

Evaluation of Patterns and Binding Forces of Tablets in Dissolution Processes

Jung-Woo Kim
Chong Kun Dang Corporation

(Received March 22, 1985)

For the model tablets using mannitol and Avicel PH 101 as excipients, the patterns of disintegration and dissolution from the differences of physical properties were investigated. It was found that the patterns in the dissolution and binding forces in the interaction of materials by estimates of solid-solid or liquid surface free energy due to cohesive or adhesive properties of materials, and solid surface free energy in binding forces of tablet should be considered as an important factor in dissolution processes.

The compression of powered or granular material into a cohesive or adhesive mass during the formation of tablet plays an important role in dissolution processes.^{1~2)}

However, the dissolution of a tablet immersed in a liquid appears to be essentially a mechanical phenomenon; wetting, penetration of liquid, and then destruction of compressed structure. The structure and properties of tablets, such as chipping, lamination, and capping occur from the properties of its cohesive or adhesive of materials used, while the differences of patterns in the dissolution and rates in disintegration of tablets are predicted. In general, tablets manufactured from compression of powers or granules may be explained by the use of spring-dashpot models.^{3~7)} On the other hand, it is suggested that disintegration or dissolution of tablets may occur by the breaking from the weak parts either spring or dashpot amid models. However, this may be classified into the following 4 cases;

- 1) weak adhesive materials with strong cohesive materials.
- 2) strong adhesive materials with weak cohesive materials.
- 3) strong adhesive materials with strong cohesive materials.
- 4) weak adhesive materials with weak cohesive materials

Chong Kun Dang Corporation

In this point of view, this report presents its patterns in the dissolution and binding forces in the interaction of materials by estimates of solid-solid or liquid surface free energy from contact angle according to cohesive or adhesive properties of materials, and solid surface free energy in binding forces of tablet should be considered as an important factor in dissolution processes.

Experimental

Experimental Formulation—Formula (A) is composed of 12g of phenobarbital, 87g of Avicel PH 101 and 1g of magnesium stearate, and formula(B) is composed of 12g of phenobarbital, 87g of mannitol and 1g of magnesium stearate. All materials used are pharmaceutical grade. Tablets are manufactured by compressing at 75 or 100MPa with machine speed of 4,101 rad/sec.⁵⁾

Disintegration Test—Disintegration is performed in 900ml of water at $37 \pm 2^\circ$ according to USP XX.

Dissolution Test—Dissolution is performed in 900ml of acetate buffer (pH 4.75) consisting of 0.005M sodium acetate solution and 0.005M acetic acid and at 50 rpm by the paddle method in USP XX.

Assay⁸⁾—Accurately take 5.0ml of sample solution at appropriate intervals. Place 5.0ml of each sample solution and 5.0ml of 0.1M borate buffer (pH 9.5) in 25 or 50ml volumetric flask. Then add water to volume. Measure the absorbances of solutions in 1cm cell at 240nm against the blank, in comparison of a standard solution having a known concentration of phenobarbital reference standard.

Results and Discussion

The meaning of "Broken" in tablet includes the phenomena in tableting processes such as chipping, lamination and capping, and destruction in disintegration and/or dissolution processes. Recently many studies about the causes of these phenomena in tableting have been reported by use of Maxwell fluid and Kelvin solid basic models.^{4,5,16)} If a material may be bonded by certain forces such as dipole-dipole interaction, dipole-hydrogen bond interaction and van der Waal's forces etc., the state of various binding forces can be expressed by using the spring-dashpot models.

The phenomena of chipping, lamination and capping can be assumed to occur by breaking of certain weakest part of spring-dashpot amid model. After tableting, first

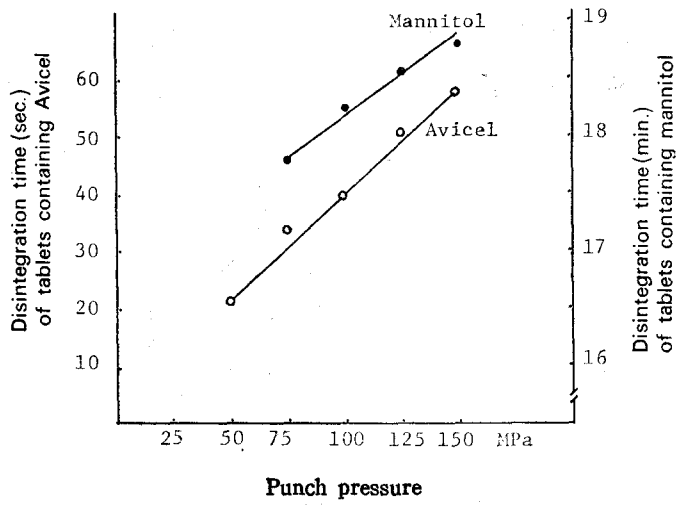


Figure 1—Effect of punch pressure on disintegration of tablets.

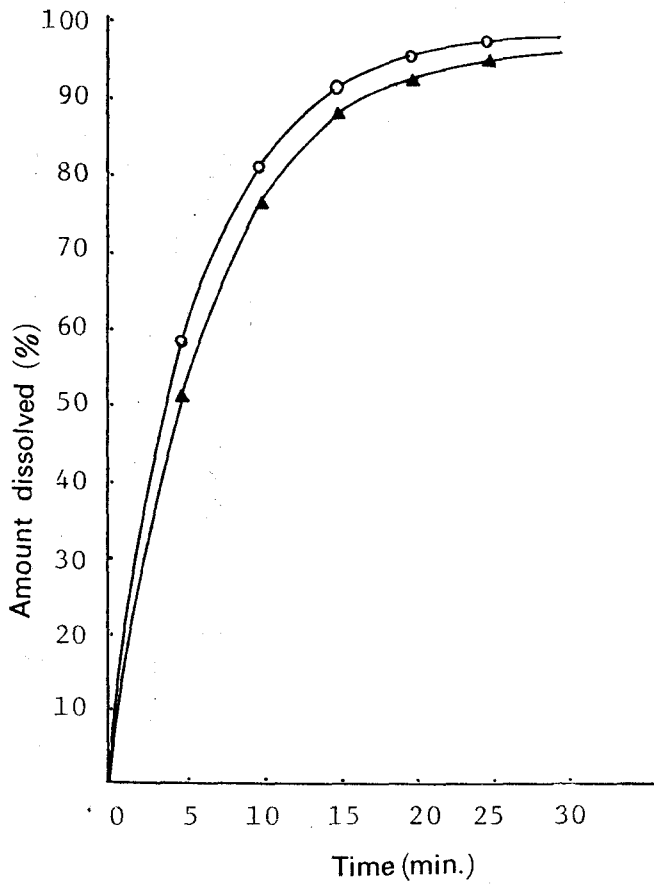


Figure 2—Dissolution of formula (A) at pH 4.75
Key : ○, 75MPa; ▲, 100MPa

of all, the wetting of tablet occurs in the dissolution process, and the wetting and penetration in tablet depend on the characteristics of materials, forces added, and formulation etc. And the tablet is destructed completely through disintegration and dissolution process.⁹⁻¹¹⁾

The destruction of tablet in the solution can be suggested to occur by the following three cases;

- 1) Dissolution processes after disintegrating
- 2) Dissolving process of the active ingredient from surface of tablet without disintegrating.
- 3) Dissolving and disintegrating process of tablet at the same time. At this point of view, to illustrate the disintegration and dissolution phenomena, formula (A) using the hydrophillic mannitol as a filler and formula (B) using Avicel PH 101 as a disintegrating agent are formulated.

Effect of Punch Pressure on Disintegration of Tablet^{12,13)}—Tablets using mannitol and Avicel PH 101 which have different physical properties each other are made by various punch pressure. Observation of disintegration curves shows the linear relationship between disintegrating time and punch pressure, and only change of disintegration time according to formulas (Fig 1).

Dissolution Pattern—In the case of formula (A), comparing with the dissolution curves, tablet is disintegrated and dissolved simultaneously, independent of tableting pressure. The relationship between time and dissolved amount of active ingredient from tablet is shown in Fig.2 and these tablets are dissolved about 90% within 15 minutes and dissolved completely within 30 minutes.

In the case of formula (B) mannitol mass is wetted, penetrated and dissolved, and then phenobarbital of the active ingredient starts to release slowly after mannitol mass is almost dissolved.

As shown in Fig.3, about 50% of active ingredient in these tablets is dissolved for 4 to 5 hours and the rest amount in these tablets is dissolved within 1 hour.

Generally, the phenomena like this may depend on the characteristics of wetting and penetration of tablet. Therefore, it can be suggested that various dissolution patterns come from the interaction of the interfacial free energy, surface tension, the contact angles of materials and the relationship between the adhesive and the cohesive forces of materials.

Considering the phenomenon in formula (B) in the theoretical aspects gives foll-

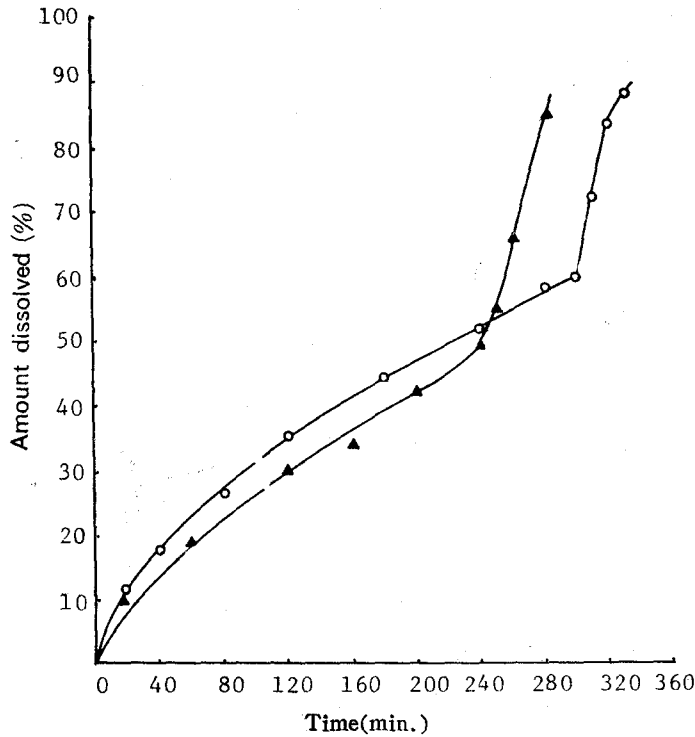


Figure 3—Dissolution of formula (B) at pH 4.75
Key : ○, 75MPa; ▲, 100MPa

ows.^{14~17)}

Comparing with adhesive forces between water/phenobarbital and water/mannitol, more hydrophilic mannitol mass is wetted faster than phenobarbital mass. Therefore, adhesive forces of water/phenobarbital (s_1) are smaller than those of water/mannitol- (s_2). Comparing cohesive forces between phenobarbital/phenobarbital with adhesive forces between phenobarbital/mannitol, in order that mannitol mass is wetted and dissolved faster than phenobarbital mass, cohesive forces of phenobarbital must be larger than adhesive forces of phenobarbital/mannitol. According to Dupre equation¹⁸⁾, the work of adhesion, $W_{O/W}$ is given by; $W_{O/W} = \gamma_{O/A} + \gamma_{W/A} - \gamma_{O/W}$

and the work of cohesion, $W_{O/A}$, is given by; $W_{O/W} = 2\gamma_{O/A}$. Where subscripts O, A, W and γ refer to oil, air, water and surface free energy, respectively. Substituting oil and water for solid 1 (s_1) and solid 2 (s_2) respectively gives;

$$W_{S_1/S_2} = \gamma_{S_1/A} + \gamma_{S_2/A} - \gamma_{S_1/S_2} \dots\dots\dots(1)$$

$$W_{S_1/A} = 2\gamma_{S_1/A} \dots\dots\dots(2)$$

Spreading coefficient, S , is given by;

$$S_{S_2/S_1} = \gamma_{S_2/A} - \gamma_{S_1/A} - \gamma_{S_1/S_2} \dots\dots\dots(3)$$

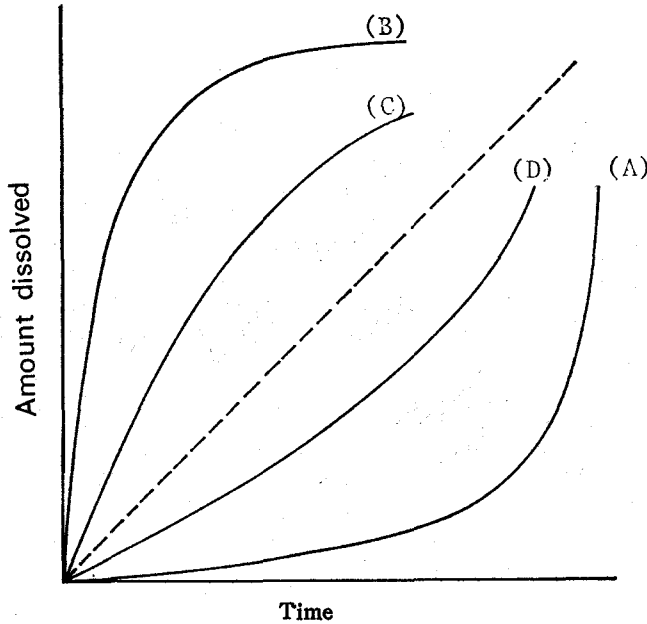


Figure 4—Dissolution profiles of tablets

From equation (1) and (3),

$$W_{S_1/S_2} = S_{S_2/S_1} + 2\gamma_{S_1/A} \dots\dots\dots(4)$$

(or $W_{S_2/S_1} = S_{S_1/S_2} + 2\gamma_{S_2/A}$)

Rearranging equation (4) results in;

$$S_{S_2/S_1} = W_{S_1/S_2} - 2\gamma_{S_1/A} \dots\dots\dots(4')$$

In the case of formula (B), comparing with spreading coefficients of S_1 and S_2 , spreading coefficient of water/mannitol is larger than that of water/phenobarbital.

$$(S_{water/S_1} = W_{S_1/water} - 2\gamma_{S_1/A} < S_{water/S_2} = W_{S_2/water} - 2\gamma_{S_2/A})$$

Therefore, rearranging above equation results in;

$$W_{S_1/water} - W_{S_2/water} < 2(\gamma_{S_1/A} - \gamma_{S_2/A}) \dots\dots\dots(5)$$

From equation (1) and (2), since cohesive forces of phenobarbital/phenobarbital are larger than those of mannitol/mannitol, the following equation can be obtained;

$$\gamma_{S_1/A} > \gamma_{S_2/A} - \gamma_{S_1/S_2} \dots\dots\dots(6)$$

While, combination of spreading coefficient of liquid (L) on a solid and adhesive forces gives the following equation;

$$W_{S/L} = \gamma_{L/A}(\cos \theta - 1) + 2\gamma_{L/A}$$

The adhesive forces of phenobarbital/water ($S_1/water$) and mannitol/water ($S_2/water$) by above equation are given by;

$$W_{S_1/water} = \gamma_{water/A}(\cos \theta_1 - 1) + 2\gamma_{water/A} \dots\dots\dots(7)$$

$$W_{S_2/water} = \gamma_{water/A}(\cos \theta_2 - 1) + 2\gamma_{water/A} \dots\dots\dots(7)'$$

Taking $W_{S_1/water}$ and $W_{S_2/water}$ from equaion (7) and (7)' respectively, and rearranging equation (5) gives equation (8).

$$\gamma_{water/A}(\cos \theta_1 - 1) - \gamma_{water/A}(\cos \theta_2 - 1) < 2(\gamma_{S_1/A} - \gamma_{S_2/A}) \dots\dots(8)$$

From equation (6) and (8),

$\gamma_{water/A}(\cos \theta_1 - 1) - \gamma_{water/A}(\cos \theta_2 - 1) < 2(\gamma_{S_1/A} - \gamma_{S_1/A}) < 2\gamma_{S_1/S_2}$ and rearranging results in;

$\gamma_{water/A}(\cos \theta_1 - \cos \theta_2) < 2(\gamma_{S_1/A} - \gamma_{S_2/A}) < 2\gamma_{S_1/S_2}$ Hence, the following equations are obtained;

$$\gamma_{S_1/A} - \gamma_{S_2/A} < \gamma_{S_1/S_2} \dots\dots\dots(9)$$

$$\gamma_{water/A}(\cos \theta_1 - \cos \theta_2) / 2 < \gamma_{S_1/S_2} \dots\dots\dots(10)$$

It means that we can approximately calculate the surface free energy with the contact angle of two materials and we can find that the differences between the surface free energies of each material are smaller than those of materials in contact with each other.

The contact angle of phenobarbital (θ_1) is 70° and that of mannitol is 0° approximately (more hydrophilic), and then the surface tension of water is 71.8 dyne/cm^2 .

Calculating from equation (10) gives that γ_{S_1/S_2} is smaller than 23.62 dyne/cm^2 .

In the case of formula (B), Adhesive forces of water/phenobarbital (S_1) are smaller than those of water/Avicel(S_2).

$$[W_{S_1/water} - W_{S_2/water} < 2(\gamma_{S_1/A} - \gamma_{S_2/A})]$$

Cohesive forces of phenobarbital/phenobarbital are much smaller than adhesive forces of phenobarbital/Avicel.

$$(\gamma_{S_1/A} \ll \gamma_{S_2/A} - \gamma_{S_1/S_2})$$

Combination of the above mentioned equation gives;

$$W_{S_1/water} - W_{S_2/water} < 2(\gamma_{S_1/A} - \gamma_{S_2/A}) \ll -2\gamma_{S_1/S_2}$$

Hence, we can get the following equation;

$$\gamma_{S_2/A} - \gamma_{S_1/A} \gg \gamma_{S_1/S_2} \dots\dots\dots(11)$$

$$\gamma_{water/A}(\cos \theta_2 - \cos \theta_1) / 2 > \gamma_{S_1/S_2} \dots\dots\dots(12)$$

It means that we can approximately calculate the surface free energy with the contact angle of two materials and we can find that the difference between the surface free energy of each material is much larger than that of materials in contact with each other.

Since the contact angle of Avicel PH 101¹⁹⁾, θ_2 is 17° , we can find that γ_{S_1/S_2} is smaller than 22.04 dyne/cm^2 . It means that the surface free energy between phenobarbital and Avicel is smaller than 22.04 dyne/cm^2 and the difference between the surface free energy of the materials in contact with each other is larger than the interfacial free energy.

Conclusively, more than two dissolution patterns may be suggested as follows:

The adhesive forces of water/solid₁ are smaller than those of water/solid₂. If cohesive forces of solid₁/solid₂ are smaller than adhesive forces of solid₁/solid₂, the curve C can be expected, and if larger, the curve D can be expected, as shown in Fig. 4.

References

- 1) H. Leuenberger, *International J. of Pharmaceutics*, **12**, 41 (1982)
- 2) H. Søger, P.J. Ruž, I. Burt, J. Ryder and J.K. Warrack, *Int. J. Pharm. Tech & Prod. Mfr.*, **2**(2), 41(1981)
- 3) Frank A. McClintock and Ali S. Argon, *Mechanical Behavior of Materials*, Addison-Wesley Publishing Company, Inc. (Canada)
- 4) Wilhelm Flügge, *Viscoelasticity*, 2nd Edition (1975)
- 5) Edward G. Rippie and Douglas W. Danielson, *J. Pharm. Sci.*, **70**(5), 476(1981)
- 6) Herbert A. Lieberman, Leon Lachman, *Pharmaceutical Dosage Forms* (vol.2), p.153~184, Marcel Dekker Inc.
- 7) M.E. Aulton, *Int. J. Pharm. Tech & Prod. Mfr.*, **3**(1), 9(1982)
- 8) Per Finholt and Sissel Solvang, *J. Pharm. Sci.*, **57**, 1322(1968)
- 9) C.F. Lerk, A.J.M. Schoonen, and J.T. Fell, *J. Pharm. Sci.*, **65**(6), 843(1976)
- 10) George Zografis and Stanley S. Tam, *J. Pharm. Sci.*, **65**(8), 1145(1976)
- 11) Lewis J. Leeson and J. Thuro Carstensen, *Dissolution Technology* (1974)
- 12) A.M. Guyot-Hermann, J. Ringard, *Drug Development and Industrial Pharmacy*, **7**(2), 155(1981)
- 13) E.M. Rudnic and C.T. Rhodes, S. Welch and P. Bernardo, *Drug Development and Industrial Pharmacy*, **8**(1), 87(1982)
- 14) Lieng-Huang Lee, *Recent Advances in Adhesion*, Gordon and Breach Science Publisher(1971)
- 15) J.J. Bikerman, *The Science of Adhesive joint*, 2nd Edition, Academic Press (1968)
- 16) Symposium on Properties of Surfaces ASTM Materials Science series-4, Presented at the 4th Pacific Area National Meeting American Society for Testing and Materials (1962), ASTM special Technical Publication No.340
- 17) Nazik A. El Gindy and Magda W. Samaha, *International Journal of Pharmaceutics*, **13**, 35(1983)
- 18) J.T. Davies, K.E. Rideal, *Interfacial Phenomena* (2nd), Academic Press(1963)
- 19) T.M. Jones, *Int. J. Pharm. Tech & Prod. Mfr.*, **2**(2), 17(1981)