[Chem. Pharm. Bull. 14(2) 152~158 (1966)]

UDC 615.412.1 : 615.772

24. Hisashi Nogami, Tsuneji Nagai, and Hiroshi Uchida : Studies on Powdered Preparations. XIV.*1 Wetting of Powder Bed and Disintegration Time of Tablet.*2

(*Faculty of Pharmaceutical Sciences, University of Tokyo**3)

Drug absorption and action of powdered preparations are expected to be caused through the process of disintegration and/or dissolution in body fluid, which may be related to the wetting of powder system, because the contact of powder with fluid is initiative on the processes. The tablet disintegration is much complicated and influenced by many complicated factors such as the content and type of disintegrator and binder, particle size of compressed powder, and compressional force, as has been reported by many workers. It is very difficult to know what mechanism is operative on the tablet disintegration. However, during the process of tablet disintegration the first step is surely taken through the interaction between tablet and liquid. The immersional wetting, therefore, is considered to be necessary on the disintegration of many kinds of tablets. The wettability of solid may be indicated by contact angle, adhesion tension, heat of wetting, and penetration rate according to Washburn's equation. The heat of wetting is the most severe measure, but the penetrating rate is considered most suitable for the study of tablet disintegration because the principle is concerned with the powder bed which is similar in condition to tablet. The wetting of powder with liquid depends essentially on various conditions of powder surface such as surface moisture content, crystal structure and crystallinity, and thus penetrating rates would be considered to be affected by such factors. Aoki, *et al.*1) and Nogami, *et al.*2) have examined effects of penetrating rate on the disintegration of granule and of tablet, respectively.

The present study was attempted to investigate dependence of the penetrating rate constant of liquid into powder bed on temperature and surface moisture content, and to discuss the relationship between the penetrating rate constant and the disintegration time of tablet.

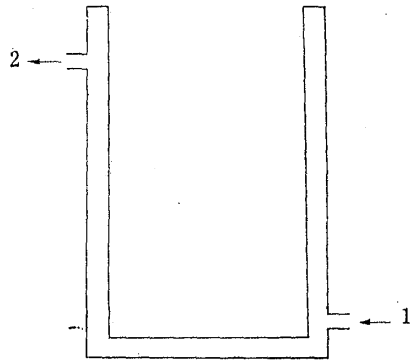

Fig. 1. Thermally Controlled Beaker

Temperature constant water was circulated by the way from 1 to 2.

Experimental

Materials——Natural aluminum silicate J.P. (AS), heavy magnesium oxide J.P. (MgO), and potato starch J.P. (PS) were used in this study. These insoluble powders were suitable for test samples to investigate the wetting itself, because the dissolution accompanied with wetting made the discussion complicated.

Preparation of Sample and Procedure——1) Measurement of penetrating rate : MgO of relatively uniform particle size passing through 149 μ sieve and very fine AS were dried under reduced pressure of 10^{-2} mm.Hg for two days, and then moistened in an atmospheric humidity controlled using saturated solution of a kind of inorganic salt for two or three weeks, while PS was used without similar treatments. A given amount of

---

*1 Part XIII : H. Nogami, T. Nagai, A. Suzuki : This Bulletin, **13**, 1387 (1965).

*2 Presented at the 84th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April 1964.

*3 Hongo, Tokyo (野上 寿, 永井恒司, 内田 広).

1) M. Aoki, T. Fukuda : Yakuzaigaku, **20**, 106 (1960).

2) H. Nogami, H. Fukuzawa, Y. Nakai : This Bulletin, **11**, 1398 (1960).

each powder was packed in a graduated tube by tapping mechanically for 6 min. At the moment when this packed tube was immersed in water in the thermally controlled beaker in Fig. 1, the measurement of the penetrating length was started.

2) Measurement of disintegration time: A given amount of PS granules (prepared using 300 ml. of 10% PS paste per kg. of PS powder) passing through 500 μ sieve and MgO passing through 149 μ sieve, respectively, was compressed for 10 sec. by Kimura K-II tabletting machine, using a pair of plain faced punches of 13 mm. diameter under a given compressing rate and force of the upper punch controlled according to the indication of strain meter (Kyowa-Dengyo DM-H type). On the 2.23 mm. sieve in the liquid in the thermally controlled beaker in Fig. 1, the tablet was disintegrated without being stirred and the time when all disintegrated fractions finished to pass through the sieve was defined as disintegration time, t_D.*4

Results and Discussion

Examination on the Tapping Time to Prepare Powder Bed

Penetrating of water into powder bed packed by tapping mechanically (190 times per min. of a drop of 1 cm.) depended on the tapping time as shown by the data on AS in Fig. 2. 1 minute tapping time was too short to obtain a satisfactorily packed bed and a reproducible linear line of wetting curve according to Washburn's equation. The penetrating rate had a decreasing trend to reach a certain value with the increase of the tapping time, and this was considered due to the decrease of the average diameter of void space in Washburn's equation as the powder bed was packed satisfactorily. 6 minutes tapping was considered appropriate because the penetrating rate of water into the powder bed packed by this tapping was almost the same to that by 15 minutes tapping, and thus all powder beds for measurement were packed by tapping for 6 minutes in this study.

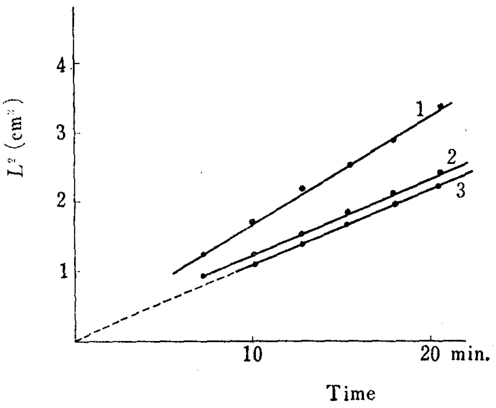

Fig. 2. Penetration of Water into Natural Aluminum Silicate Bed packed for Various Periods

1: 1 min. 2: 6 min. 3: 15 min.

Penetrating Rates and their Temperature Dependences

On the penetrating rate of liquid into powder bed, Peek-McLean's equation (1) has been known[3)]

$$\frac{dL}{dt}=\frac{r\gamma\cos\theta}{4\eta L}-\frac{r^2dg}{8\eta} \qquad (1)$$

where L is the penetrating length at time t, r the average radius of void space, θ the contact angle between liquid and powder surface, g the acceleration constant of gravity, and γ, η and d are the surface tension, viscosity and specific gravity of liquid, respectively. Since measurements in this study were made on fine powder bed and in the initial period of the penetration, the second term in the right of equation (1) can be neglected. Integrating equation (1) and putting $h=0$ at $t=0$, the following so-called Washburn's equation is obtained,[4)]

$$L^2=\frac{r\gamma\cos\theta}{2\eta}t. \qquad (2)$$

---

*4 This measure is different from that obtained according to Disintegration Test in J.P. VII.

3) R.L. Peek, D.A. McLean: Ind. Eng. Chem., Anal. Ed., **6**, 85 (1934).

4) E.H. Washburn: Phys. Rev., **17**, 273 (1921).

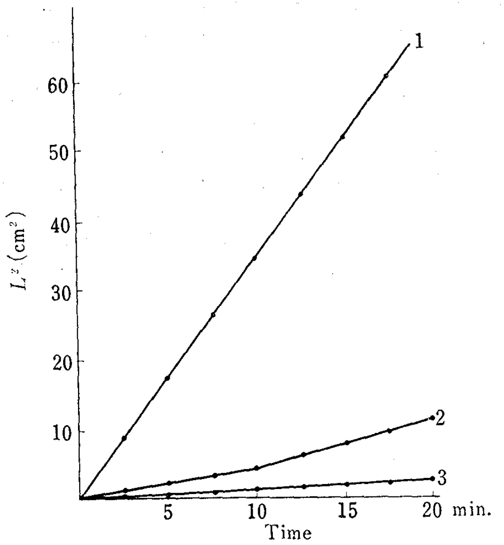

Fig. 3. Penetration of Water into Powder Bed at 30°

1 : Potato starch
2 : Heavy magnesium oxide
3 : Natural aluminum silicate

Writing $\frac{r\gamma\cos\theta}{2\eta}=k$, which is called penetrating rate constant in this study,

$$L^2=kt. \qquad (3)$$

It is shown in Fig. 3 that the penetration of water into powder bed can be expressed by equation (3) and also k varied with materials used, *i.e.* depending on the average radius of void space r, and the contact angle θ. Such a bending point in magnesium oxide/water system as shown in Fig. 3 have been reported in also calcium carbonate/methanol system by Kuno *et al.*,[5] but the causes are not well known.

As expected from equation (2), penetrating rate constant is related to surface tension and viscosity of liquid, and thus penetrating rate constant might depend on liquid temperature. The viscosity of liquid is known to depend on temperature according to Andrade's equation (4),

$$\eta=Ae^{\frac{E}{RT}} \qquad (4)$$

where E is the activation energy of viscosity, A the constant, and R the gas constant. On the other hand, the adhesion tension, $\gamma\cos\theta$, depends on temperature at a constant pressure p, as

$$\varDelta H=\gamma\cos\theta-T\left(\frac{\partial\gamma\cos\theta}{\partial T}\right)_p \qquad (5)$$

where $\varDelta H$ is the heat of wetting. If systems are not disturbed during the wetting process, $\varDelta H$ is independent on temperature. In this experiment, pressure p is considered constant; solving equation (5),

$$\gamma\cos\theta=\varDelta H-CT \qquad (6)$$

is obtained, where C is the positive constant; combining equations (2), (4), and (6),

$$k=\frac{r}{2A}(\varDelta H-CT)e^{-\frac{E}{RT}} \qquad (7)$$

Since generally $\varDelta H/CT$ is coming between one and two, taking logarithm of equation (7), approximating log ($\varDelta H/CT$-1) to $\varDelta H/C'T+C''$,

$$\log\frac{k}{T}=\alpha-\frac{\beta}{RT} \qquad (8)$$

where $$\alpha=\log\frac{rC}{2A}+C'', \qquad \beta=E-\frac{R}{C'}\varDelta H \qquad (9)$$

Penetrating rate of water into PS powder bed, for example, depended on temperature of water as shown in Fig. 4. Obtaining k from the slope of each straight line and then plotting log k/T *vs.* $1/T$, the result obtained was expressed by equation (8)

---

[5] H. Kuno, R. Abe : Kogyo Kagaku Zasshi, **61**, 1445 (1958).

as shown in Fig. 5. The similar results were obtained on also all other samples examined in this study. From these linear relationships the apparent activation energies of wetting (β) were obtained as shown in Tables I and II *e.g.*, β value of PS/water system in Fig. 5 was calculated as 1.67 kcal.

From Tables I and II, it was known that magnesium oxide was wetted more easily by water than by ethanol, whereas AS have an inverse tendency. From values in

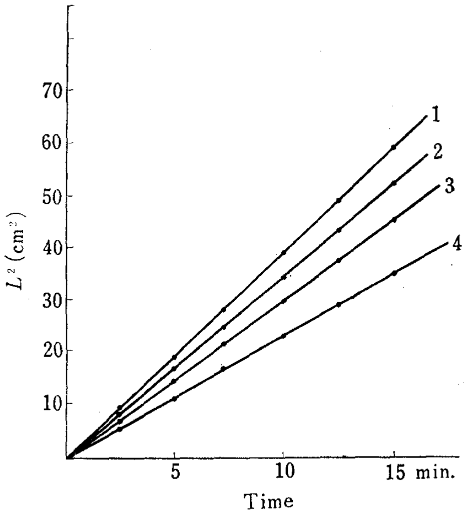

Fig. 4. Penetration of Water into Potato Starch Bed at Various Liquid Temperatures
1 : 38° 2 : 30.4° 3 : 20.1° 4 : 0.6°

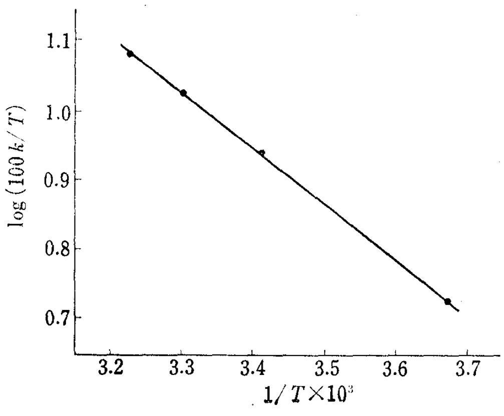

Fig. 5. Temperature Dependence of Penetrating Rate Constant of Water into Potato Starch Bed

Table I. Penetrating Rate Constant[a] and Apparent Activation Energy β, of Natural Aluminum Silicate

Liquid	Moisture Content (%)	Temperature			β kcal.
		20°	30.8°	39°	
Water	0	0.40	0.54	0.74	5.2
	2.32	0.58	0.78	0.98	4.4
	9.28	1.09	1.49	1.95	4.4
Ethanol	0	4.4	6.2	7.6	4.8
	2.19	4.1	5.9	7.2	4.8
	9.23	5.5	7.9	10.3	5.2

[a] Each value is the mean of 3 determinations in cm^2/10 min.

Table II. Penetrating Rate Constant[a] and Apparent Activation Energy β, of Heavy Magnesium Oxide

Liquid	Moisture Content (%)	Temperature			β kcal.
		20°	30.8°	39°	
Water	0	5.8	7.1	8.3	2.6
	5.73	7.0	9.6	11.5	3.7
	8.36	6.8	9.2	12.9	4.8
Ethanol	0	1.5	1.8	2.3	3.5
	2.53	3.9	4.8	6.1	3.5
	15.22	5.2	7.0	9.2	4.3

[a] Each value is the mean of 3 determinations in cm^2/10 min.

these tables on the powder of no moisture content, ratios of $(\gamma \cos \theta/\eta)$ of water to that of ethanol at 30.8° were calculated as 3.95 in the case of magnesium oxide and 0.087 in the case of AS. Comparing these values with the ratio of (γ/η) of water to that of ethanol at 30° (3.66), the followings were estimated: contact angle of magnesium oxide with water was smaller than with ethanol; that of AS with water was fairly larger than with ethanol. This result would indicate that magnesium oxide powder is of more hydrophilic and polar surface than AS powder.

The dependence of penetrating rate constant on moisture content was remarkable in systems of relatively small k values like AS/water and magnesium oxide/ethanol as shown in Tables I and II. It seemed possible that the surface of powder was made to be more affinitive with such hydrophilic liquids on account of the water adsorbed on it by moistening.

Apparent activation energies shown in Tables I and II were reasonable in these systems, because the wetting process was considered to be controlled by physical factors such as viscosity of liquid and adhesion tension between liquid and powder surface. The measurement on activation energies of wetting of powder surface has never been reported, but that of the wetting of metal surface with molten glass has been reported as 40~60 kcal./mol., corresponding to the activation energy of viscous flow of molten glass.[6] This would indicate that heat of wetting of metal/molten glass system is negligible in equation (9). According to equation (9), it would be expected that the apparent activation energies (β) of wetting of hydrophilic solid such as magnesium oxide increased with the amounts of pre-adsorbed water and amounted to the value (4.5 kcal.) corresponding to the activation energy of viscous flow of water at a saturated condition, as represented in Table II, because heat of wetting of hydrophilic solid decreased with the amounts of adsorbed water and at a saturated condition the powder surface was covered with liquid layer. On the other hand, in the case of powder of less hydrophilic character, the heat of wetting with water was small, being a little affected by surface moisture content or rather increased with amounts of pre-adsorbed water, and thus the apparent activation energy of wetting of AS did not depend on moisture content or rather decreased as shown in Table I. As well, the apparent activation energy of PS (1.67 kcal.) indicated that PS was of hydrophilic surface and heat of wetting with water was very large. The influence of moisture content on the activation energy of diffusion of water vapor into a starch gel film has been described by Fish, *et al.*[7] *i.e.*, decreasing from 9.8 to 4.5 kcal. of activation energy with the increase of moisture content of film from 0.8 to 80%. This water vapor diffusion was considered to be controlled by a mechanism different from that of the wetting process, but at a fully swollen condition its activation energy became that of viscosity of water.

In the case of magnesium oxide, although the apparent activation energy increased with moisture content, penetrating rate also increased with moisture content due to the increase of an average pore diameter of magnesium oxide bed, as expected from the fact that an apparent bulk density decreased with moisture content.

Tablet Disintegration

The disintegration time of tablet was dependent on the temperature of liquid as well as on the compressional force, as shown by the data on magnesium oxide in Table III. Here, to discuss such a tablet as is disintegrated when it is wetted, the followings are assumed: 1) the water-powder interfacial area in the system, S,

---

6) K. Semba: J. Ceramic Assoc. Japan, **66**, 213 (1958).

7) B.P. Fish: "Diffusion and Equilibrium Properties of Water in Starch," p. 22 (1957), Her Majesty's Stationary Office, London.

Table III. Disintegration Time of Heavy Magnesium Oxide Tablet in Water

Compressional force (ton)	20°	29°	37.5°
0.1	68.6	54.7	47.7
0.2	50.8	39.0	30.4
0.3	43.0	41.1	34.4

Unit : second

increases in proportion to the penetrating length of capillary void, L,

$$S=fL \tag{10}$$

where f is the constant characteristic to tablet; 2) S reaches to a certain value S_D, at disintegration time t_D. Differentiating equation (10), combining equations (10) and (2), and then putting $S=0$ at $t=0$ and $S=S_D$ at $t=t_D$,

$$S_D^2=\frac{f^2}{2}\cdot kt_D. \tag{11}$$

Accordingly, it follows that,

(Penetrating rate constant)×(Disintegration time)=constant.

The average pore diameters could be considered to be almost equal for tablets made under the same compressional condition, the values of k on tablets depended only on temperature. Experimental results were in substantial accord with equation (11) as shown in Fig. 6. It was, therefore, understood that the immersional wetting might be a controlling factor on the disintegration of the tablet made under a low compressional force, the limiting value of which was dependent on the materials used, the compressional conditions, etc. According to equation (11), the straight lines in Fig. 6 must pass the original point, when they are extrapolated. But, in the case of PS, from the fact that the straight line deviated a little from the original point as shown in Fig. 6, it seemed

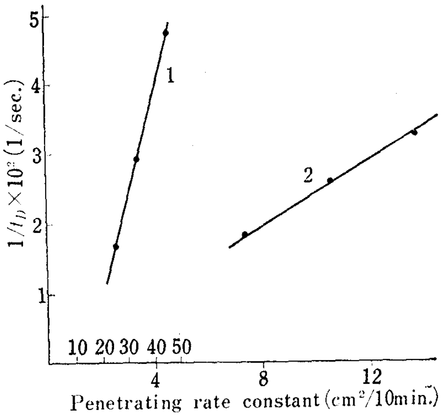

Fig. 6. Relationship between Disintegration Time t_D and Penetrating Rate Constant

1 : Potato starch (0.5 ton)
2 : Heavy magnesium oxide (0.2 ton)

Table IV. Sedimention Volume and Disintegration Time* of Potato Starch

Liquid	Sedimentation volume[a] (ml./g.)	Disintegration time[b] (sec.) 38°	20.5°	0.75°
Pyridine	0.92	10.8	18.3	50.0
Acetone	1.02	13.0	28.6	—
Ethanol	1.20	19.6	19.7	33.5
Dioxane	1.30	14.8	24.0	—
Water	1.37	20.4	30.1	55.3
Benzene	1.79	none[c]	none	none

a) Each value is the mean of 4 determinations obtained at 38°.
b) Each value is the mean of 7 determinations.
c) This represents that potato starch tablets were not disintegrated.
* This measure is disintegration time of potato starch tablet compressed at 0.5 ton.

possible that this was the case when the disintegration could not begin until the penetrating of water reached a certain rate.

Additionally, the relationship between disintegration time and sedimentation volume was examined as shown by the data on PS in Table Ⅳ. It may be questionable that disintegration time is directly related to sedimentation volume, but it is possible that sedimentation volume is dependent on wettability of powder with liquid. PS tablets were disintegrated more easily in the liquid where PS powder gave less sedimentation volume. These results also show that wetting must play an important role in the tablet disintegration.

This study was supported in part by a Grant in Aid for Fundamental Scientific Research from the Ministry of Education, to which the authors are grateful.

Summary

1. The penetrating rate constants of water and ethanol into magnesium oxide and AS powder beds were obtained with a satisfactory reproducibility. These results were in accord with Washburn's equation.

2. The penetrating rate constants in these systems were dependent on the temperature of liquid according to log $k/T=\alpha-\beta/RT$ and apparent activation energies of wetting were obtained as a few kcal.

3. Dependence of the penetrating rate constant on moisture content of powder was remarkable in systems of relatively small k values like AS/water and magnesium oxide/ethanol.

4. The apparent activation energy of wetting was concerned with the moisture content of powder.

5. The disintegration time of tablet was dependent on the temperature of liquid as well as on the compressional force. The temperature dependence of disintegration time was almost the same as that of penetrating rate constant.

6. The immersional wetting might be a controlling factor on the disintegration of the tablet made under a low compressional force.

(Received July 5, 1965)