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# The Effect of Crystal Hardness on Compaction Propensity

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The effect of crystal hardness on the compaction mechanism and tensile strength of tablets was investigated by using twelve different materials. The tensile strength of tablets was found to be independent of crystal hardness. This result suggests that crystal hardness is not directly associated with the binding force between crystal particles, and this result can be ascribed to differences in the mode of crystal deformation, that is, fragmentation, plastic flow, *etc.* The reciprocal of crystal hardness was correlated to the $K$ value in the Heckel equation for organic materials. Furthermore, at constant pressure there was a linear relationship between the reciprocal of crystal hardness and the logarithm of the reciprocal of fractional voidage.

**Keywords**——crystal hardness; tensile strength; compaction; tablets; fragmentation; plastic flow

## Introduction

In previous paper, the effect of particle size on the compaction properties and mechanism was reported for sulfadimethoxine and sulfaphenazole as model drugs.[1] Since crystal hardness might be a significant factor with respect to compaction propensity, we next investigated the effect of crystal hardness (measured with a Vickers hardness tester) on the binding between crystal particles of twelve different materials. The results are presented here.

## Experimental

**Materials**——The materials examined in this study were sulfadimethoxine (Dainippon Seiyaku Co., Ltd.), sulfaphenazole (Dainippon Seiyaku Co., Ltd.), acetaminophen (Hoei Yakko Co., Ltd. (JP grade)), aspirin (Tsukishima Yakuhin Co., Ltd. (JP grade)), hexamethylenetetramine (Wako Junyaku Kogyo Co., Ltd. (reagent grade)), lactose (Hoei Yakko Co., Ltd. (JP grade)), phenacetin (Sankou Seiyaku Kogyo Co., Ltd. (JP grade)), salicylamide (Iwaki Seiyaku Co., Ltd.), sucrose (Wako Junyaku Kogyo Co., Ltd. (reagent grade)), urea (Wako Junyaku Kogyo Co., Ltd. (reagent grade)), potassium chloride (Wako Junyaku Kogyo Co., Ltd. (reagent grade)), and sodium chloride (Wako Junyaku Kogyo Co., Ltd. (reagent grade)). For compression, sulfadimethoxine and sulfaphenazole were separated into 42/48, 80/100, and 170/200 mesh fractions and other materials were sieved to obtain 42/48 mesh powder by the use of J.I.S. sieves fitted on a sonic sieve tester made in this laboratory. For measuring crystal hardness, lactose, potassium chloride, and sodium chloride were recrystallized from distilled water, acetaminophen, hexamethylenetetramine, phenacetin, salicylamide, sulfadimethoxine, and sulfaphenazole were recrystallized from ethanol, aspirin was recrystallized from acetone, and sucrose and urea were not recrystallized but were used as intact crystals.

**Compression Apparatus and Procedures**——Compression was carried out as described previously.[1]

**Tensile Strength**——The measurement of tensile strength was carried out as reported in the previous paper.[1]

**Crystal Hardness**——A crystal was fixed on a glass plate and the crystal hardness was determined by the use of a Vickers hardness tester. A load of 10, 25, or 50 g applied to the crystal and after 30 s, the diagonal length of the indentation was measured. Then, the value measured was converted to the Vickers hardness number ($H_v$) from the following relationship:

$$H_v = \frac{\text{applied load}}{\text{contact area of indenter}} \quad (1)$$

## Results and Discussion

Crystal hardness measured under various applied loads and the tensile strength of tablets[2] produced under $100 \times 10^7$ dyn/cm$^2$ are shown in Table I. The crystal face possessing the largest area, that is, the face that grew most slowly during crystallization, was used to measure crystal hardness. The compaction properties are greatly influenced by the crystal face having the largest area, since the broadest face aligns itself parallel to the punch face as a preferred orientation during compression; *i.e.*, the compression pressure is mainly resisted by that face. The results indicated that the tensile strength of tablets is independent of crystal hardness. For example, sulfaphenasole possessed about 3 times the crystal hardness of aspirin, but sulfaphenazole tablets showed the same tensile strength as those of aspirin. This result can be ascribed to differences of crystal deformation, fragmentation, plastic flow, and so forth. Heckel[3,4] has proposed the following equation:

TABLE I. Vickers Hardness Number, $H_v$, and Tensile Strength for Various Materials

| Material | Applied load (g) | Vickers hardness number, $H_v$[a] ($\times 10^8$ dyn/cm$^2$) | Standard deviation ($\times 10^8$ dyn/cm$^2$) | Tensile strength ($\times 10^5$ dyn/cm$^2$) |
|---|---|---|---|---|
| Acetaminophen | 10 | 35.8 | 3.03 | 29.9 |
| | 25 | 37.0 | 5.12 | |
| | 50 | 29.7 | 3.69 | |
| Aspirin | 10 | 9.81 | 0.814 | 110 |
| | 25 | 9.29 | 1.89 | |
| Hexamethylenetetramine | 10 | 4.71 | 0.638 | 40.0 |
| | 25 | 4.20 | 0.186 | |
| | 50 | 3.65 | 0.432 | |
| Lactose | 10 | 53.5 | 2.75 | 58.5 |
| | 25 | 52.7 | 4.80 | |
| | 50 | 50.6 | 10.3 | |
| Phenacetin | 10 | 18.3 | 0.981 | 22.0 |
| | 25 | 16.2 | 0.589 | |
| | 50 | 17.0 | 0.726 | |
| Salicylamide | 10 | 14.0 | 1.35 | 70.3 |
| | 25 | 10.4 | 0.903 | |
| | 50 | 12.5 | 1.72 | |
| Sucrose | 10 | 49.6 | 11.5 | 85.8 |
| | 25 | 56.2 | 10.5 | |
| | 50 | 49.1 | 5.68 | |
| Sulfaphenazole | 10 | 29.1 | 0.245 | 110 |
| | 25 | 28.9 | 0.196 | |
| | 50 | 28.6 | 0.353 | |
| Sulfadimethoxine | 10 | 24.0 | 3.33 | 22.0 |
| | 25 | 26.3 | 7.14 | |
| | 50 | 19.1 | 2.58 | |
| Urea | 10 | 8.30 | 0.540 | 84.3 |
| | 25 | 9.20 | 2.74 | |
| | 50 | 7.26 | 0.186 | |
| Potassium chloride | 10 | 10.6 | 0.177 | 235 |
| | 25 | 9.64 | 0.441 | |
| | 50 | 10.1 | 0.618 | |
| Sodium chloride | 10 | 19.1 | 0.677 | 230 |
| | 25 | 18.1 | 0.275 | |
| | 50 | 17.6 | 0.392 | |

a) The number of measurements was three.

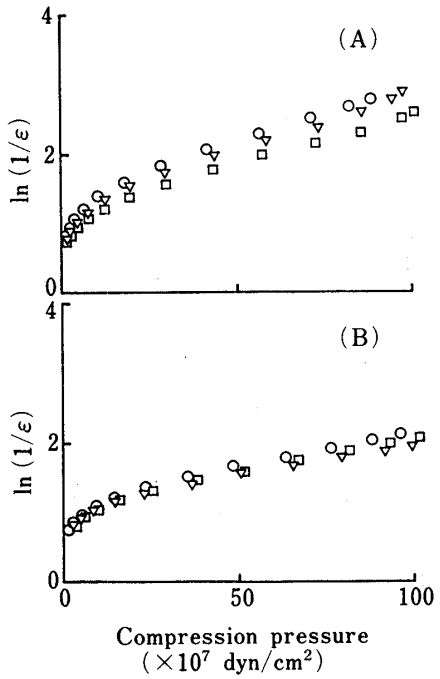


Fig. 1. Heckel Plots for the Three Size Fractions of Sulfadimethoxine and Sulfaphenazole

(A) SD, (B) SP. ○, −42+48 mesh; ▽, −80+100 mesh; □, −170+200 mesh.

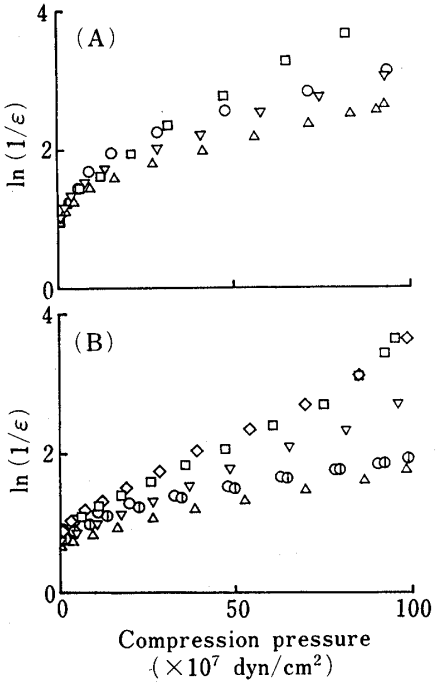


Fig. 2. Heckel Plots for Various Materials

(A) △, acetaminophen; ○, aspirin; ▽, phenacetin; □, salicylamide.
(B) ◇, hexamethylenetetramine; ○, lactose; ▽, potassium chloride; △, sodium chloride; ⓘ, sucrose; □, urea.

$$\ln(1/(1-D)) = KP + A \tag{2}$$

This equation is the most widely used equation relating the relative density, $D$, of a powder bed during compaction to the applied pressure, $P$, $K$ and $A$ are constants, and $1-D$ is the fractional voidage, $\varepsilon$. Equation 2 may thus be written in the form:

$$\ln(1/\varepsilon) = KP + A \tag{3}$$

Figure 1 shows Heckel plots for sulfadimethoxine and sulfaphenazole. Sulfadimethoxine, which undergoes particle fragmentation during compaction,[1] also showed a clear particle size effect in the Heckel plots. An increase in the particle size of sulfadimethoxine resulted in an increase in the relative density for a given applied pressure. It seems probable that the fractured particles occupy the interparticle voids between the larger crystal particles. Heckel plots for various materials are shown in Fig. 2. The slope ($K$) in the linear region takes various values among the materials. Heckel has reported that the $K$ value is related to the reciprocal of hardness in the case of metals. Plots of $K$ value against the reciprocal of crystal hardness (applied load: 10 g) are shown in Fig. 3. It was also found with regard to organic materials that the $K$ value tended to increase with the reciprocal of crystal hardness. Furthermore, as there is a relationship between the $K$ value and the reciprocal of crystal hardness, the following relationship can be derived from Eq. 3 at constant pressure.

$$1/H_v \propto \ln(1/\varepsilon) \tag{4}$$

Figure 4 shows plots of $1/H_v$ against $\ln(1/\varepsilon)$ for the tablets (compression pressure: $100 \times 10^7$ dyn/cm$^2$). There was a linear relationship between $1/H_v$ and $\ln(1/\varepsilon)$, and the equation of the line of best fit was

$$1/H_v = 0.0646 \times 10^{-8} \ln(1/\varepsilon) - 0.104 \times 10^{-8} \tag{5}$$

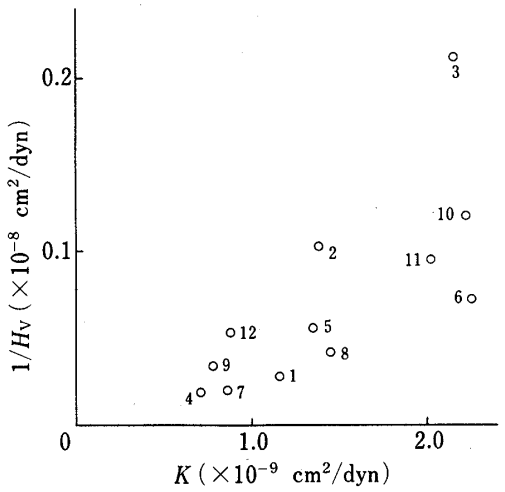


Fig. 3. Relation between Reciprocal of Crystal Hardness (Applied Load: 10 g), $1/H_v$, and $K$ Value in Heckel Plots (Particle Size: 42/48 Mesh)

1, acetaminophen; 2, aspirin; 3, hexamethylenetetramine; 4, lactose; 5, phenacetin; 6, salicylamide; 7, sucrose; 8, sulfadimethoxine; 9, sulfaphenazole; 10, urea; 11, potassium chloride; 12, sodium chloride.

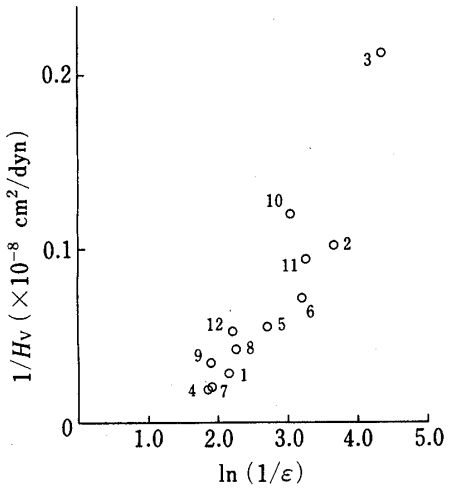


Fig. 4. Relation between Reciprocal of Crystal Hardness (Applied Load: 10 g), $1/H_v$, and Natural Logarithm ($1/\varepsilon$)

Key as in Fig. 3 (particle size: 42/48 mesh). The regression equation is $1/H_v = 0.0646 \times 10^{-8} \ln(1/\varepsilon) - 0.104 \times 10^{-8}$; $r = 0.927$, $F = 61.1$, $p < 0.01$ and $n = 12$.

with a correlation coefficient of 0.927 ($F = 61.1$, $p < 0.01$ and $n = 12$). Figure 4 shows that material of higher $H_v$ had a larger fractional voidage, and this result suggested that crystals which show higher crystal hardness did not readily undergo fragmentation or plastic deformation. However, there did not appear to be direct relationship between $H_v$ and the binding force between the crystals in tablets.

## References

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