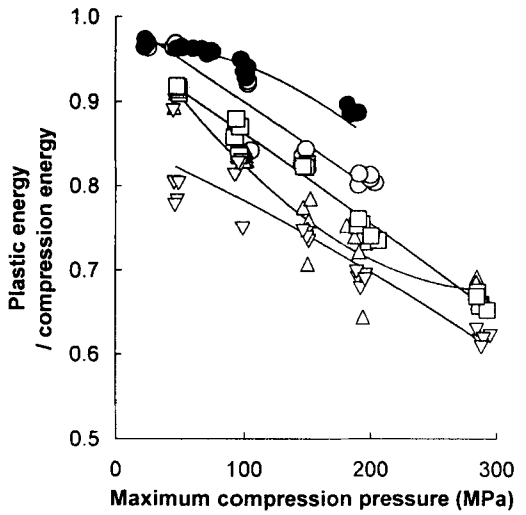

Figure 4. Relationship between maximum compression pressure and plastic energy/compression energy. ●, FLR; ○, MCC; Δ, ADCP; □, CS; ▽, LAC.

during the compression process. In addition, the change of powder column length from the beginning to maximum stress, designated as *A–C* in Fig. 1(a), is remarkably larger with FLR than with the others. The values of that change for FLR, MCC, ADCP, CS, and LAC at 200 MPa of maximum compression pressure were 12.87, 6.87, 3.33, 3.99, and 2.71 mm, respectively. As shown in Table 1, FLR powder has much lower bulk density compared with the other excipients, although the true densities of FLR and ADCP are almost the same. Therefore, this result is thought to be caused by the bulk of FLR. The physical and morphological properties of FLR seem to be closely related to the large plastic deformation shown in Fig. 3. The details of this will be discussed later.

The ratio of plastic energy (*PE*) to compression energy (*CE*), which is often used as index of plasticity of materials (10), is plotted against the maximum compression pressure (*MCP*) in Fig. 4. The value (>0.9) of *PE/CE* for FLR is the highest among the 5 excipients over the *MCP* observed. Thus FLR is again confirmed to possess higher plasticity than the other excipients. MCC also has a high *PE/CE* value at a low *MCP* (around 20–30 MPa), but the decrease in *PE/CE* with the increase in *MCP* is more significant than with FLR. As shown in Table 1 and Fig. 2, LAC and CS have rigid crystalline structures and a fine sphere-like particle, so their relatively low plasticity may result from these characteristics.

Figure 5 shows the relationship between hardness and *PE* for each tablet compressed up to 200 MPa. Tablet hardnesses of FLR and MCC increased considerably with increase in *PE*, and are particularly high over the *PE* observed, respectively. Furthermore, the largest *PE* occurring at 200 MPa of compression pressure was obtained with FLR and MCC. On the other hand, *PE* values of the other excipients are in the relatively small range. These results mean that the energy consumed by plastic deformation is used effectively to increase the mechanical strength of FLR and MCC tablets. Thus, the

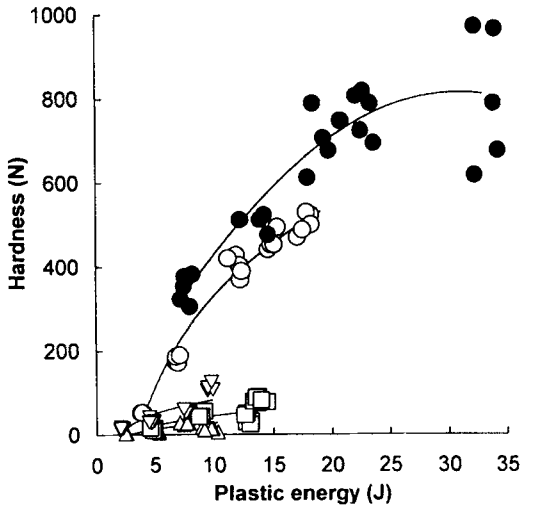

Figure 5. Relationship between plastic energy and hardness of tablets. ●, FLR; ○, MCC; Δ, ADCP; □, CS; ▽, LAC.

use of FLR or MCC as an excipient can be expected to improve tablet hardness.

Volume Reduction Percentage and Elastic Recovery

The relationship between volume reduction percentage and elastic energy (*EE*) as shown in Fig. 6 indicates that *EE* for LAC, CS, ADCP, MCC, and FLR markedly increases beyond 1 J of EE at around 45, 55, 60, 70, and 80% of volume reduction, respectively. As previously reported (2,4), FLR has a petal structure due to scaly crystals of calcium silicate, so *EE* of FLR is thought to not increase until the destruction of this characteristic structure is completed. On the other hand, *EE* of MCC should increase after a loose structure of MCC powder column formed by fibrous particles is changed into a packed, dense structure by compression. As shown in Fig. 2, ADCP is a granule with a porous structure. Because of the destruction of this structure, although it has the highest bulk density, *EE* does not begin to increase at higher volume reduction percentage than with CS and LAC. Yuasa et al. (6) have reported that brittleness fracture and plastic deformation of CS particles hardly occur up to about 200 MPa of compression pressure. LAC particles have rigid crystalline structures. So, CS and LAC attain to the close packing state; in other words, these volumes are hardly reduced at low compression pressure. Therefore, *EE* of CS and LAC begin to occur at low volume reduction percentage.

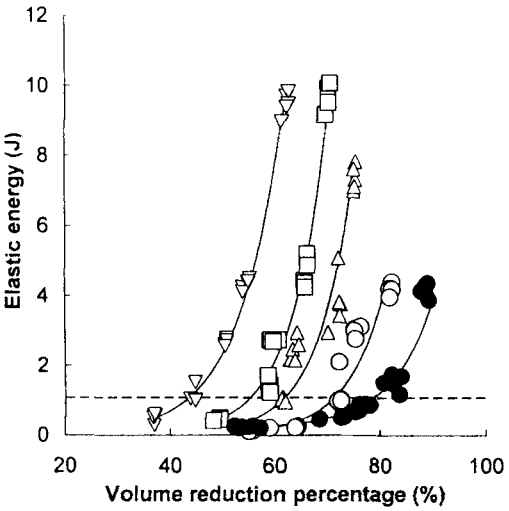

Figure 6. Relationship between volume reduction percentage and elastic energy. ●, FLR; ○, MCC; △, ADCP; □, CS; ▽, LAC.

Hardness and Elastic Recovery

Elastic recovery (*ER*) is also important property for evaluating the compactibility of excipients, since large *ER* values sometimes cause serious problems such as a coating failure and large friability. Figure 7 shows the relationship between *ER* and tablet hardness for each excipient. In ADCP, CS, and LAC tablets, *ER* increased at low hardness (<20 N), while in FLR and MCC tablets, *ER* increased remarkably at very high hardness, around 600 and 400 N, respectively. *ER* of both tablets can therefore be controlled to make it low and constant over a wide range of hardness.

As described in Fig. 6, there is a volume reduction at which *ER* is markedly increased. A hardness at which *ER* is increased (Fig. 7) is thought to be related to this volume reduction. This means that an increase in *ER* of FLR and MCC tablets occurs after 80% and 70% volume reduction, respectively. The contact points and contact area among particles due to the plastic deformation and brittleness fracture of FLR increase with the increase in compression force until the structure is completely packed. This structure is achieved at 80% volume reduction in FLR tablets and its hardness would not increase after the achievement of this structure because no further increase in contact points or contact area inside of FLR tablet is possible. Similar changes are assumed to occur in MCC tablets, but twining of fibrous MCC rather than fracture of the MCC particle seems to play an important role in this tablet. Yuasa et al. (6)

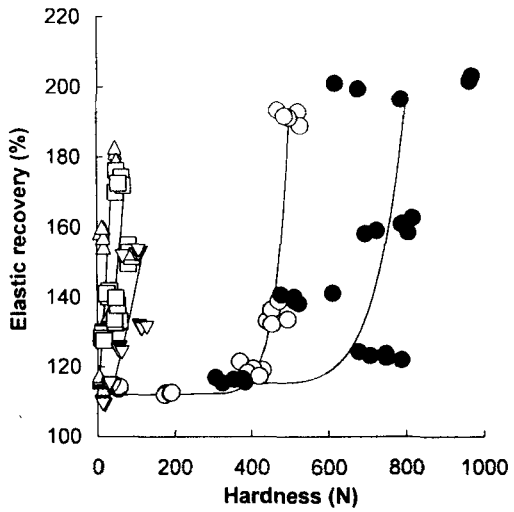

Figure 7. Relationship between hardness and elastic recovery. ●, FLR; ○, MCC; △, ADCP; □, CS; ▽, LAC.

suggest that this structure affects the mechanical strength and internal structure of MCC tablets.

CONCLUSION

In the present study, FLR was found to have higher plasticity than 4 other excipients, due to plastic deformation and brittleness fracture. This high plasticity appears to be responsible for the high hardness of FLR tablets. Further, elastic recovery can be controlled to remain at low values over a wide range of tablet hardnesses. These characteristics suggest that FLR would be a versatile excipient in tablet formulation.

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