[Chem. Pharm. Bull. 29(1) 205—212 (1981)]

The Rate of Penetration of Liquid into Tablets[1)]

Eihei Fukuoka, Shintaro Kimura,* and Midori Yamazaki

Faculty of Pharmacy, Toho University, 2-2-1 Miyama Funabashi-shi Chiba, 274, Japan

(Received July 15, 1980)

A direct measuring method for the liquid penetration rate into tablets was devised and compared with the usual powder method. The effect of the diameter and shape of tablets on the penetration rate was examined by using a two-dimensional model and confirmed to be negligible in practice. Directly compressed tablets of several powders used as excipients were tested as samples.

The weight variation of tablets had little effect on penetration. Since the penetration rate depends on the compression pressure, all tablets were prepared at a constant pressure of 215 kg/cm^2. Both in the present method and in the usual powder method most samples were in conformity with Washburn's equation, but the rate constants (K) were considerably different in the two methods. The results for crystalline cellulose could be described by such an equation in the case of the powder method but not in the case of the tablet method. The reason is considered to be the swelling of tablets and the accompanying generation of cracks. In this case, an L *vs.* t plot showed good linearity instead of an L^2 *vs.* t plot. The penetration patterns of crystalline cellulose tablets were also different from those of the other samples.

Most of the tablets were not disintegrated after completion of penetration; calcium carbonate, lactose and crystalline cellulose were exceptions.

Keywords——penetration test; wetting of powder; penetration rate of tablet; disintegration of tablet; Washburn's equation; excipient; swelling of powder; contraction of powder

When tablets are administered to humans or dropped into a test solution, in the first place, wetting and penetration of liquid into the tablets occur almost simultaneously. Next, water intake and subsequent swelling of the disintegrating agent take place and the tablets are dispersed by the swollen disintegrating agent into their original granules or powders.

Many investigations have been made on tablet disintegration. However, there has been little work on the wetting or penetration of water into tablets, which necessarily precedes disintegration. The main reason for this is considered to be as follows. When the tablets are dropped into a test solution, wetting naturally occurs first at the surface and progresses to the center; this makes it difficult to measure the rate of water penetration into tablets directly. In addition, dissolution of the ingredient and swelling of the disintegrating agent make it even more difficult to measure the rate of penetration of water.

For water penetration into a powder column, Washburn's equation[2)] (Eq. 1) has been widely used.

$$L^2 = \gamma \cdot r \cdot t \cdot \cos\theta / 2\eta \qquad \text{(Eq. 1)}$$

where L is the penetration length at time t, r is the average radius of the capillary, θ is the contact angle between the liquid and the powder surface, and γ and η are the surface tension and viscosity of the liquid. Nevertheless, the applicability of Eq. 1 to compressed tablets has not yet been determined. Ganderton[3)] *et al.* measured the volume of liquid taken up by compressed tablets and discussed the effect of some factors such as particle size, method of granulation and addition of lubricants on liquid uptake. However, Eq. 1 is concerned with the length of water penetration and dose not predict directly the volume of liquid taken up by tablets, especially when the distribution of capillary diameter cannot be ignored, as is the case in most tablets. L does not run parallel to the volume of liquid taken up by tablets

(V), since L is concerned with larger capillaries but V is concerned with the total capillary volume except for spaces unavailable for penetration.

In the present study, a simple method to measure the length of penetration of a liquid into tabletes has been devised. By using the present method and the usual powder method, the applicability of Washburn's equation to both samples was examined and the characteristics of penetration of water into powder and tablets were discussed in terms of K, ($K=\gamma \cdot r \cdot \cos\theta/2\eta$), obtained as the slope of a plot of L^2 *vs.* t.

Experimental

Apparatus——The apparatus used for measurement of the penetration rate of liquid into tablets is shown in Fig. 1. It consists of a sample-supporting arm, an illuminator, a vessel filled with liquid and a laboratory jack. The tablet was mounted on the supporting arm, and the vessel filled with distilled water was elevated slowly with the jack until the liquid just contacted the lowest part of the tablet. The time (t) necessary for the liquid to pass from the first mark to other marks which had previously been made on the surface of the tablets at intervals of 0.25 cm was measured (Fig. 1). It is extremely difficult and sometimes impossible to discern the boundary layer between the wetted and unwetted portions, especially when the sample has no intrinsic color. To overcome this difficulty, the tablet was observed through transmitted light by using a diaphragm (D in Fig. 1) designed not to illuminate the observer's eye directly.

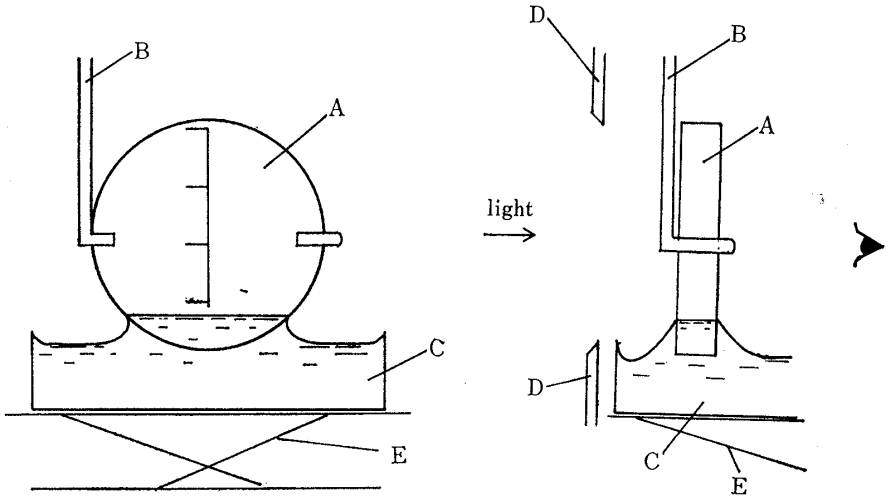

Fig. 1. Apparatus for Measurement of the Penetration Rate of a Liquid into a Tablet

A: tablet, B: supporting arm, C: liquid, D: diaphragms, E: laboratory jack.

Preparation of Tablets——The tablets were prepared by direct compression. The powder, equilibrated with environmental humidity (56—68% R.H.), was screened through a 100 mesh sieve and undersize powder was used. The weighed amount of powder was compressed to a disk-shaped tablet with a flat-faced punch and die of 1.3 cm i.d. by using an oil press. The pressure applied to the tablet was measured with a pressure gauge in the oil press. Tablets thus prepared were weighed one by one and the thickness of the tablets was measured with a micrometer.

Effect of Size and Shape of Tablets——Unlike the conventional powder method, in the present method, the boundary area between the wetted and unwetted portions changes with penetration. To examine the effect of size and shape on the penetration, circular filter papers, 3, 4 and 5.5 cm in diameter, were used as a two-dimensional model for a disk-shaped tablet. As a model for the usual powder method, in which the boundary area described above is expected to be constant, filter paper cut into a rectangular shape (3×5.5 cm) was examined and compared with circular paper.

In addition, the effect of the shape on penetration into actual tablets was examined. Thus, magnesium oxide tablets were prepared by the usual method described above and the arc-shaped parts of both sides of the tablets were scraped off as shown in Fig. 4. The penetration rates into intact tablets were compared with those into scraped ones.

Penetration of Liquid into a Powder Bed——A glass tube of 0.8 cm i.d. was used. The bottom of the tube was covered with a cotton cloth. The samples that had passed through a 100 mesh sieve were packed

into a tube by tapping 500 times from a height of 5 cm to make a homogeneous capillary distribution throughout the powder bed. The bottom of the tube was immersed in the liquid and the time t required for the liquid to rise to some height, L, was measured at a temperature of about 23°. From the data obtained by the two methods, L^2 was plotted against t to check the applicability of Eq. 1.

Materials——Four materials of J.P.IX grade (Table I) were selected on the basis of utility as a tablet excipient, insolubility in water and applicability of direct compression for tablet making. In addition to these, lactose, which is widely used as a soluble excipient, was examined for comparison with the insoluble materials.

Table I. Materials used and Their Characteristics

Material	Specific gravity	Specific surface[a] area(m^2/g)	Particle[a] diameter(μ)
Magnesium oxide	3.70	3.7	0.43
Magnesium carbonate	3.04	4.5	0.57
Crystalline cellulose	1.55	1.17	3.67
Magnesium silicate	3.28	13.8	0.08
Lactose	1.53	0.17	226

a) Air permeability method.

Results and Discussion

Effect of Tablet Shape——Although slight variation in the slope of the L^2 against t curve is apparent, as shown in Fig. 2-A, the results with both circular and rectangular filter papers were in good accord with Eq. 1. The variation of slope K with diameter of the filter paper is shown in Fig. 2-B. With decrease of the diameter, the slope K for the circular filter paper approaches that of the rectangular paper. In the case of penetration into a circular sample, liquid may be supplied through the cross section A to B, as shown in Fig. 3. Except in the final stage of penetration, the area A is smaller than the area B, but in the rectangular sample both areas are the same. When the diameter of the circle becomes small, as in the present study, the difference between areas A and B may be neglected. This is the reason why penetration into a small circle proceeds in the same way as that into a rectangular sample.

There was no significant difference between the original tablets and the scraped tablets, and the results for both samples were in good accord with Eq. 1 (Fig. 4). This agrees with

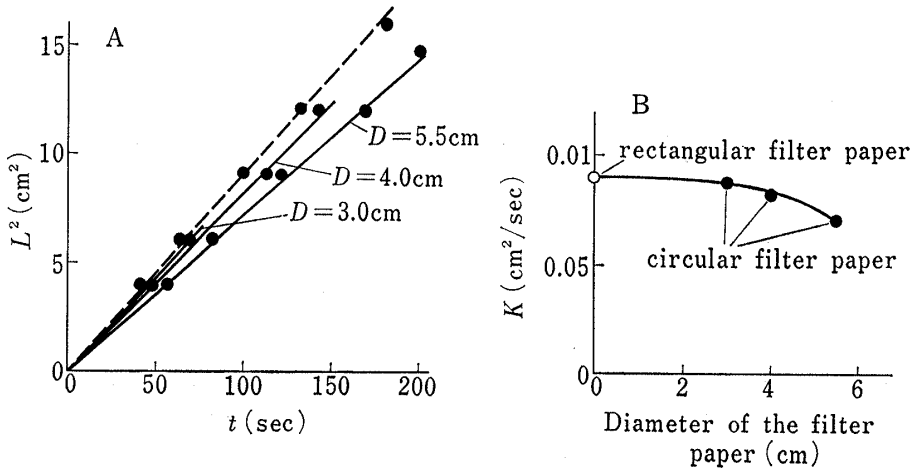

Fig. 2. Effects of Shape and Size of Filter Papers on Liquid Penetration

The filter papers were used as two-dimensional models for tablets.
A: relation between L^2 and time, t.
·····rectangular filter papers.
——circular filter papers.
B: relation between slope, K, and diameter, D, of the filter papers.

the results predicted by the two-dimensional model and confirms that the effect of tablet shape on the penetration behavior is negligible in tablets having relatively small diameter.

Reproducibility

Scatter diagrams of L^2 *vs.* t for magnesium oxide as obtained by the present tablet method and the usual powder method are shown in Fig. 5. These tablets were all prepared under a pressure of 215 kg/cm^2. Variations of penetration time in the tablet method are apparently larger than those in the powder method. This is attributable for the most part to reading errors caused by the small size of the tablets. Another reason may be inhomogeneity in the tablets arising in the preparation process.

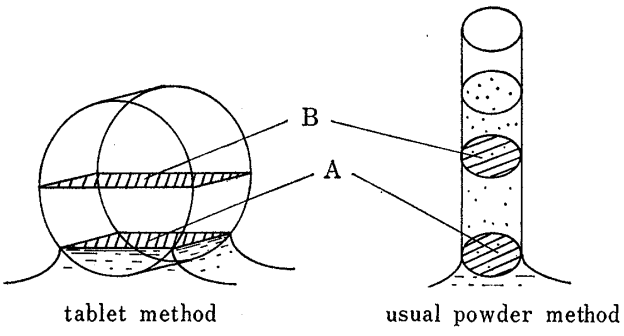

Fig. 3. Schematic Explanation of the Penetration of Liquid into a Tablet and a Powder Column

A: the area through which the liquid is supplied.
B: the area to which the liquid is supplied.

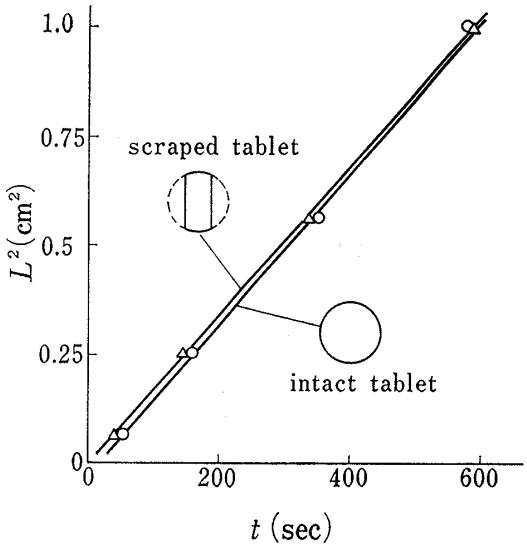

Fig. 4. Effect of Scraping on Liquid Penetration into Magnesium oxide Tablets

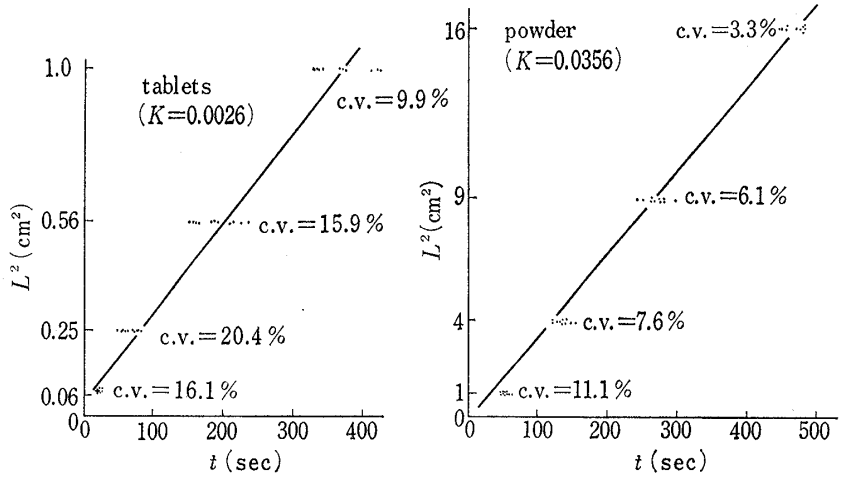

Fig. 5. Scatter Diagrams of L^2 and t for the Tablet Method and the Powder Method

K: slope of the L^2 *vs.* t regression line, c.v.: coefficient of variation.

Effect of Weight of Tablets

Magnesium oxide tablets having various weights from 0.1 to 0.5 g were prepared under a pressure of 430 kg/cm^2. Washburn's plots for these tablets and the effect of tablet weight on the slope K are shown in Fig. 6-A and B. It is evident from Fig. 6-A and B that the rate

of penetration is not affected by the weight of tablets. Thus, the diameters of capillaries seem to be constant regardless of the weight of tablets.

Since transmitted light was used for observation, a thinner tablet is more convenient in the present method. However, tablets must be hard enough for handling, and thin tablets are not used commercially, so a tablet of 250 mg in weight was chosen as a standard.

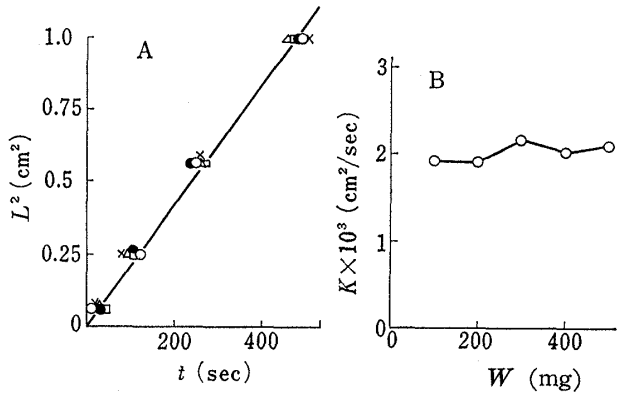

Fig. 6. Effect of Weight on Liquid Penetration into Magnesium oxide Tablets Prepared at a Pressure of 215 kg/cm^2

A: relation between L^2 and t for tablets having different weights.
○ 0.1 g, × 0.2 g, △ 0.3 g, ● 0.4 g, □ 0.5 g.
B: relation between K and weight of tablets (W).

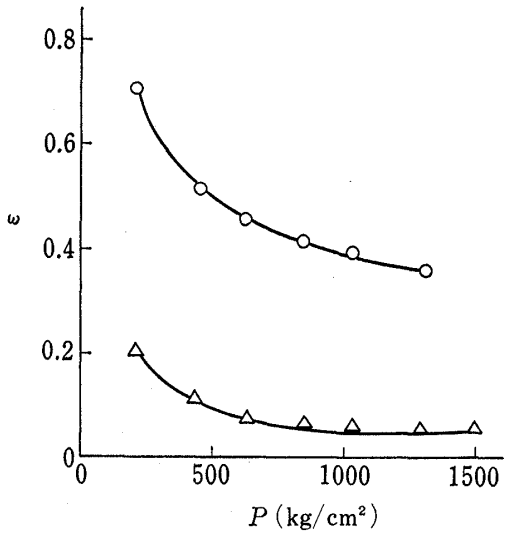

Fig. 7. Relation between Porosity (ε) and Compression Pressure (P)

○ magnesium oxide, △ crystalline cellulose.

Effect of Tableting Pressure

To examine the effect of tableting pressure on the penetration rate into tablets, magnesium oxide (showing a low penetration rate) and crystalline cellulose (showing a high penetration rate) were chosen as samples. The materials were compressed under pressure in the range from 215 to 1500 kg/cm^2. The effects of compression pressure on porosity (ε) and on penetration rate are shown in Fig. 7 and Fig. 8, respectively. It is evident that porosity and penetration rate decrease with increasing pressure. The L^2 *vs.* t plot for magnesium oxide was linear, but, in contrast, the plot for crystalline cellulose shows an apparently concave line (Fig. 8-B). In this case, the L *vs.* t plot instead of the L^2 *vs.* t plot shows good linearity (Fig. 8-C).

Since the penetration rate was recognized to vary with compression pressure, tablets were usually prepared at low pressure (215 kg/cm^2), to shorten the measuring time.

Penetration into Various Tablets and Powders

The results obtained are shown in Fig. 9-A and B. All samples except for crystalline cellulose in the tablet method gave results consistent with Eq. 1. The slopes (K) of these samples are shown in Table II. It is clear from this table that tablets show considerably smaller K values than the corresponding powders. The value of K depends on both r and $\cos\theta$, but the change of θ is considered to be small, because the compression pressure was comparatively low (215 kg/cm^2) and the particles may not be greatly crushed in tableting. Thus, if the influence of change of θ on K is neglected, these results apparently indicate that the capillary diameter in tablets is smaller than in powder, since the same materials and liquid were used in the experiments. The order of magnitude of K obtained by each method is the same, but magnesium silicate seems to be exceptional. Awata[4] *et al.* stated that the penetration of liquid into a powder packed in a glass tube was frequently interrupted halfway by contraction of the powder bed due to wetting, and liquid penetration became extremely slow or ceased.

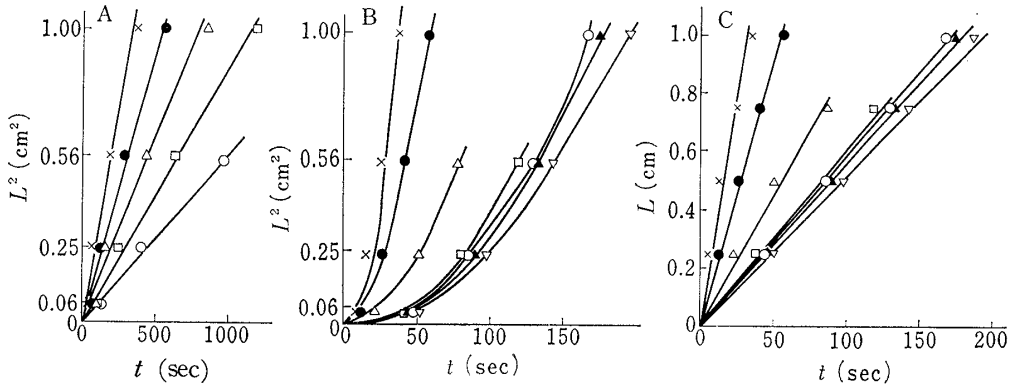

Fig. 8. Effect of Compression Pressure on Liquid Penetration

A: 0.25 g magnesium oxide tablets.
B: 0.25 g crystalline cellulose tablets.
C: L *vs.* t plot for the same sample as B.
× 215 kg/cm^2, ● 430 kg/cm^2, △ 645 kg/cm^2, □ 860 kg/cm^2, ○ 1075 kg/cm^2, ▲ 1290 kg/cm^2, ▽ 1505 kg/cm^2.

Magnesium silicate shows usual penetration behavior in the tablet method, but in contrast exhibits a remarkably low penetration rate in the powder method (Fig. 9-B). This phenomenon arises from contraction of the wetted powder bed, as described by Awata *et al.* The reason for the contraction of the powder bed on wetting is obscure, but the mechanism is beyond the scope of the present report.

The tablets of lactose gave a linear L^2 *vs.* t plot, but tablets of crystalline cellulose showed a concave plot (Fig. 9-A); thus, the penetration rate of compressed lactose is initially faster than that of crystalline cellulose but then this order is reversed. The concave line in the L^2 *vs.* t plot for crystalline cellulose can be interpreted in this way. The tablets of crystalline cellulose swell freely when water is taken up. This swelling causes the generation of cracks or lamination of tablets. The liquid penetration rate is increased by these cracks and it is for this reason that Eq. 1 is not applicable to crystalline cellulose. In this case, K in Table II means the slope of the L *vs.* t plot and has dimensions of cm/sec.

In contrast with the result obtained by the tablet method, crystalline cellulose gave a linear plot in the powder method (Fig. 9-B). This can be explained in terms of both the swelling of powder and generation of cracks being restricted by the glass tube, so that the liquid penetration behavior in crystalline cellulose in the glass tube is similar to that of other non-swelling materials.

In the case of lactose, linearity holds in the L^2 *vs.* t plot in both the powder and tablet methods, so that the effect of dissolution of particles on the penetration rate seems to be small.

Table II. Comparison of Porosity and Penetration Constant (K) of Powders and of Tablets prepared at a Pressure of 215 kg/cm^2 (0.25 g in Weight and 1.3 cm in Diameter)

Excipients	Tablets			Powders	
	Thickness (mm)	Porosity (−)	K (cm^2/sec)	Porosity (−)	K (cm^2/sec)
Lactose	1.60	0.231	0.0279	0.431	0.0746
Crystalline cellulose	1.53	0.206	(0.0369[a])	0.785	0.0495
Magnesium silicate	1.92	0.700	0.0227	0.819	0.0013
Magnesium carbonate	1.66	0.627	0.0026	0.911	0.0100
Magnesium oxide	1.74	0.707	0.0017	0.927	0.0074

a) Obtained from an L *vs.* t plot and having the dimensions of cm/sec.

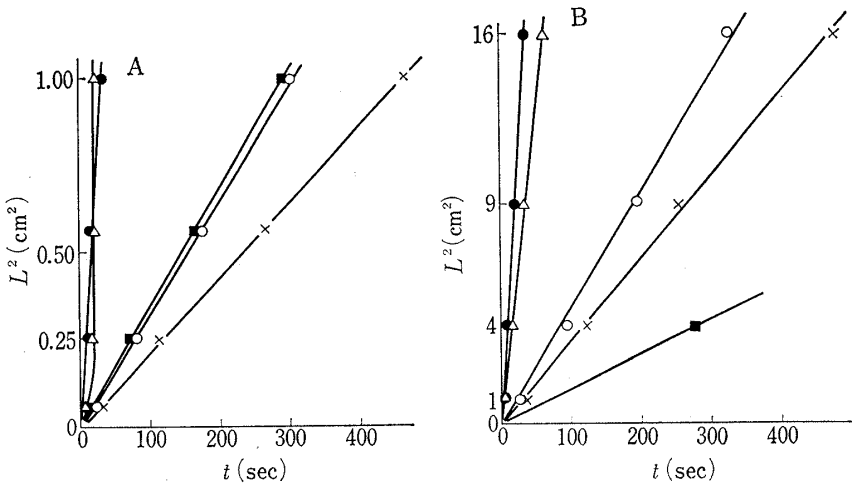

Fig. 9. Comparison of the Rates of Liquid Penetration into Various Excipients Determined by Two Methods

A: tablet method, B: usual powder method.
△ crystalline cellulose, ● lactose, ■ magnesium silicate, ○ magnesium carbonate, × magnesium oxide.

Penetration Patterns

With the progress of liquid penetration, various patterns (illustrated in Fig. 10) are observed. Most tablets belong to type A. Some tablets which belong to type A occasionally show patterns of type B, so that the difference between types A and B may not be fundamental. A pattern of type C is observed only in crystalline cellulose tablets. A feature of type C is that the penetration rate in the lateral surrounding portion of tablets is faster than that in the middle portion. These phenomena become more marked in the case of tablets prepared at pressures from 645 kg/cm^2 to 860 kg/cm^2 (type D in Fig. 10). The central portion of the tablet is left as an unwetted island in a short time. The particles at the peripheral portion of the tablet have a larger degree of freedom as regards swelling than particles in the bulk portion. Thus, when penetration occurs, peripheral particles are considered to swell more quickly than bulk particles. Once swelling occurs, it generates cracks and promotes further penetration, as mentioned above. This is the reason why penetration of type C or D occurs.

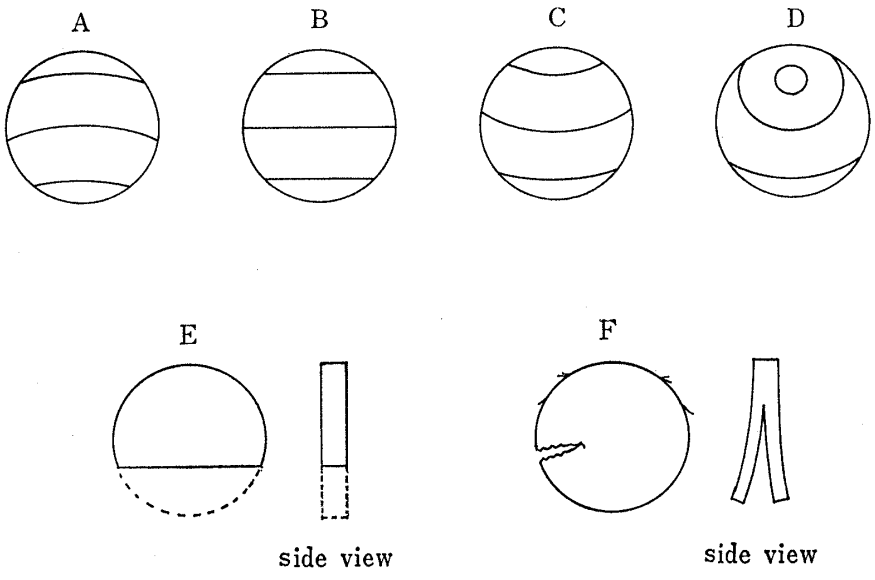

Fig. 10. Classification of Penetration Patterns and Disintegration Patterns

A,B,C,D: penetration patterns, E,F: disintegration patterns.

Disintegration Patterns

Most tablets change little in external appearance even after completion of penetration, but a few samples such as lactose and calcium carbonate tablets change in form, with disintegration. The latter intact powders are difficult to compress into tablets, and furthermore the tablets disintegrate immediately after wetting, so the binding force between particles must be very weak. In these cases, shortly after penetration occurs, particles separate from the bottom of the tablets immersed in water, so that the bottom gradually moves upwards. The final forms after penetration are illustrated in Fig. 10-E. The liquid is drawn up to some height until the weight of the rasied portion of the liquid overcomes the surface tension of the liquid, and the raised portion separates from the bottom of the tablet, so that penetration stops since the supply of liquid has stopped. The pattern shown in Fig. 10-F is observed only in the case of crystalline cellulose tablets. They separate into two sheets or crack due to swelling during penetration.

References and Notes

1) This work was presented at the 19th annual meeting of the Kanto branch of the Pharmaceutical Society of Japan, Chiba, October 1975.
2) E.H. Washburn, *Phys. Rev.*, **17**, 273 (1921).
3) D. Ganderton and D.R. Fraser, *J. Pharm. Pharmac.*, **22**, *Suppl.*, 95S (1970); D. Ganderton, *J. Pharm. Pharmac.*, **21**, *Suppl.*, 9S (1969).
4) E. Awata and T. Suyama, *Takamine Kenkyunenpo* **9**, 67 (1957).