[Chem. Pharm. Bull. 24(8)1789—1794(1976)] UDC 615.453.6.011.4 : 615.014

Influence of Tablet Dimensions on the Disintegration Time[1)]

Nobuyuki Kitamori and Tsugio Shimamoto

Pharmaceutical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd.[2)]

(Received October 30, 1975)

A study was made on the effect of dimensions on the disintegration time of tablet. The ln-ln plot of the disintegration time against the tablet thickness gave a straight line. The relation may be expressed simply by the equation,

$$t_D = KT^n$$

where t_D is the disintegration time of the tablet which is compressed at a fixed pressure and has a constant diameter and thickness T, and K and n are constants. The relation expressed by this equation held good not only for directly compressed tablets but also for tablets made from granules. A tablet disintegration mechanism can be assumed by this equation. The rate of deaggregation of particles from the surface of the tablet changes with time depending upon the degree of the acceleration of deaggregation through the swelling of the disintegrant.

The values obtained by the disintegration test in J.P. VIII are not related directly to the physical properties of tablets. However, since the disintegration test is a efficient screen for the formulator as well as a valuable quality control tool, disintegration time of tablets is still one of the important tablet characteristics.

There are many factors affecting disintegration time of tablets. For example, these are variables involved in the disintegration test such as the type of apparatus used, the composition of the test media and the temperature of the disintegration test liquid, and variables involved in the dosage form and manufacture employed such as the disintegrant and its concentration, the binder used, the compressional pressure, the method of the granulation process, *etc.*

The discussion on the effect of these factors on the tablet disintegration usually referrs to the comparison of disintegration time values. It should be noted, however, that even the tablets containing the same ingredients and having the same physical properties do not have the same disintegration time. This is because the form and size of tablets can also affect disintegration time.

Selmeczi and Lenart[3)] studied the physical properties of tablets containing the same ingredients, but differing in shape and size and described that the disintegration time of tablets was affected by the surface areas. The object of this paper is to report the correlation between the disintegration time and the dimensions of tablets. An application of such correlation to analysis of the mechanism in tablet disintegration is also shown.

Experimental

Compression of Tablet——Flat-faced punches and dies of 6.0, 8.0, 10.0 and 12.0 mm diameter were used. The proper quantities of powder or granule were compressed in each die on the physical testing instrument[4)] at 1000, 2000, and 4000 kg/cm^2 to obtain the tablets differing in thickness. Tablets were compressed at a constant strain rate of 5 mm/min and ejected at a strain rate of 100 mm/min. Before each compression, the

1) This work was presented at the 95th Annual Meeting of Pharmaceutical Society of Japan, Nishinomiya, April 1975.
2) Location: *2-17-85 Juso-hommachi, Yodogawa-ku, Osaka, 532, Japan.*
3) B. Selmeczi and J. Lenart, *Pharmazie*, **23**, 577 (1968).
4) Autograph IS-5000, Shimazu Seisakusho Ltd., Kyoto.

punches and die were dusted by magnesium stearate powder in order to obtain the uniform density of tablet. Tablet thickness was measured by a dial gauge,[5] before the determination of the disintegration time.

Disintegration Time——The disintegration time for each tablet in distilled water was determined according to the modification of J.P. VIII method, so that only one tablet was disintegrated at a time and the attached disk was not used.

Materials——Lactose, corn starch and hydroxypropyl cellulose (HPC-L) used were of J.P. VIII grade. Anhydrous β-lactose used was prepared from usual lactose in our laboratories.[6] Lactose or lactose/corn starch mixture (7 : 3 by weight) was granulated with aqueous HPC-L solution to be equivalent to 1.0, 3.0, 5.0 and 7.0% w/w dry binder in the final tablet. After massing in a mortar, the moistened powder was forced through the 32 mesh screen, dried in a vacuum dryer at 35° for 16 hours and rescreened (32 mesh). All granules obtained were stored in a chamber of relative humidity of 11% at 25° to regulate their moisture content.

Results

The disintegration time of a tablet increased exponentially with an increase in tablet thickness. A typical example of the relation between the tablet thickness and the disintegration time is given in Fig. 1, where a linear relation was observed at a fixed compressional pressure, irrespective of their diameters. The ln–ln relationship in Fig. 1 shows that the disintegration time is related to the thickness of tablets by the following equation,

$$t_D = KT^n \qquad (1)$$

where t_D is the disintegration time of the tablet having the thickness T, and K and n are constants respectively. Furthermore, it is evident from Fig. 1 that the straight lines at three compressional pressure levels are almost parallel to each other.

The relation between the constant K in equation (1) and the compressional pressure, P, was given by equation (2) as shown in Fig. 2.

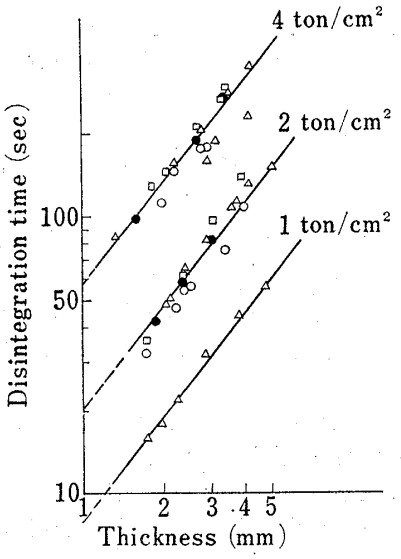

Fig. 1. Ln-ln Plots of Disintegration Time *versus* Thickness of Anhydrous β-Lactose Tablet having Different Thickness and Diameter at Several Compressional Pressures

—○—: 6 mm diameter
—●—: 8 mm diameter
—△—: 10 mm diameter
—□—: 12 mm diameter

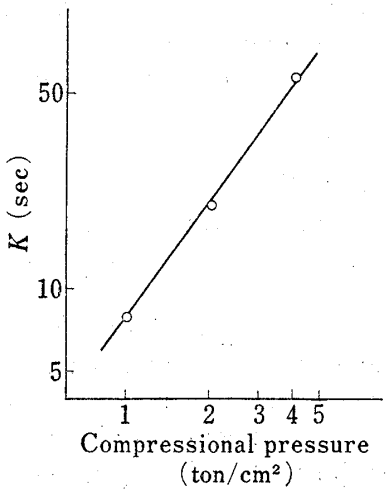

Fig. 2. Relationship between the Constant K in Equation (1) and the Compressional Pressure P for Directly Compressed Tablet of Anhydrous β-Lactose

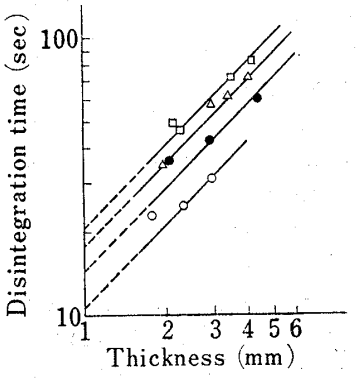

Fig. 3. Effect of Diameter on the Relationship between Disintegration Time and Thickness for Lactose/Corn Starch Tablet

—○—: 6 mm diameter
—●—: 8 mm diameter
—△—: 10 mm diameter
—□—: 12 mm diameter

5) Dial Thickness Gauge, Mitutoyo Mfg. Co. Ltd., Tokyo.
6) Its preparation followed by general method. The β-lactose used contained *ca.* 10% by weight of α-lactose.

$$K = k_1 P^l \quad (2)$$

where k_1 and l are constants. Substituting for the constant K in equation (1) from equation (2) gives

$$t_D = k_1 P^l T^n \quad (3)$$

The disintegration time was affected by the diameter of a tablet in some cases. However, the effect of the diameter of a tablet on the disintegration time is insignificant. The ln–ln relation between the disintegration time and the tablet thickness for the directly compressed tablets of lactose/corn starch mixture is shown in Fig. 3. The straight lines for four different diameters are also parallel to each other so that the constant k_1 in equation (3) is a function of the tablet diameter, D, irrespective of the thickness of tablets. The relation between k_1 and the tablet diameter could also be given by the exponential equation (4),

$$k_1 = k_2 D^m \quad (4)$$

where k_2 and m are constants. Then the equation may be written in more general form:

$$t_D = k_2 P^l D^m T^n \quad (5)$$

The relation between tablet dimensions and the disintegration time expressed by equation (5) can be applied not only to the directly compressed tablets but also to tablets made from granule. The results obtained with tablets which were prepared by wet granulation of lactose/corn starch mixture and of lactose are shown in Fig. 4 and 5.

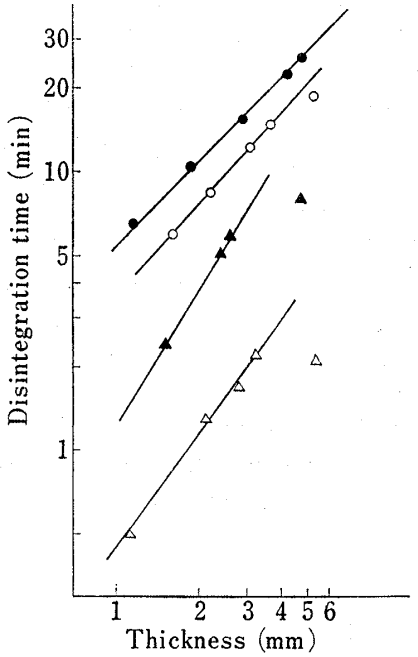

Fig. 4. Ln-ln Plots of Disintegration Time *versus* Thickness of Tablets made from Lactose/Corn Starch Granule with varing Concentration of HPC-L

—△—: 1% HPC-L —▲—: 3% HPC-L
—○—: 5% HPC-L —●—: 7% HPC-L

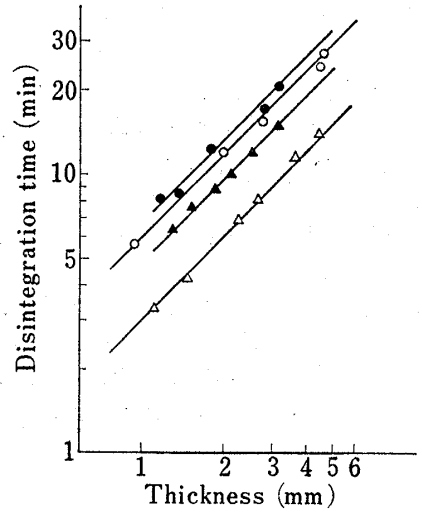

Fig. 5. Ln-ln Plots of Disintegration Time *versus* Thickness of Tablets made from Lactose Granule with varing Concentration of HPC-L

—△—: 1% HPC-L —▲—: 3% HPC-L
—○—: 5% HPC-L —●—: 7% HPC-L

These figures clearly show that increase in binder concentration increases in the disintegration time of tablets. The slope of the straight line varies with concentration of the binder for the tablet containing corn starch, while the slope of the line does not change with concentration of the binder for the lactose tablet. The thicker tablet was often broken into two or more pieces during the disintegration test and shorter disintegration time was observed in this case than that was expected from the relation as shown in Fig. 4. This phenomenon was

observed only with the tablet containing corn starch. Such a tablet stretched in the axial direction of a tablet during the disintegration process, because of the extraordinary swelling, and the stretching of a tablet led it to break in two pieces.

Discussion

It might be expected that the effect of the compressional pressure on the disintegration time of a tablet in equation (5) would be due to the change of the porosity of the tablet by compression. It is well known that the logarithm of compressional pressure is linearly related to the porosity of a tablet. However, no further work on this subject was done to allow definite statement to be made. When a tablet is compressed at a fixed pressure, the disintegration time is expressed by the following equation,

$$t_D = k_3 D^m T^n \tag{6}$$

where k_3 is a constant which equals $k_2 P^l$.

It was found experimentally that the effect of the diameter of a tablet on disintegration time is not large, so that equation (4) can be reduced to equation (1).

Now equation (1) suggests a simple tablet disintegration process. When a tablet is immersed in water, tablet dimensions will decrease in all the directions as a tablet disintegrates. A tablet ordinarily has smaller dimension of thickness than that of diameter, so that the disintegration time might be governed mainly by the thickness of a tablet. Fig. 6 shows a plot of the disintegration time against the tablet thickness for tablets having a constant diameter over the wide range of the ratio of the thickness to the diameter.

The disintegration time increased with an increase in thickness of tablets until the ratio of the thickness to the diameter reached unity. When the ratio was greater than unity the disintegration time was independent of the tablet thickness. Fig. 6 indicates that the disintegration time is governed by the smallest dimension of a tablet.

The tablet disintegration process can be explained on the basis of the relation between the thickness and the disintegration time of tablet expressed by equation (1). In the first step of a tablet disintegration process, liquid penetration into a tablet should be necessary. And then the constituent particles separate gradually from the surface of the tablet. This process is generally called "disintegration." If the rate of particle separation from the surface of a tablet is almost the same as the rate of penetration, the rate-determining step in the tablet disintegration should be the penetration of water into a tablet. The tablet ordinarilly, however, has the porous structure and hydrophilic properties, so that the penetration of liquid

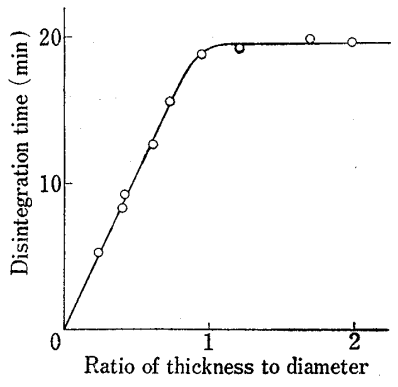

Fig. 6. Plot of Disintegration Time *versus* Ratio of Thickness to Diameter for Tablet made from Lactose Granule (6 mm diameter, 2.0 ton/cm²)

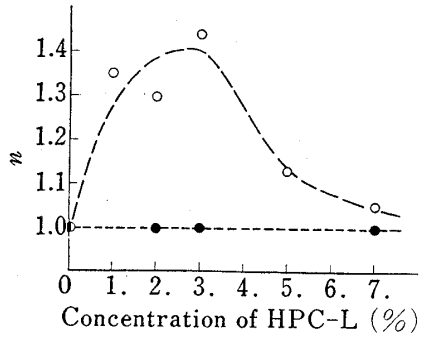

Fig. 7. Relationships between the Exponent n in Equation (1) and the Concentration of HPC-L for Tablets made from Lactose and Lactose/Corn Starch Granule

—○—: lactose/corn starch —●—: lactose

into the capillary of the tablet is predominant and the rate-determining step of the disintegration must be the deaggregation of particles from the surface of the tablet. Inspecting the section of the tablet which is disintegrating in water, it can be found that the disintegration proceeds only in the outer layer of the tablet, while water has already penetrated inside the tablet.

Cleave[7] assumed that the rate of decrease in dimension was a constant for the dissolution of the tablet. The authors now suppose the more general equation describing the tablet disintegration process, under the condition of $T<D$,

$$\frac{dT}{dt} = \alpha t^{m-1} \tag{7}$$

where T is the thickness of a tablet at time t, and α and m are constants. For the convenience of the mathematical treatment, the exponent m–1 was used. Integrating equation (7) and imposing the initial condition yields

$$T_0 - T = \frac{\alpha}{m} t^m \tag{8}$$

where T_0 is the initial thickness of a tablet. Hence, for a given tablet, the tablet will completely disintegrate, when T becomes zero. So the following relation is obtained,

$$T_0 = \frac{\alpha}{m} t_D{}^m \tag{9}$$

Rearranging and setting $n=1/m$ the same equation as the experimental one can be obtained, since T_0 in equation (9) corresponds to T in equation (1). As mentioned above, equation (7) is equivalent to equation (1) obtained experimentally.

From the experimental results, the value of the exponent n which was the slop of the ln–ln plot of data was between 1.0 and 1.5, so that m–1 was reduced to the negative value. This means from equation (7) that the rate of disintegration decreases as the disintegration proceeds. When the value of m–1 equals zero, that is $n=1.0$, the rate of disintegration is constant through the whole disintegration process.

The exponent n in equation (1) is useful for considering the difference in disintegration profile between the tablets of lactose and lactose/corn starch granule with HPC-L. The values of n in Fig. 4 and 5 are plotted against the concentration of HPC-L in Fig. 7.

Apparently the disintegration time increased with an increase in concentration of HPC-L as shown in Fig. 4 and 5. The values of n, however, behaved differently from the disintegration time with varying concentration of HPC-L.

It has been generally accepted that starch acts as a disintegrant through a swelling action when exposed to water. Patel and Hopponen[8] reported that dried corn starch increased in volume by 78% when suspended in water. The main action of corn starch as a disintegrant will be acceleration of the deaggregation of particles from the surface of the tablet by swelling.[9] In the tablet containing corn starch, the swelling of the disintegrant accelerates the deaggregation of particles from the tablet effectively at the beginning of the disintegration process, since the deaggregation of particles occurrs from the portion of the tablet, where starch has been wetted not long ago, so that the starch grains are increasing in volume. As the disintegration proceeds, however, an acceleration effect of the deaggregation by swelling of starch gradually becomes weak, since the starch grains have already swelled before the deaggregation of particles occurrs in the layer. Therefore, the disintegration rate decreases as time passes in this case.

7) J.P. Cleave, *J. Pharm. Pharmacol.*, **17**, 698 (1965).
8) N.R. Patel and R.E. Hopponen, *J. Pharm. Sci.*, **55**, 1065 (1966).
9) Y. Nakai, H. Fukuoka, T. Ogasawara and T. Fujikura, Abstracts of the 93rd Annual Meeting of Pharmaceutical Society of Japan, Tokyo, Vol. III, 233 (1973).

The situation might, however, change when the tablet contains higher concentration of HPC-L which possesses adhesive properties with a tendency to form adhesive gel when hydrates. The deaggregation of particles from the tablet will be retarded by the gel-like layer of hydrated HPC-L. The penetration of water will be also retarded by the formation of the gel-like layer. The deaggregation rate of particles will be considerably smaller than the penetration rate of water. The acceleration effect of the deaggregation by swelling of starch is ineffective through the whole disintegration process, since the starch grains have already swelled before the deaggregation of particles occurrs in the layer. The rate of disintegration is almost unchanged, so that the exponent n in equation (1) equals unity.

On the other hand, in the tablet prepared from lactose granule, the exponent n in equation (1) remained constant all over the concentration ranges of the binder, while the disintegration time increased with an increase in concentration of HPC-L. This is because there is no acceleration effect of the deaggregation of particles by swelling of disintegrant. Fig. 7 may support the assumption of the disintegration mechanism mentioned above.