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Effects of Tableting Procedures on the Preferred Orientation of Crystalline Particles[1)]

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The effects of tableting procedures on the preferred orientation of phenacetin and aspirin crystals in a tablet were investigated. Among aspects of tableting procedures which might affect the preferred crystal orientation, the granulation process, the shape of the punch and the addition of magnesium stearate were investigated.

A wet granulation method decreased the mobility of crystals during compression, and thus reduced the degree of preferred orientation. This phenomenon was considered to be one of reasons for the improved lamination properties seen with the granulation method. The shape of the punch affected the preferred orientation; a concave punch caused a more complex preferred orientation pattern than a flat punch. The preferred orientation was considered to correspond to the stress distribution in a tablet. Magnesium stearate reduced the interparticle friction and facilitated the attainmnet of preferred orientation.

The characteristic preferred orientation of crystals in the neighborhood of the upper surface and side surface of a tablet was investigated. The broadest faces of crystals were aligned in parallel to the upper punch face and the die wall.

Keywords——tablet; preferred orientation of particles within tablet; X-ray powder diffractometry; lamination; aspirin; phenacetin; magnesium stearate

In the previous study,[2)] an X-ray diffraction method was developed for evaluating the preferred orientaion of crystalline particles of aspirin, phenancetin, *etc.*, in a tablet. Selected faces of a tablet, the upper surface and faces cut parallel, oblique, and normal to the upper surface, were presented to an X-ray beam, and X-ray diffraction patterns for these faces were measured. The patterns of the faces were different from each other. These differences resulted from differences in the preferred orientation of crystalline particles in a tablet during compression, so that the degree of preferred orientation could be evaluated from the differences.[2a)]

The effects of the size and morphology of crystals on the preferred orientation were investigated, and it was reported that thin, plate-like crystals had the greater tendency to orient preferentially than pulverized crystals, and showed a greater tendency to laminate.[2b)] In addition, the changes in volume, specific surface area and pore size distribution of the tablets during the compression process were measured, and the relation between these factors and the preferred orientation of crystals was considered.[2c)]

In the present study, the effects of tableting procedures on the preferred orientation of phenacetin and aspirin crystals were investigated. Among factors in the tableting procedures which might affect the preferred orientation, the granulation process, the shape of the punch and the addition of magnesium stearate were investigated. The characteristic preferred orientation of crystals in the neighborhood of the upper surface and side surface of a tablet was also studied.

Experimental

Materials——Two kinds of aspirin were used. One (crystal A) was prepared by sieving aspirin (JP IX grade) to 32—60 mesh. The other (crystal B) was precipitated from methanol solution of aspirin (JP IX

grade) by dilution with water, then dried and passed through a 42 mesh screen. They were stored in a desiccator of P_2O_5 for one week before use. Crystals A and B correspond to crystals A and C in the previous paper,[2b] respectively. Phenacetin (JP IX grade) was sieved to 32—60 mesh and stored in a desiccator of P_2O_5 for one week before use.

Preparation of Granules——Granules for compression were prepared as follows. Phenacetin (50 g) was blended with 7.5 g of 7% hydroxypropylcellulose aqueous solution or 7% corn starch paste. Air drying was carried out at 40°C for 20 min, then the resulting moist mass was passed through a 5 mesh screen and futher dried at 40°C for 2 h. A screen of large aperture (5 mesh screen) was used to avoid fracturing phenacetin crystals. In order to avoid any effect of change in crystal shape during the granulation process on the preferred orientation of phenacetin crystals, crystals treated with water instead of binder solutions were used for direct compression.

Preparation of Tablets——Tablets of three different shapes were prepared using the Instron tension-compression machine, model TT-DM. The instrument was operated at a downward crosshead motion of 5 mm/min until a desired load was exerted. The load was maintained for one min.

Flat-faced Tablet: Flat-faced punches of 10 mm diameter were used. A sample of 1 g was compressed for measurements of X-ray diffraction patterns and 0.7 g was compressed for measurements of breaking strength of tablets.

Convex-flat Tablet: In order to investigate the effect of punch shape on the preferred orientation of crystals, a convex-flat tablet was prepared. A concave upper punch with a radius of curvature of 13.5 mm and a flat-faced lower punch of 15 mm diameter were used. A sample of 2 g was compressed at 2.25 t.

Angular Tablet: A tablet with a flat side face was prepared for the purpose of measuring the X-ray diffraction pattern for the tablet face in contact with a die wall during compression. Square punches with sides of 15 mm were used. A sample of 3 g was compressed at 2.25 t.

Measurement of X-Ray Diffraction Pattern——A Rigaku Denki Geigerflex 2027 was used (Ni filter, Cu-$K\alpha$ radiation). The procedures were the same as those reported in the previous paper.[2c]

The Tendency for Tablets to Laminate——The breaking strengths normal and parallel to the upper surface of flat-faced tablets were measured with the same attachment as previously reported[2c] using the Instron tension-compression machine, model TT-DM. The instrument was operated at a downward crosshead motion of 30 mm/min. The tendency for tablets to laminate was evaluated in terms of the ratio of breaking strength in the normal direction (H_n) to that in the parallel direction (H_p).

Results and Discussion

Effect of Granulation on Preferred Orientation

It is known that the use of a wet granulation method improves lamination and capping properties of tablets. Several reasons can be considered for this phenomenon. The first is that a granule is compressed more easily than a powder and the structure of a tablet thus will be more homogeneous. The second is the effect of a binder of increasing the hardness of a tablet.

In the previous paper,[2b] it was reported that the preferred orientation of particles within a tablet caused the lamination tendency. Therefore, since a granulation method decreases the mobility of particles during compression and thus the degree of preferred orientation of particles within a tablet, this phenomenon might be one of the reasons for the improvement of lamination properties with the granulation method.

Table I shows the X-ray diffraction intensities of a phenacetin crystal tablet (direct compression) and granule tablets (wet granulation method). In the case of the crystal tablet, the X-ray diffraction intensities of the (100) and (200) planes were strong for the flat upper surface and the face cut parallel to the upper surface, while these intensities were very weak for the face cut normal to the upper surface. This result showed that (100) faces of phenacetin crystals, that is, the broadest faces of the tabular crystals aligned themselves parallel to the upper flat punch face.[2a] On the other hand, the X-ray diffraction intensities of the (100) and (200) planes for the upper surface and the parallel face of granule tablets were weaker than those of the crystal tablet, indicating that the degree of preferred orientation of phenacetin crystals was decreased in the granulation method. The effect of granulation with hydroxypropylcellulose (HPC) was larger than that with starch.

Table II shows the breaking strength of phenacetin tablets. H_n is the breaking strength normal to the upper surface and H_p is the breaking strength parallel to the upper surface.

Table I. Effect of Granulation on X-Ray Diffraction Intensities of Selected Faces of Various Phenacetin Tablets

Phenacetin	$2\theta(°)$	$(h\ k\ l)$	Diffraction intensity		
			1[a]	2[b]	3[c]
Crystal	6.8	(100)	7	6	—
	11.4		5	4	1
	13.6	(200)	43	25	1
	14.8		—	2	12
	21.9	(012)	10	14	33
	24.2		7	5	13
	26.0		3	5	19
Granule (HPC)	6.8	(100)	3	2	—
	11.4		4	4	2
	13.6	(200)	19	8	1
	14.8		4	5	11
	21.9	(012)	18	32	36
	24.2		10	8	14
	26.0		7	8	12
Granule (starch)	6.8	(100)	6	3	—
	11.4		5	6	2
	13.6	(200)	30	14	1
	14.8		2	4	12
	21.9	(012)	18	20	41
	24.2		7	8	12
	26.0		4	7	13

a) Upper surface. *b*) Parallel face. *c*) Normal face.

Table II. Breaking Strength of Various Phenacetin Tablets

Phenacetin	H_n (kg)[a]	H_p (kg)[b]	H_n/H_p
Crystal	1.58 ± 0.270[c]	0.14 ± 0.025	11.3
Granule (HPC)	3.94 ± 0.229	0.88 ± 0.073	4.5
Granule (starch)	2.99 ± 0.262	0.53 ± 0.121	5.6

a) Breaking strength of tablets normal to the upper surface.
b) Breaking strength of tablets parallel to the upper surface.
c) Mean value $\pm$ standard deviation ($n=10$).

H_n/H_p represents the tendency of the tablet to laminate. The values of H_n/H_p of granule tablets were smaller than that of the crystal tablet, so that the tendency to laminate was reduced by granulation. The effect of hydroxypropylcellulose was greater than that of starch.

The results in Tables I and II suggest that the decrease of preferred orientation was one of the reasons for the reduced tendency of the tablet to laminate when the granulation method was used.

Effect of Punch Shape on Preferred Orientation

It has been reported that the punch shape affects the pressure distribution,[3] apparent density and the movement of particles[4] within the tablet, but little work has been done on the effect of punch shape on the preferred orientation of particles. Therefore, the effect of punch shape on the preferred orientation of aspirin crystal B was investigated.

Tablets prepared using a concave upper punch and a flat lower punch were cut parallel to the lower flat surface, and then the X-ray diffraction patterns on the cut faces were measured. Figure 1 shows the relationship between $I_{(100)}/I_{(112),(211)}$ (I') and the distance (x) from the

top of the convex surface of a tablet to the cut faces. I' represents the tendency for the (100) faces of aspirin crystal B, the broadest crystal faces, to align themselves parallel to the flat lower surface. The original thickness of a tablet was 9.50 mm.

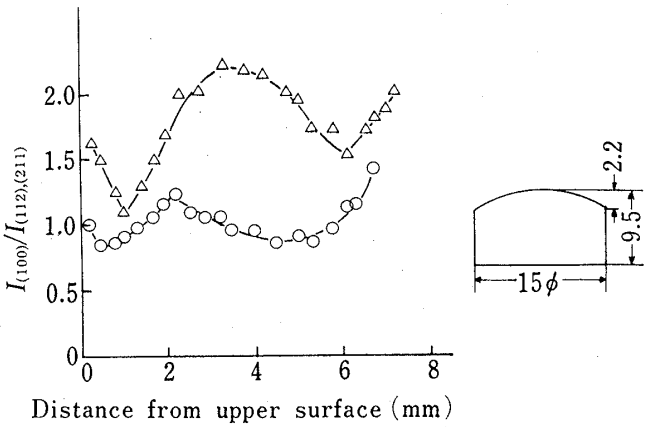

Fig. 1. Relationship between $I_{(100)}/I_{(112),(211)}$ and Distance from the Upper Surface of Tablets of Aspirin Crystal B with an Upper Convex and a Lower Flat Surface

○; no magnesium stearate.
△; 2% magnesium stearate.

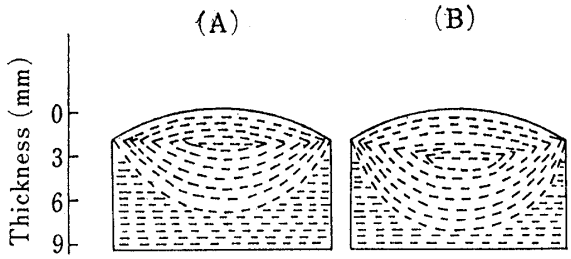

Fig. 2. Patterns of Preferred Orientation of Aspirin Crystal B with Tablets deduced from the Results in Fig. 1

(A); no magnesium stearate.
(B); 2% magnesium stearate.

As shown in Fig. 1, the value of I' was relatively large in the immediate neighborhood of the convex upper surface and decreased in the inner regions of the tablets (to 0.5 mm from the top). I' increased from 0.5 mm to 2.2 mm and showed a maximum at $x=2.2$ mm, at which point the convex part of the upper surface came to end. I' again decreased below 2.2 mm from the top, and in the neighborhood of the flat lower surface I' again increased due to the effect of the lower flat punch.

In the case of using a concave upper punch, as described above, the preferred orientation of aspirin crystals within a tablet was more complex than in a flat upper punch. Because the effect of the upper punch shape extended not only in the neighborhood of the upper surface of the tablet but also within the tablet, the preferred orientation of particles was considered to reflect the stress distribution in the tablet.

The patterns of preferred orientation of aspirin crystal B deduced from the results in Fig. 1 are shown in Fig. 2. Figure 2 shows a face cut normal to the upper surface and represents the mode of preferred orientation of thin plate-like crystals. Horikoshi *et al.*[3] reported the stress distribution and the powder movement in convex type tablets of bacterial alkaline proteinase. The mode of the preferred orientation shown in Fig. 2 is in reasonable accord with their result.

In the previous paper,[2b] it was reported that the broadest face (100) of thin plate-like aspirin crystal B aligned itself parallel to the flat tablet surface in the compression process using flat punchs, and the tablet showed a strong tendency to laminate. Thus, the preferred orientation of particles in a tablet as shown in Fig. 2 might be one of the reasons for capping phenomena in the compression process using concave punches.

Figure 1 (△) and Fig. 2 show the effect of magnesium stearate on the preferred orientation of aspirin crystal B. Because magnesium starate reduces interparticle friction and facilitates the transmission of upper punch pressure into the tablet, $I_{(100)}/I_{(112),(211)}$ was increased, In addition, the minimum and maximum points of $I_{(100)}/I_{(112),(211)}$ were shifted to lower positions in the tablet.

Preferred Orientation on the Side Surface of Tablets

It is of interest to know how particles preferentially orient on the side surface of a tablet in contact with the die wall during compression and how a lubricant affects the preferred orientation of particles on the surface. There has been little work on this subject because a suitable method for evaluating the degree of preferred orientation of particles has not been available.

The X-ray diffraction method reported in the previous paper[2] was used to investigate this subject. Aspirin and phenacetin crystals were compressed into angular tablets. Then, the X-ray diffraction patterns for selected faces of the tablet, the side surface, the upper surface and faces cut parallel and normal to the upper surface, were measured. Table III shows the X-ray diffraction intensities for these faces of the tablets.

Table III. X-Ray Diffraction Intensities of Selected Faces of Various Tablets

Substance	2θ(°)	(h k l)				Diffraction intensity			
						1[a]	2[b]	3[c]	4[d]
Aspirin	7.7	(100)				32	16	1	30
crystal A	15.5	(200)	(002)	(110)	(011)	32	23	36	32
	20.6	(210)	(012)			1	2	11	1
	22.6	(211)	(112)			3	9	15	5
	23.2	(202)				6	8	2	5
	27.0	(212)	(310)			8	23	16	9
	31.4	(400)	(022)	(220)		8	4	2	6
Aspirin	7.7	(100)				34	16	—	26
crystal B	15.5	(200)	(002)	(110)	(011)	25	17	41	21
	20.6	(210)	(012)			1	3	12	2
	22.6	(211)	(112)			4	10	14	9
	23.2	(202)				2	7	2	4
	27.0	(212)	(310)			14	28	14	21
	31.4	(400)	(022)	(220)		7	5	3	3
Phenacetin	6.8	(100)				7	6	—	6
	11.4					4	5	2	11
	13.6	(200)				44	35	—	19
	14.8					2	2	15	4
	21.9	(021)				7	7	45	20
	24.2					6	4	8	7
	26.0					4	4	10	5

a) Upper surface. *b*) Parallel face. *c*) Normal face. *d*) Side surface.

In the case of aspirin crystals, a strong (100) X-ray diffraction peak was observed for the upper surface and parallel face, while this peak was weak for the normal face. This result showed that (100) faces of aspirin crystals, that is, the broadest faces[2a] of tabular (crystal A) and plate-like (crystal B) crystals, aligned themselves parallel to the upper flat punch face during compression. The (100) peak was also observed for the side surface at the same intensity as for the upper surface, it was found that the broadest (100) faces of aspirin crystals aligned themselves parallel to the die wall during compression.

In the case of phenacetin crystals, (100) is also the broadest face.[2a] The X-ray diffraction peaks of the (100) and (200) faces, which were observed on the upper surface, the parallel face and the side surface, were not observed on the normal face. This result shows that phenacetin crystals behave in the same way as aspirin crystals during compression.

On the side surface of aspirin tablets, the (100) faces aligned themselves parallel to the surface. Within the tablets, however, the (100) faces aligned themselves normal to the side surface. Thus, the preferred orientation of crystals at various positions within a tablet, from the side surface to the center of a tablet, appear to be different. Angular tablets of aspirin

were cut parallel to a flat side surface, then X-ray diffraction patterns of the cut faces were measured. Figures 3 and 4 show the values of $I_{(100)}/I_{(112),(211)}$ on each cut face of aspirin crystal A and B tablets, respectively. The (100) faces aligned the side surface in the immediate neighborhood of the die wall in both cases. Within the tablet, however, the (100) faces oriented preferentially parallel to the upper punch, that is, normal to the side surface. Crystal A is a tabular one having a thickness of several dozen micrometers and B is a plate-like crystal having a thickness of several micrometers.[2b] In spite of the difference of thickness, the effect of the die wall on preferred orientation extended to the same distance (about 0.2 mm) for crystals A (Fig. 3) and B (Fig. 4). This result showed that the plate-like crystal B oriented more readily than tabular crystal A.

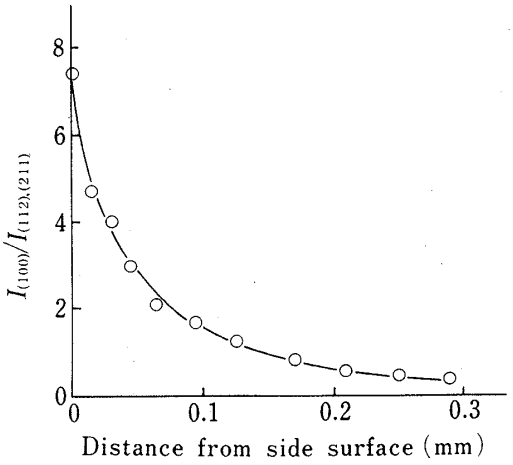

Fig. 3. Relationship between $I_{(100)}/I_{(112),(211)}$ and Distance from the Side Surface of an Angular Tablet of Aspirin Crystal A

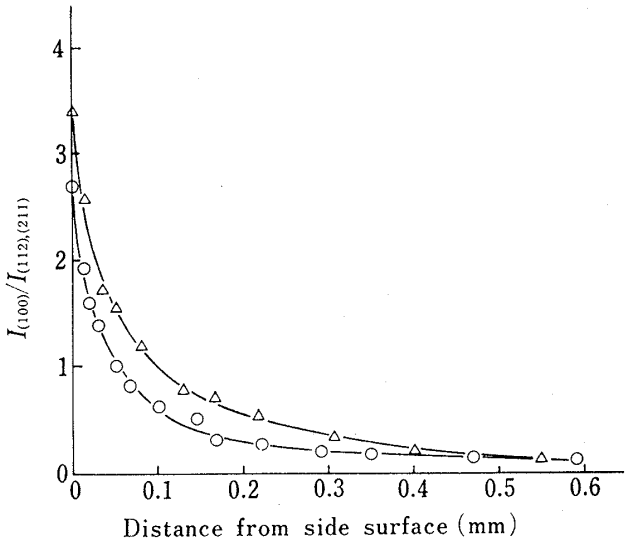

Fig. 4. Relationship between $I_{(100)}/I_{(112),(211)}$ and Distance from the Side Surface of Angular Tablets of Aspirin Crystal B

○; no magnesium stearate.
△; 2% magnesium stearate.

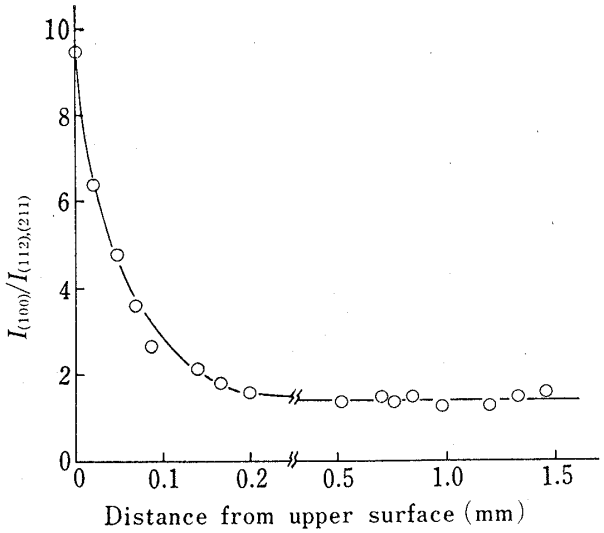

Fig. 5. Relationship between $I_{(100)}/I_{(112),(211)}$ and Distance from the Upper Surface of a Flat Tablet of Aspirin Crystal A

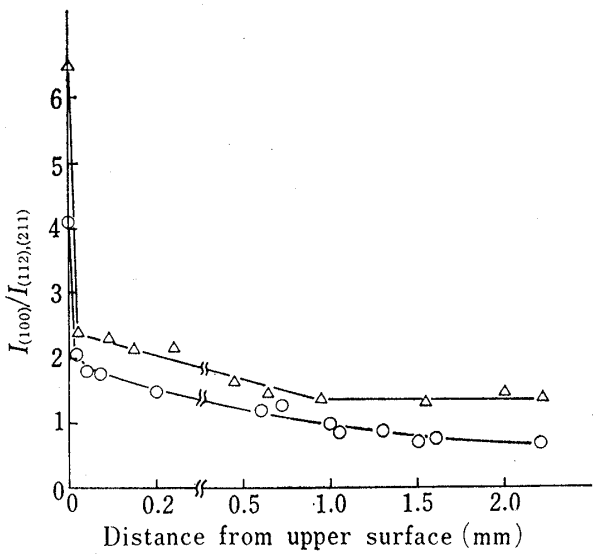

Fig. 6. Relationship between $I_{(100)}/I_{(112),(211)}$ and Distance from the Upper Surface of Flat Tablets of Aspirin Crystal B

○; no magnesium stearate.
△; 2% magnesium stearate.

Figure 4 shows the effect of magnesium stearate on the preferred orientation of aspirin crystal B in the neighborhood of the side surface of a tablet. Because magnesium stearate reduces interparticle friction and facilitates the preferred orientation of crystals in the neighborhood of the die wall during compression, the value of $I_{(100)}/I_{(112),(211)}$ was increased by adding magnesium stearate.

Preferred Orientation in the Neighborhood of the Upper Surface

Flat-faced tablets of 10 mm diameter were cut parallel to the flat upper surface, and the X-ray diffraction patterns of the cut faces were measured. Figures 5 and 6 show the change in preferred orientation of aspirin crystal A and B tablets in the neighborhood of the upper surface. The value of $I_{(100)}/I_{(112),(211)}$ decreased sharply within a tablet. This result showed that preferred orientation is most marked in the immediate neighborhood of the flat upper punch face during compression. In the case of crystal A (Fig. 5), the value of $I_{(100)}/I_{(112),(211)}$ became constant at a distance of about 200 μm from the upper surface. On the other hand, I' of crystal B, which is thinner, changed down to about 1.5 mm (Fig. 6). The thin, plate-like crystal B presumably can orient preferentially rather easily because of its shape, and the effect of the upper punch on preferred orientation extended into the inner part of the tablet.

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References and Notes

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