was not recognized.

b) The disintegration and solution rate of $CaCO_3$ granule that contained starch paste was not rapid and larger particles remained undissolved in the final stage.

c) It was evidenced that the tablet prepared from $CaCO_3$ granule disintegreted more slowly than the tablet prepared by direct compression.

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65. Hisashi Nogami, Jun Hasegawa, and Yoshinobu Nakai[*1] : Studies on Powdered Preparations. III.[*2] Studies on Disintegration of Basic Magnesium Carbonate Tablet.

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In the preceding paper,[*2] a new method for testing disintegration of a tablet and granule was proposed, and the result on calcium carbonate was reported. Because calcium carbonate was not suitable for studying the effects of binder, disintegrator, and compressional force, these effects were examined with basic magnesium carbonate, and apparent particle-size distribution of a tablet was compared and described in this report.

Experimental

Materials—Basic Magnesium Carbonate : Reagent grade, 1st class, was dried over P_2O_5 at 80° for 72 hr. and kept in a $CaCl_2$ desiccator. About 0.3 g. of the powder passed through 100-mesh sieve was weighed and used for thermal analysis.

Granule : Two kinds of granule were prepared.

Granule A : 190 g. of basic magnesium carbonate was mixed with 4 g. of potato starch, prepared from 6 g. of starch and 50 cc. of water, granulated with 20-mesh sieve, dried in warm air stream of 50°, and kept in a desiccator. This granule contained 95.2% of the carbonate.

Granule B : Starch paste described above was added to a mixture of 186 g. of basic magnesium carbonate and 8 g. of starch, granulated, dried, and kept in the same manner. This granule contained 93.1% of the carbonate.

Temperature rise of the starch and the dried starch paste was determined as described in the preceding paper.[*2] The tablet prepared from 300 mg. of the granule B contains 12 mg. of starch and 9 mg. of dried starch paste, and the temperature rise caused by them, $2.1\times10^{-3\circ}$, is negligible as described before.

Apparatus, Procedure, etc.—Same as described in the previous paper. Temperature rise of basic magnesium carbonate is given in Table I.

Table I. Temperature Rise of Basic Magnesium Carbonate in 1*M* Acetate Buffer (pH 4.2) (°C/g.)

1.91.	1.86,	1.85,	1.85,	1.86,	1.78
	mean			1.85	

Result and Discussion

The disintegration and solution were studied as shown in Fig. 1, in which the curves (1), (2), and (3) show the temperature change of basic magnesium carbonate powder, the granule A, and the graule B, and the curves (1′), (2′), and (3′) show the change of surface area of these materials. Marked difference in the results obtained with the

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[*2] Part II. This Bulletin, **7**, 331(1959).

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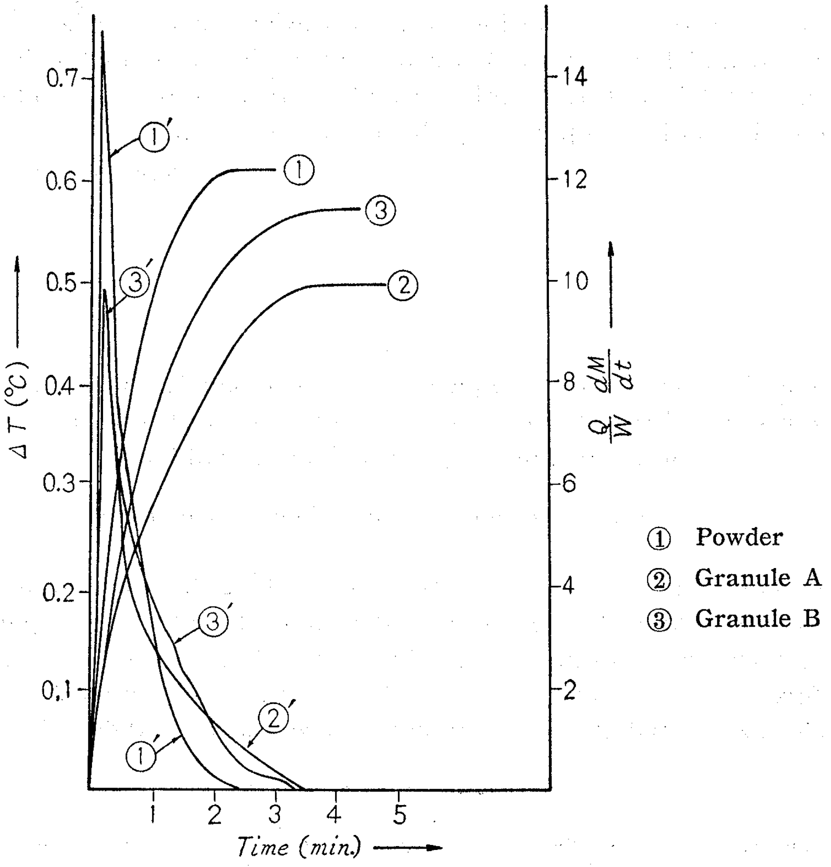

Fig. 1. Reaction Rate of Powder and Granules of Basic Magnesium Carbonate

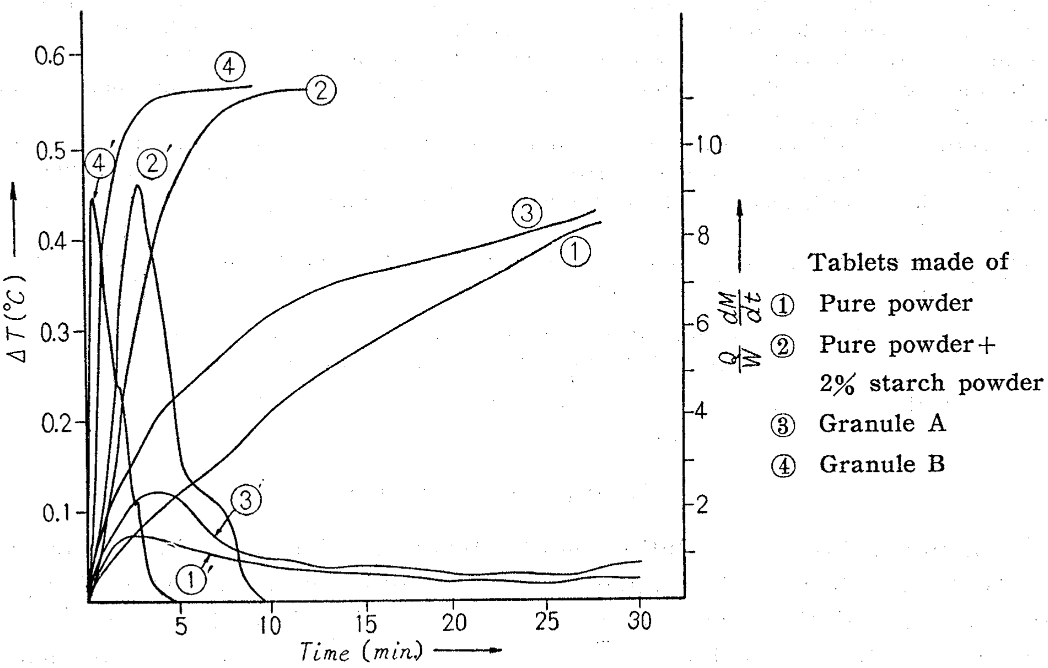

Fig. 2. Effect of Disintegrator and Binder on Disintegration of Tablets
(Compressional force : 1 ton)

powder and the granules was not recognized, but some larger particles remained undissolved and the granule B dissolved somewhat faster than the graunle A. This phenomenon is the same as those described in the preceding paper, but the difference between granule A and B became evident when they were compressed into tablets.

The effects of a binder and a disintegrator were examined as seen in Fig. 2, in which the curves (1), (2), (3), and (4) are the temperature rise of tablets prepared from the carbonate by direct compression, mixture of the powder and 2% of potato starch, the granule A, and the granule B. The curves (1′), (2′), (3′), and (4′) represent the change of surface area of the corresponding tablets. These tablets were compressed with the same force of 1 ton.

The tablet obtained from the carbonate powder showed slow temperature rise and the increase and decrease of surface area was not so marked as seen in the curves (1) and (1′). It might have been caused by partial disintegration of the tablet. This result is evidently different from the result obtained with basic magnesium carbonate powder or of the tablet prepared from it described in the preceding study.

The tablet prepared with a mixture of the original powder and 2% of potato starch by direct compression disintegrated rapidly and showed a notable change in surface area as seen in curve (2′). Therefore, it was considered that the result showed the effect of 2% of starch and the characteristic of the tablet resembled the reactivity of original powder.

The result of the tablet obtained from granule A is shown by the curves (3) and (3′). The effect of disintegrator was weakened by the binder. The curve of temperature rise lies between the curves (1) and (2), and the change of surface area is similar to the curve (1′). The relation was quite different from that of granule B which contained more disintegrator, as will be explained later.

The tablet prepared from granule B showed a marked change in temperature rise and surface area. The characteristics were similar to those of the original granule but a slight difference was recognized in the tail of the curves. The prolonged tail might be due to the remaining of larger particles.

The effect of compressional force on disintegration was studied and the result is given in Fig. 3, in which the granule B was compressed into three kinds of tablet with the forces of 0.5, 1.5, and 2.0 tons. The difference was not evident within 1.5 mins. in the curves (1), (2), and (3), but the degree of temperature rise became small and prolonged with the increase of compressional force. The relation was seen more clearly in curves (1′), (2′), and (3′), the time necessary for complete dissolution became large, and larger particles remained undissolved with the increase of pressure.

From these results, it may be considered that there is no notable difference in the relation between disintegration and compressional force, when a tablet is made from the granule that contains a large amount of disintegrator. A linear relationship between logarithm of disintegration time and compressional force has been reported.[1,2]

The conflicting circumstance described above may be due to the presence of a fundamental difference between the method proposed and the one of U.S.P. or B.P., or because the material used is a carbonate.

Disintegration of a tablet is evaluated in U.S.P. and B.P. by the time that takes all the fragments of tested tablet to pass through a 10-mesh sieve but in the present method, it was evaluated by the increase and decrease of surface area of the solid particle. The disintegration time of four kinds of tablet compressed with the force of 0.5, 1.0, 1.5, or 2.0 tons was determined and given in Fig. 4 and Table II.

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1) T. Higuchi, *et al.*: J. Am. Pharm. Assoc., **42**, 194(1953).
2) J. Hasegawa: Yakugaku Zasshi, **75**, 480(1955).

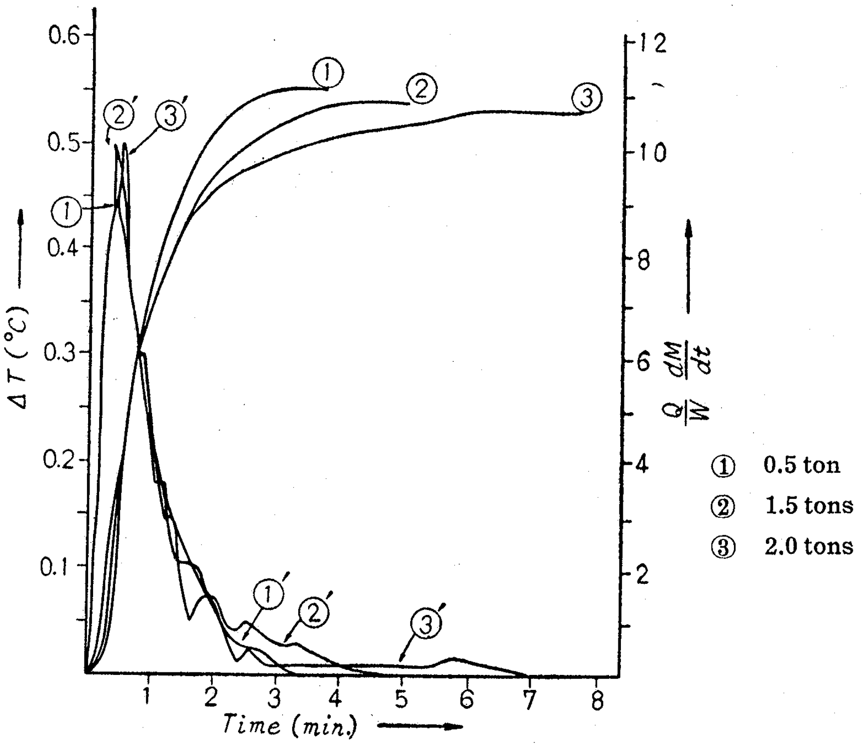


Fig. 3. Effect of Compressional Force on Tablets Disintegration

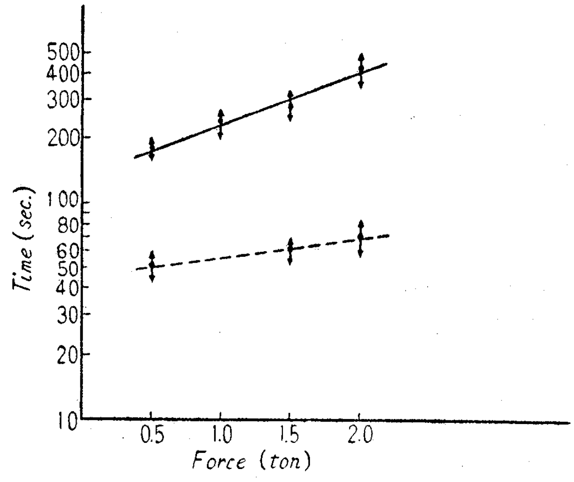


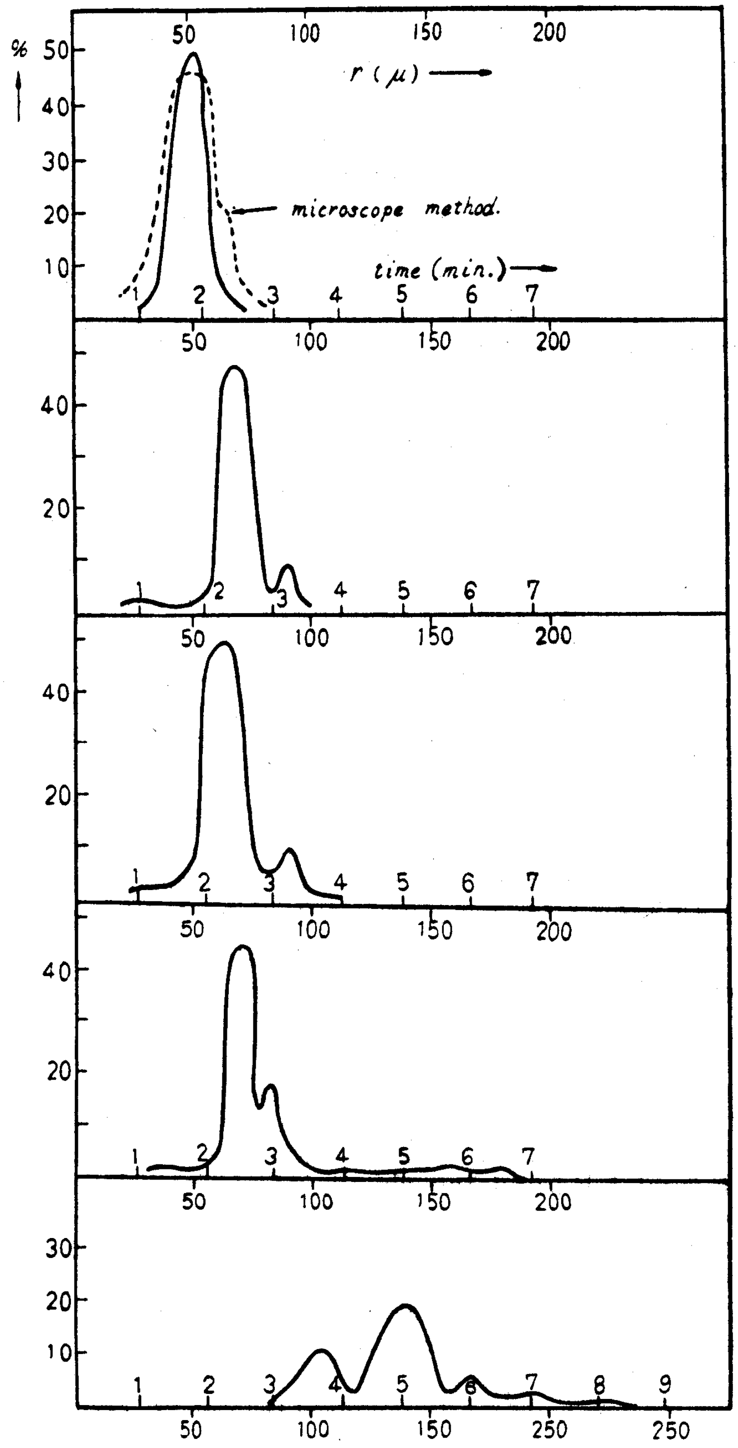
Fig. 4. Effect of Compressional Force on Tablet Disintegration determined by U.S.P. Method and Thermal Analysis

Table II. Disintegration Time determined by U.S.P., J.P., and Thermal Analysis Method

Method / Compress. force (ton)	U.S.P. (sec.)	J.P. (sec.)	Thermoanalytical method	
			Max. surf. area (sec.)	Zero surf. area (sec.)
0.5	52	30	20	180
1.0	—	—	25	240
1.5	60	30	25	280
2.0	70	30	30	420

The linear relation described above is recognized in Fig. 4, where the mean value and standard deviation of three determinations are given. It was very interesting that the same linear tendency was found between the logarithm of solution time of solid and the compressional force. The result determined by the J.P. method was about 30 sec. for these tablets as given in Table II.

Considering the results mentioned above, it is assumed that J.P. or U.S.P. method intends to evaluate disintegration by the time it takes for a tablet to reach the maximum surface area or all the particles to dissolve to below 10-mesh size.



(A) Powder

(B) Granule B

(C) Tablet made of granule B (Compressional force, 0.5 ton)

(D) Tablet made of granule B (Compressional force, 2 tons)

(E) Tablet made of Mg-Carbonate + 2% starch powder (Compressional force, 1 ton)

Fig. 5. Apparent Particle-size Distribution of Powder, Granule, and Tablets

It is necessary for a complete estimation of a medicinal effect of tablet to examine and observe the detailed process from the beginning of disintegration to the end of solution through the maximum of surface area. Therefore, it is considered that the effect of tablet cannot be estimated by a single determination obtained by J.P. or U.S.P. method, and the proposed method is evidently more suitable for the purpose stated above.

As for the use of a carbonate as the material, carbon dioxide may affect disitegration of a tablet and further investigation will be carried out for the elucidation of this point.

Apparent particle-size distribution was determined and disintegration was evaluated from this standpoint. It is desirable that the tablet has the same medicinal effect as the original powder used, as Berry[3] stated, and it may be compared directly by the present proposed method.

The results determined on the original powder, granule B, the tablet prepared from granule B with force of 0.5 and 2.0 tons, and the tablet obtained from a mixture of original powder and 2% of starch, are given by curves (A), (B), (C), (D), and (E) in Fig. 5.

Particle-size distribution was determined by thermal analysis and microscopic method, and compared in (A), where 1000 crystals were measured by a microscope and the maximum was found at 50 μ or 100 sec. The maximum of distribution shifted to about 68 μ in granule B and another maximum was recognized at 85 μ, as shown by (B) in Fig. 5. The result showed the prolongation of time for solution by granulation. When granule B was compressed to a tablet with the force of 0.5 ton, as shown by (C) in Fig. 5, apparent particle-size distribution of the tablet was quite similar to that of the original granule, but the maximum of distribution was reduced to 60 μ. It might be due to the fact that the action of binder was decreased by the relatively weak pressure and the disintegration was prompted by the starch contained. This circumstance is very interesting from the mechanism of disintegrator. The same granule was compressed into a tablet with the force of 2.0 tons, and the result is given by (D) in Fig. 5, where two peaks of distribution were found at about 70 μ and 80 μ. The tail of distribution might mean the effect of a higher pressure. A mixture of the carbonate and 2% of potato starch was compressed into a tablet and apparent distribution was determined as shown in (E) of Fig. 5. The maximum of distribution curve shifted to 140 μ, the deviation of distribution expanded from 80 μ to 240 μ, and the delay of disintegration was recognized. It may mean that the effective mean diameter of micropore in the tablet was decreased by the effect of pressure. It is understood that the disintegration of tablets prepared by direct compression or slugging may not be good since higher pressure is necessary in these procedures.

Summary

Disintegration of a granule and the tablet of basic magnesium carbonate was investigated, apparent particle-size distribution was compared, and the effects of binder and disintegrator was studied by thermal analysis. The relation between testing method for disintegration by U.S.P. and J.P., and the change of surface area was discussed, and the following conclusions were drawn.

1) Judging from the change of surface area, the effect of compressional force was not notable in a tablet prepared with well-disintegrating granule.

2) The disintegration time of a tablet prepared by direct compression was very prolonged and this relation was clearly recognized by the evaluation of apparent particle-size distribution of a tablet.

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[3] H. Berry: J. Pharmacol., 2, 619(1950).