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Comparison of the compression characteristics between new one-step dry-coated tablets (OSDRC) and dry-coated tablets (DC)

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Abstract

One-step dry-coated tablets (OSDRC) were prepared using materials which are generally used in pharmaceutical tablets. The radial tensile strength of OSDRC was measured for various compression pressures and core porosities before the final compression to compare with that of conventional dry-coated tablets (DC). Furthermore, stress relaxation in the compression process was investigated. Radial tensile strength and stress relaxation profiles of OSDRC were the same as those of conventional DC. X-ray computerized tomography (CT) of the tablets showed that the density distribution of both tablets was also the same. Thus, we concluded that OSDRC and conventional DC have the same compression characteristics and physical properties. The OSDRC-system was executed by the use of upper and lower punches, which had a double structure, a center punch, and an outer punch surrounding the center punch. The OSDRC process consists of three compressions to make the lower-outer layer (1st-outer layer), the core, and the whole tablet including the upper-outer and side-outer layers (2nd-outer layer). At first, the powder for the 1st-outer layer fills a space, which is made by the lower-center punch and lower-outer punch, and is pre-compressed by the upper-center punch. Then, while the upper-center punch pushes the pre-compressed 1st-outer layer, the lower-center punch is slid down. The upper-center punch is then pulled away to make a space, which is filled with the powder for the core. This is then pre-compressed by the upper-center punch. Finally, the lower-outer punch is slid downward and the powder for the 2nd-outer layer fills and surrounds the pre-compressed core/1st-outer layer completely. The core/1st-outer layer and the 2nd-outer layer complex is then compressed by the upper and lower punches in which the center punches are unified with the outer punches, respectively. This system can be assembled onto the turn table of a rotary tableting machine, and can make a dry-coated tablet in a single turn.

Keywords: One-step dry-coated tablets; Dry-coated tablets; Compression coated tablets; OSDRC-system; Compression test; Stress relaxation; Tensile strength

1. Introduction

The manufacturing method of conventional dry-coated tablets (DC) requires the preparation of the core tablets beforehand. The conventional method is: (1) the powder for the outer layer fills the inside of the die,

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(2) the core tablet is placed on the powder from Step 1, (3) the remaining powder for the outer layer surrounds the core tablet, and (4) the powder containing the core tablet is compressed. However, the manufacturing cost of this method is high because of the necessity to compress the core tablets in advance. In addition, this method can cause problems such as non-core, double-core, off-center, inlay, and cooking, caused by the core tablet supply system. For these reasons, DC have not been as widely used as normal tablets. Hence, we report a novel one-step dry-coated tablet manufacturing method (one-step dry-coated tablet-system: OSDRC-system) (Ozeki et al., 2001) to solve the problems associated with the conventional DC.

The new manufacturing method for DC was executed with the use of upper and lower punches, which had a double structure, a center punch, and an outer punch surrounding the center punch. The OSDRC process consists of three compressions to make the lower-outer layer (indicated as 1st-outer layer), the core, and the whole tablet, including the upper-outer and side-outer layers (indicated as 2nd-outer layer). At first, the powder for the 1st-outer layer fills a space, which is made by the lower-center punch and lower-outer punch, and is pre-compressed by the upper-center punch. Then, while the upper-center punch pushes the pre-compressed 1st-outer layer, the lower-center punch is slid down. The upper-center punch is then pulled away to make a space, which is filled with the powder for the core. This is then pre-compressed by the upper-center punch. Finally, the lower-outer punch is slid downward and the powder for the 2nd-outer layer fills and surrounds the pre-compressed core/1st-outer layer completely. The core/1st-outer layer and the 2nd-outer layer complex is then compressed by the upper and lower punches, in which the center punches are unified with the outer punches, respectively.

This manufacturing method does not require the preparation of the core tablets beforehand, allowing the DC to be made in one process. Furthermore, this method causes no problems with the core, which are observed for conventional DC; namely, we can produce DC as easily as normal tablets.

This study was conducted to compare the physical properties, compression characteristics, and internal structures between OSDRC and conventional DC. We also clarified the effects of the initial core porosity (core porosity before the last compression) as a factor of DC on the tablet's compression characteristics.

2. Materials and methods

2.1. Materials

The sample powders used were α-lactose monohydrate (DMV 200), cornstarch (Nihon shokuhin kako Co., Ltd.; Cornstarch) and hydroxypropylcellulose (Nippon Soda Co., Ltd.; HPC-L) as high polymer binders, and ascorbic acid(Roche Co., Ltd.; L-ascorbic acid) as a model core medicine. These materials are well known to cause tablet failure due to brittleness. The core and outer layer ingredients of the sample are listed in Table 1.

2.2. Granulation method

The powder mixtures for the core and outer layer were granulated, respectively, before the compression with a fluidized bed granulator (Freund Co., Ltd.; FLO-5) after sieving the materials with 42 meshes. The following granulating conditions were kept constant during the granulation process: inlet air temperature, 80 °C; outlet air temperature, 30 °C; and the purified water, 1100 ml, sprayed onto the 2100 g compound.

2.3. Compression test

All samples were compressed using a universal tension and compression tester (Simadzu Co., Ltd.; Autograph AG-5000D) with 6 mm + 8 mm double structure flat-face punches. Moreover, the compression characteristics were evaluated by Heckel's equation:

$$\ln\left(\frac{1}{1-D}\right) = KP + A \qquad (1)$$

Table 1
Ingredients of OSDRC and DC

Material	Core (mg/tablet)	Outer layer (mg/tablet)	Total (mg/tablet)
Lactose	70	100	
Cornstarch	30	43	
Ascorbic acid	43	–	
HPC-L	7	7	
Total	150	150	300

where D is the relative density of the powder bed during compression to the applied pressure, P (Danjo et al., 1994).

2.4. Measurement of radial tensile strength

Using tablet hardness measurement equipment (Toyama Chem. Co., Ltd.; TH-203), we subjected the model tablets to a diametrical compression test after they had been allowed to remain at room temperature for 24 h in a desiccator. The maximum load, F, which was applied diametrically to fracture the tablet, was determined. The radial tensile strength, T_s, was calculated using the following equation (Fell and Newton, 1970):

$$T_s = \frac{2F}{\pi d L} \tag{2}$$

where d is the tablet diameter and L is the tablet thickness.

2.5. Measurement of stress relaxation

Stress relaxation experiments were performed using the Autograph equipped with 6 mm + 8 mm double structure flat-face punches, on a tablet weighting 300 mg. The evolution of the force in relation to time caused by the upper punch displacement was then recorded for 15 min (Kawashima et al., 1995; Imai et al., 2001). The measurement value of stress relaxation under these conditions, without being filled with powder, was deducted from the measurement value, and was rectified.

The rate of relief, $Y(t)$, was calculated using the following equation:

$$Y(t) = \frac{P_0 - P_t}{P_0} \tag{3}$$

where P_0 is the initial force, and P_t is the decaying force after time t. The determined $Y(t)$ with t was fitted to Eq. (5), obtained by the modification of Kawakita's equation, Eq. (4), to estimate constants a and b, which characterize stress relaxation (Danjo et al., 1996, 1998):

$$Y(t) = \frac{abt}{1 + bt} \tag{4}$$

$$\frac{t}{Y(t)} = \frac{1}{ab} + \frac{t}{a} \tag{5}$$

2.6. Evaluation of the internal structure

The internal density of a dry-coated tablet was measured using high resolution X-ray CT equipment (JFCC Foundation specification). The image obtained was analyzed with image analysis equipment (BIR Co., Ltd.; ACTIS+3).

3. Results and discussion

3.1. OSDRC-system and its features

The outline of the devised novel OSDRC-system is shown in Fig. 1. This system was devised to be applied to a rotary-type tableting machine. However, for this study we used a single set of punches and die for OSDRC (Fig. 2). The model punches and die are shown in Fig. 2. The upper and lower punches consisted of the center punches (diameter: 6 mm) and the outer punches (outside diameter: 8 mm) surrounding the center punches. The OSDRC process consisted of three compressions to make the 1st-outer layer, the core, and the whole tablet, including the 2nd-outer layer.

To make the 1st-outer layer, the lower-center punch (b1) was slid down, and the powder for the 1st-outer layer filled the space made by the lower-center punch (b1) and the inside wall of the lower-outer punch (b2). The powder was pre-compressed by the upper-center punch (a1).

Then, while the upper-center punch pushed the pre-compressed 1st-outer layer, the lower-center punch was slid down. The upper-center punch was pulled away to make a space which was filled with the powder for the core, and was then pre-compressed by the upper-center punch (a1).

Finally, after sliding the lower-outer punch (b2) downward, the pre-compressed core/1st-outer layer was surrounded completely by the powder for the 2nd-outer layer. On the last compression, the upper-center punch (a1) and the upper-outer punch (a2) were united by a joint part (c), as were the lower punches. Thereby, they could be used as one punch and compressed the whole powder together. Additionally, the compression speed and pressure of the center and outer punches was the same during the last compression. When these punches were united,

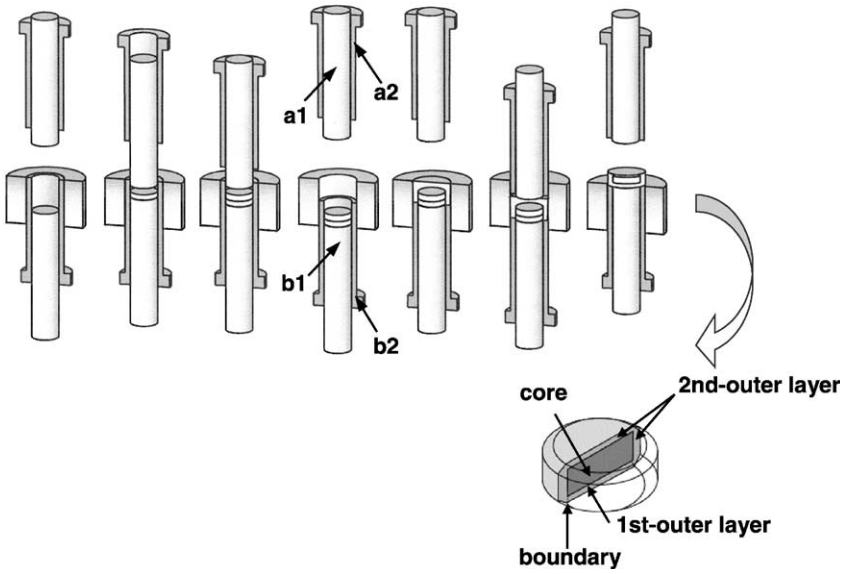

Fig. 1. Mechanism of OSDRC-system.

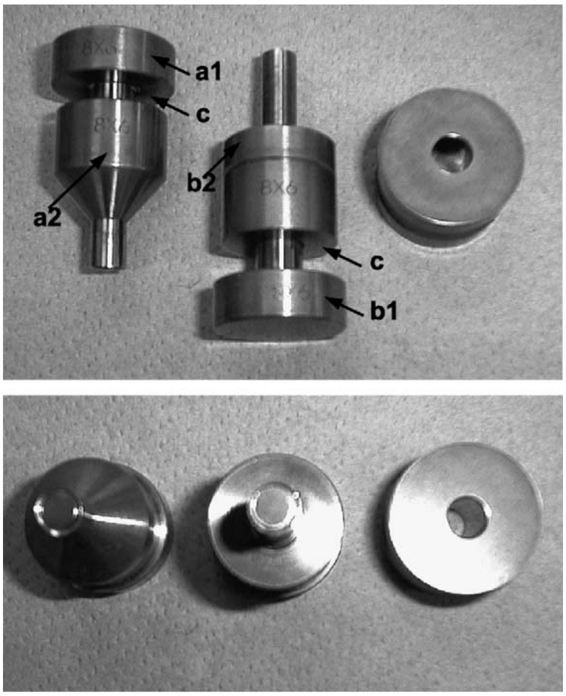

Fig. 2. Experimental punch and die for OSDRC-system.

the tip of the punches had a flat face, like a normal punch.

3.2. Comparison of the compression characteristics between OSDRC cores and conventional DC cores

In the pre-compression of the OSDRC process, the core could not be compressed individually from the 1st-outer layer. The comparison of the compression characteristics between OSDRC cores (core/1st-outer layer) and conventional DC cores was made in order to clarify the influence of the 1st layer upon the core compression.

The Heckel's plots of both cores were very similar (Fig. 3). Both cores exhibited a curve under a low pressure, but were linear under a high compression pressure. Generally, the rearrangement of the particles occurs under a low compression pressure. In contrast, the particles plastic deformation, adhesion, and union occur under a high compression pressure. From the Heckel's plots, we assumed that the same compression process occurred in both cores in this study. This experiment demonstrated that the core, including the outer layer, of OSDRC and the core tablet of conventional DC were similar in their compression characteristics.

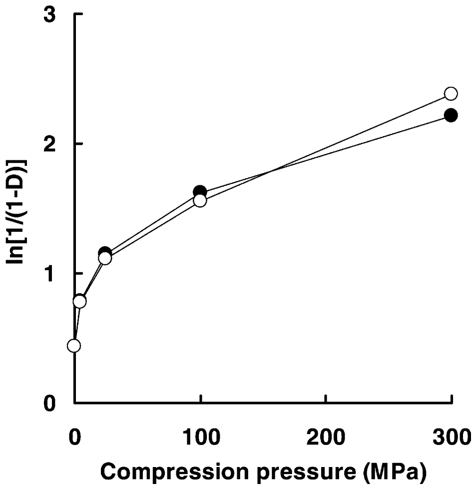

Fig. 3. Heckel's plot for OSDRC cores and conventional DC cores. (●) core and outer layer of OSDRC; (○) core tablet of conventional DC.

The porosity of the core/1st-outer layer of OSDRC and the core of conventional DC for various compression pressures is shown in Fig. 4. Both porosities similarly decreased with increasing compression pressure and showed a good correlation with the logarithm of compression pressure, which is described with Eq. (6) as:

$$\varepsilon = \varepsilon_0 - \frac{1}{R} \ln P \quad (6)$$

where ε_0 is the initial porosity and R is the experimental constant.

We calculated the ε_0 and R values for OSDRC cores and conventional DC cores by computer fitting of data to Eq. (6). The initial core porosity, ε, for the compression test and the stress relaxation examination at various compression pressures, P, was estimated with the ε_0 and R values.

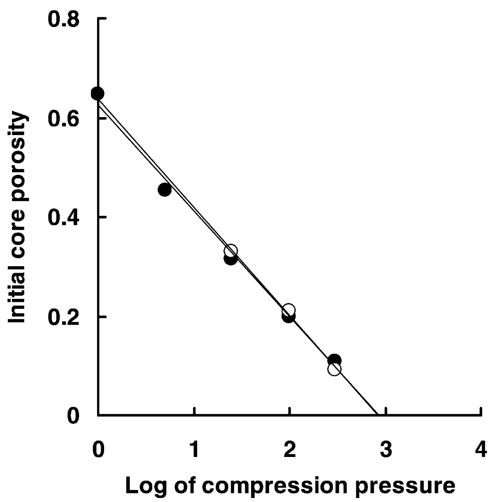

Fig. 4. Relationship between compression pressure and core porosity of OSDRC and conventional DC. (●) core of OSDRC, $y = 0.6254 - 0.2134x$ ($R^2 = 0.9933$); (○) core of conventional DC, $y = 0.6381 - 0.2181x$ ($R^2 = 0.9953$); y: porosity of core, and x: log of compression pressure.

3.3. Comparison of radial tensile strength between OSDRC and conventional DC

The radial tensile strength of OSDRC and conventional DC (150 mg of core) was examined at various compression pressures, as shown in Fig. 5. The tensile strength increased with compression pressure in both tablets, and the strength of OSDRC was similar to that of conventional DC for various pressures. The

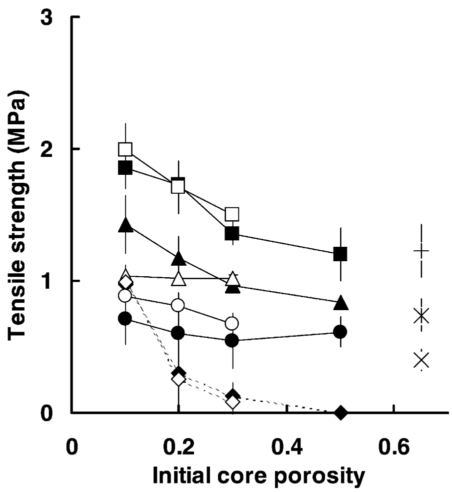

Fig. 5. Relationship between tensile strength of OSDRC and conventional DC and core porosity. core: 150 mg; outer layer: 150 mg; compression pressure: (●, ○) 100 MPa, (▲, △) 150 MPa, (■, □) 200 MPa, and (◆, ◇) core only. Tablets were prepared using the OSDRC method (closed symbols) or the conventional DC method (open symbols) at various compression pressures, or only the outer layer ingredient (non-core tablet) was compressed at 100 MPa (×), 150 MPa (∗), or 200 MPa (+). Error bars indicate S.D. ($n = 3$).

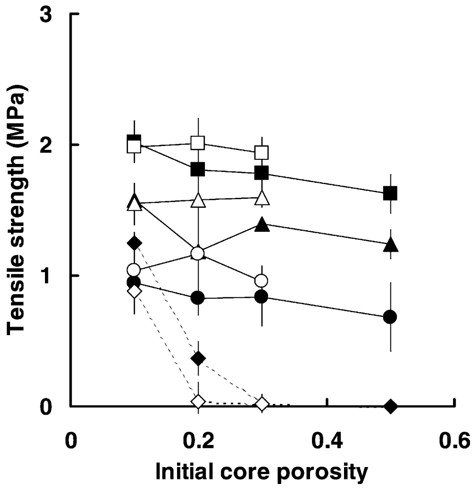

Fig. 6. Relationship between tensile strength of OSDRC and conventional DC and core porosity. core: 90 mg; outer layer: 210 mg; compression pressure: (●, ○) 100 MPa, (▲, △) 150 MPa, (■, □) 200 MPa, and (◆, ◇) core only. Tablets were prepared using the OSDRC method (closed symbols) or the conventional DC method (open symbols) at various compression pressures. Error bars indicate S.D. ($n = 3$).

same result was observed when the weight of the core tablet was changed to 90 from 150 mg, as shown in Fig. 6.

The outer-layer of OSDRC is made in two steps by the first and last compressions. However, the destruction of the outer layer boundary of OSDRC was not observed during the tablet hardness measurement. Therefore, we considered that the effect of the pre-compression of the 1st-outer layer on the radial tensile strength of the whole tablet was very small.

3.4. Effect of initial core porosity on compression characteristics

The tensile strength of both OSDRC and conventional DC slightly increased with decreasing initial core porosity, as shown in Fig. 5. This effect was greater at high compression pressures rather than at low pressures. This was not so obvious in tablets with a small core (90 mg), as shown in Fig. 6.

In an additional experiment conducted to explain this phenomenon, the tensile strength of a tablet consisting of only the ingredients for the outer layer (non-core tablet) was lower than that of a tablet including a core, as shown in Fig. 5 (symbols: ×, *, and +). This suggested that uncompacted particles decayed the pressure-transmission and increased the variation of the density distribution in the tablet with no lubricant, since the powder had a high coefficient of internal friction. In other words, the non-uniform filling structure inside the non-core tablets or the tablets with high initial core porosity resulted in the decreased tensile strength, because no lubricant was used in the present study.

3.5. Effect of initial core porosity on both tablet's stress relaxation

In order to examine the effect of the initial core porosity and compression characteristics of OSDRC and conventional DC in detail, the stress relaxation profile was measured as an index of the particle re-arrangement and plastic deformation. Then, both tablets with different initial core porosities were compressed by various pressures. There was no difference between the stress relaxation curves of both tablets (data not shown), and the amount of relaxation decreased with an increase in compression pressure. Although various equations for stress relaxation exist, we used Eqs. (3) and (4) proposed by Peleg and Moreyra (1979) and Kawakita and Ludde (1971), respectively. Eq. (5), obtained by modifying Eq. (4), predicts a linear relationship between $t/Y(t)$ and t. Plotting data for OSDRC and conventional DC according to Eq. (5) showed good linearity (Fig. 7).

The relationship between the initial core porosity, the compression pressure, and each constant is shown in Fig. 8. The constant a values of OSDRC and conventional DC showed no difference, regardless of the initial core porosity and compression pressure, and both plots showed the same tendency.

Generally, constant a shows the value of relaxation in infinite time (Imai et al., 2001), and a large a value means that the stress relaxation is large. As shown in Fig. 8, constant a decreased with increasing compression pressure. The stress relaxation is caused by the re-arrangement, crushing of particles, and plastic deformation of the particles themselves (Cutt et al., 1987). Thus, the internal filling structure inside a tablet becomes dense with increasing compression pressure.

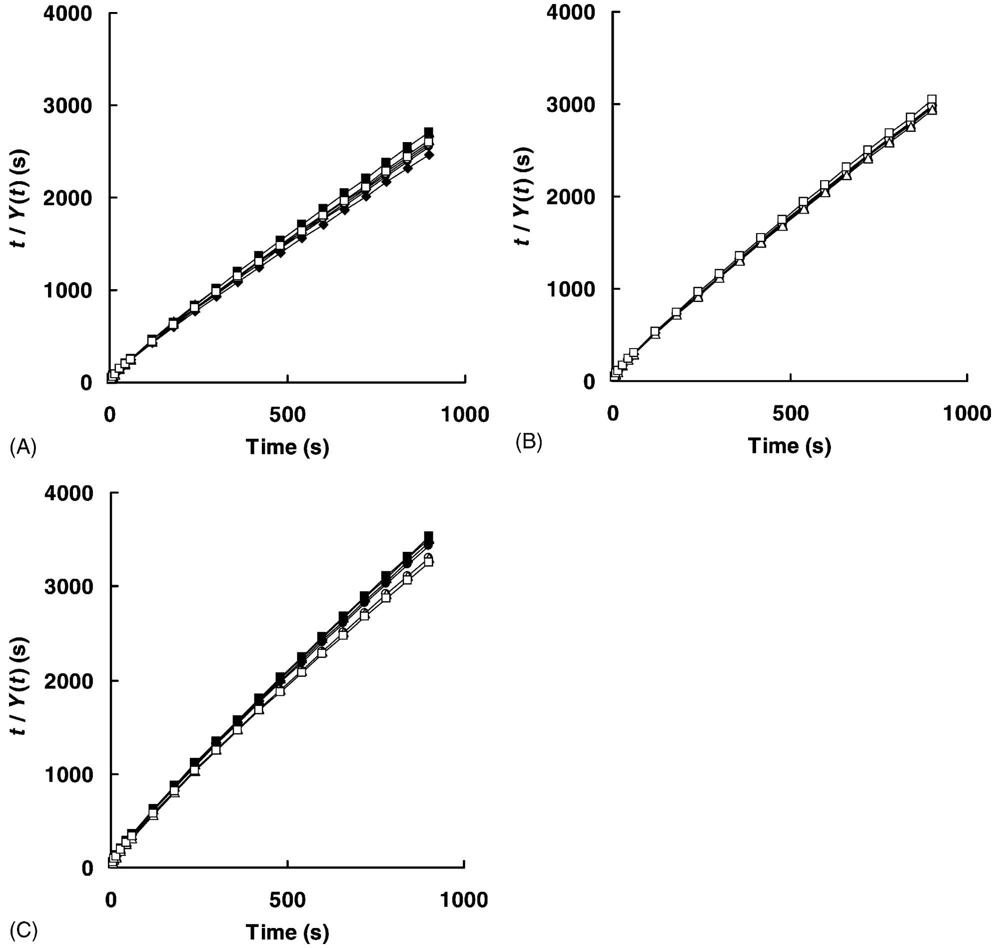

Fig. 7. Relationship between $t/Y(t)$ and t. porosity of core: (◆) 0.5, (●, ○) 0.3, (▲, △) 0.2, and (■, □) 0.1. Tablets were prepared using the OSDRC method (closed symbols) or the conventional DC method (open symbols) at various compression pressures. compression pressure: (A) 100 MPa, (B) 150 MPa, and (C) 200 MPa.

Fig. 8 suggests that neither re-arrangement nor plastic deformation could occur easily while the upper punch was held in position, and the extent of relaxation was decreased. In addition, the relaxation already occurred during the compression, due to low speed compression in this study.

Constant b is an index showing relaxation speed, and the relaxation speed is quick when the b value is large. There was no difference between OSDRC and conventional DC regardless of the initial core porosities and compression pressures for constant b, and both plots showed the same tendency. Constant b was almost independent of the initial core porosity. On the other hand, it varied by the compression pressure. However, no clear relationship between constant b and the compression pressure was observed.

3.6. Evaluation of the internal structure

The internal structure of OSDRC and conventional DC was evaluated using X-ray CT equipment. The result is shown in Fig. 9. The density distribution of OSDRC and conventional DC was similar. Both

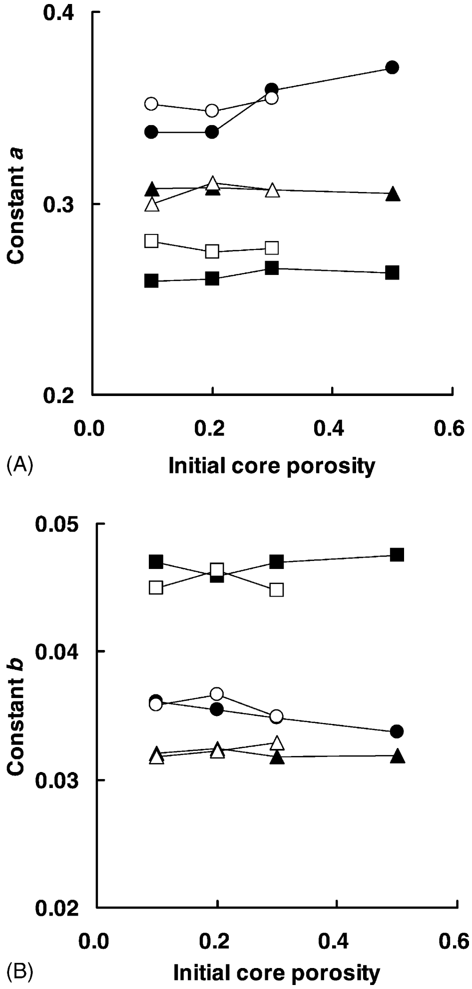

Fig. 8. Relationship between porosity of the core and the constant for OSDRC and conventional DC. (A) The constant *a*, (B) the constant *b*; compression pressure: (●, ○) 100 MPa, (▲, △) 150 MPa, and (■, □) 200 MPa. Tablets were prepared using the OSDRC method (closed symbols) or the conventional DC method (open symbols) at various pressures.

tablets were compressed at pressures of 100 and 200 MPa. Although the porosities of the initial core (0.1) and the powder for the 2nd-outer layer (0.63) were different, there was no exfoliation between the 1st-outer layer and the 2nd-outer layer.

After measuring the tablets with the X-ray CT equipment, the values of the X-ray absorption per unit volume (CT value) were reconstructed into two-dimensional images. The high density point is

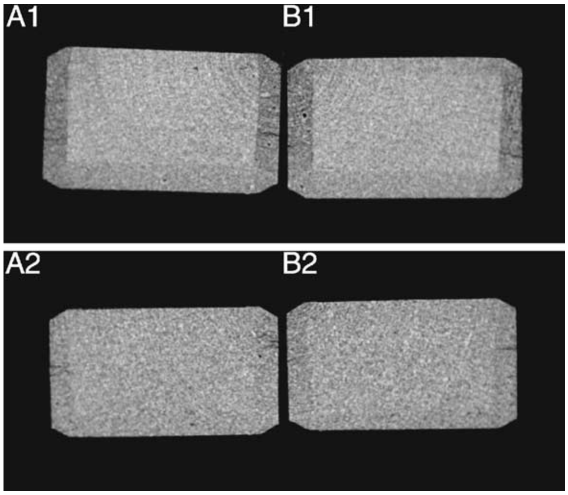

Fig. 9. X-ray computerized tomography image of a cross section OSDRC and conventional DC. A1, A2: OSDRC; B1, B2: DC; A1, B1: compression pressure 100 MPa; and A2, B2: compression pressure 200 MPa. All initial core porosities were 0.1.

shown brighter in Fig. 9. For the compression pressure 100 MPa, the difference in the density of the core and the outer layer was clear, as indicated in A1 and B1 in Fig. 9. The side densities of the OSDRC and conventional DC were especially low. We assumed this result was due to a high density of the core (hard to shrink), which prevented enough pressure-transmission to the side portion of tablet. At 200 MPa the boundary of the core and the outer layer for OSDRC and conventional DC was indefinite, which supported that both internal structures were equalizing.

We concluded that the compression characteristics of OSDRC and conventional DC were very similar due to the internal density distribution being the same. Furthermore, exfoliation of the 1st- and 2nd-outer layers of OSDRC was not observed.

4. Conclusion

When comparing compression characteristic between OSDRC made by the new manufacturing method and conventional DC, it was found that:

(1) Both tablets had equivalent radial tensile strengths for the various compression pressures, and the

strength increased with an increase in compression pressure. From this result, we assumed there was no influence of the difference in manufacturing method on the physical characteristics of the tablets.

(2) The radial tensile strength of both tablets increased a little with a decrease in the initial core porosity. We considered that the internal density of the tablets became uniform due to the internal pressure-transmission being improved with the high-density core.

(3) Both tablets showed almost equivalent curves for the stress relaxation examination. This was due to the same re-arrangement manner of the particles and compression flow in the compression processes.

(4) The internal structure X-ray CT showed that the internal distribution of density in both tablets was similar.

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