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The Disintegration Behaviors of Insoluble Tablets Containing Different Disintegrants.(พฤติกรรมการแตกตัวของยาเม็ดไม่ละลายน้ำที่ประกอบด้วยสารช่ว...

G.C. Ritthidej

C. Thongplengsri

S. Dumrongpisudthikul

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ORIGINAL ARTICLE

The Disintegration Behaviors of Insoluble Tablets Containing Different Disintegrants.

*G.C. Ritthidej, Ph.D.**
*C. Thongplengsri, M.Sc.***
*S. Dumrongpisudthikul, M.Sc.****

Abstract

Dibasiccalcium phosphate dihydrate with different types and varying percentages of disintegrants were directly compressed into tablets. The mechanisms of action from moisture sorption and water penetration were investigated to elucidate the disintegration behaviors of tablets.

The amount of moisture adsorbed and the density change of tablets increased with the amount of disintegrant. On the contrary, the hardness decreased except of those containing microcrystalline cellulose. The initial water penetration rate was the highest except those from tablets containing sodium starch glycolate. An obstacle in water penetration occured in tablets containing high amount of disintegrants except corn starch. An optimum percentage of each disintegrant produced the lowest disintegration time. Of the four disintegrants investigated, cross-linked polyvinylpyrrolidone provided the fastest disintegration. The disintegration behaviors were discussed and related to the initial or highest rate of watere penetration from tablets containing disintegrants excent microcrystalline cullulose. (Th. J. Pharm. Sci., Vol. 13 No. 2, 141-154 (1988)).

* Assistant Professor, Department of Manufacturing Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok.

** Pharmacist, Chew Brothers & Co., Bangkok.

*** Lecturer, Department of Manufacturing Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok.

INTRODUCTION

It is already known that the disintegrated and dissolved drug must be presented to the absorption site as rapidly as possible after oral administration. During the course of this evolutionary process, incorporation of efficient disintegrant prior to tabletting provides pharmaceutical formulations with the means of quantitatively controlling the disintegration of solid dosage form.

Various disintegrants are employed in tablet formulation. Among most widely used are corn starch, sodium starch glycolate, and cross-linked carboxymethylcellulose (1). Most investigators showed that an increase in concentration of disintegrant caused a decrease in disintegration time (2, 3, 4, 5). However some disintegrants showed optimum concentrations (6, 7). Several mechanisms of action of disintegrants were reported (8). They are water uptake, swelling, deformation, particle repulsion and heat of hydration. There is no doubt that water uptake is the first step in any process of disintegration. The rate of water absorption had been implicated as an important mechanism. Equilibrium moisture absorption and desorption have also been used to evaluate the interaction of disintegrants with moisture both quantitative and qualitative manners such as volume, percent moisture sorption and hardness. It was demonstrated that the disintegrants with the highest moisture sorption were generally the most effective in most tablet systems (9).

The purpose of this study was to investigate the effect of type and amount of disintegrant of different mechanisms on the disintegration time of insoluble tablets and to study if moisture sorption and water uptake could elucidate the disintegration behaviors of these tablets. Four disintegrants of different properties, sodium starch glycolate with high swelling volume and high water uptake, corn starch with limited swelling and high water uptake, cross-linked polyvinylpyrrolidone with moderate swelling volume and high water uptake, and microcrystalline cellulose with heat of hydration and particle/particle repulsion force were used. The percentages of disintegrants were varying between the range commonly used including a higher and a lower percentages than the range used. An insoluble diluent, dibasic calcium phosphate dihydrate, was employed to exclude the influence of excipient.

MATERIALS AND METHODS

A) Materials

The following substances were obtained from commercial sources: dibasic calcium phosphate dihydrate **1**, sodium starch glycolate **2**, corn starch**3**, cross-linked polyvinylpyrrolidone**4**, microcrystalline cellulose**5**, magnesium stearate**3**.

B) Equipment

The following equipment were used: single punch tablet machine **a** instrumented with strain gauze **b**, strain indicator amplifier **c** and oscilloscope **d**, micrometer **e**, hardness tester **f**, disintegration apparatus **g**, twin-shell V-blender **h**, and apparatus for water uptake measurement which was setted as

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1 Emcompresses, Edward Mendell Co., USA
2 Explotab, Edward Mendell Co., USA
3 Pharmaceutical Sciences Co., Thailand
4 Kollidon CL, BASF, Germany
5 Avicel PH101, FMC Corporation, USA

a Modified Stoke, Model A3, Thailand
b Kwoya, Type KFC-5-C1-IIL30, Japan
c Shikoh, Model 6003-F, Japan
d Tedtronic, series 3030367, USA
e Teclock Corporation, 0.01 mm, Japan
f Schleuniger -2E, Germany
g Hanson Research Corporation, USA
h Kan Seng Lee Machinery (1960) Ltd., Part., Thailand

shown in Figure I. The apparatus consists of a sinterglass filter connected to a horizontal graduated pipette by a rubber bung. A continuous water column was maintained from the sintered glass filter through the glass bottle to the end of the pipette. A piece of filter paper was placed on top of the sintered glass base. The top of rubber bung was covered with a slide to prevent evaporation of penetration liquid. The entire assembly was immersed in a water bath, thermostatically controlled at $37 \pm 1^{\circ}C$.

C) Preparation of Tablets

The tablet compositions in each formula were listed in Table 1. A batch of 500 grams of the formulation was prepared by mixing dibasic calcium phosphate dihydrate with disintegrant in a laboratory scale twin-shell V-blender. The rotation speed was 60 rpm. After ten minutes mixing, magnesium stearate was added. Mixing procedure was continued for another 5 minutes. The powder was then dried in hot air oven at $70^{\circ}C$ for 30 minutes.

Before mixing, all excipients were passed through a # 60 mesh handle screen to break agglomerates except magnesium stearate which was passed through a # 80 mesh handle screen.

The powder was compressed into tablets at 2400 psi using an instrumented single punch tablet machine tooled with 3/8 inch, round flat faced punch. The tablets were adjusted to have a weight of 350 mg.

D) Tablet Evaluation

1. Moisture Sorption Tablets from each batch were stored in a dessicator at room temperature. This dessicator was equilbrated to have a relative humidity of 98%. If any care was taken to minimal opening the dessiator, the humidity remained quite constant. Samples were evaluated at the time intervals of 0, 6, 24, 48 and 72 hours.

1.1 percent moisture uptake The moisture uptake of the tablet was gravimetrically determined. Ten tablets were weighed on an analytical balance. Moisture pickup at time interval was expressed as percent weight increase from initial tablet weight.

1.2 volume change The volume change was calculated from the thickness and the diameter of tablets which were measured in millimeter by using a micrometer spring gauge. The mean of ten determination was employed. The ratio of volume change was expressed as the ratio of the apparent tablet density at time interval and the initial tablet density.

1.3 hardness The hardness of tablet was determined by using a hardness tester. An average of ten determinations was expressed in Strong-Cobb-Arner unit.

2. Water Penetration The water penetration was measured by using the apparatus previously mentioned. A tablet was placed on top of the filter paper. The volume of water uptake was read in millilitre from the graduated pipette. A mean of at least five determinations was represented the uptake volume.

3. Disintegration The disintegration time of tablets was determined by using a disintegration apparatus according to the USP XX method. Distilled water was used as disintegration medium. The value was expressed in second. At least six tablets from each formulation was tested.

RESULTS

1. Moisture Sorption The data from moisture sorption of dibasic calcium phosphate dihydrate tablets containing various types and different levels of disintegrant after exposure to 98% relative humidity were listed in Table 2-5.

Table 1 Tablet Composition

Ingredient	% w/w per tablet			
dibasic calcium phosphate dihydrate	96.5	93.5	90.5	87.5
sodium starch glycolate	3.0	6.0	9.0	12.0
magnesium stearate	0.5	0.5	0.5	0.5
dibasic calcium phosphate dihydrate	96.5	93.5	90.5	87.5
corn starch	3.0	6.0	9.0	12.0
magnesium stearate	0.5	0.5	0.5	0.5
dibasic calcium phosphate dihydrate	98.5	96.5	94.5	92.5
cross-linked polyvinylpyrrolidone	1.0	3.0	5.0	7.0
magnesium stearate	0.5	0.5	0.5	0.5
dibasic calcium phosphate dihydrate	79.5	69.5	59.5	49.5
microcrystalline cellulose	20.0	30.0	40.0	50.0
magnesium stearate	0.5	0.5	0.5	0.5

Table 2 The percent increase in weight, W, ratio of tablet density, D, and hardness, H, of dibasic calcium phosphate dihydrte tablets containing various percentages of sodium starch glycolate after exposure to 98% R.H. at room temperature.

Time	3%			6%			9%			12%		
(hrs)	W	D	H	W	D	H	W	D	H	W	D	H
0	0	1.00	5.94 (0.33)	0	1.00	4.92 (0.58)	0	1.00	3.89 (0.56)	0	1.00	2.84 (0.66)
6	0.473	0.98	2.59 (1.04)	0.785	0.95	1.61 (0.61)	0.883	0.95	—	0.936	0.93	—
24	1.007	0.95	—	1.882	0.91	—	2.123	0.91	—	2.739	0.89	—
48	1.721	0.93	—	2.637	0.90	—	3.553	—	—	4.247	—	—
72	2.482	—	—	3.312	0.92	—	5.109	—	—	6.238	—	—

Table 3 The percent increase in weight, W, ratio of tablet density, D, and hardness, H, of dibasic calcium phosphate dihydrate tablets containing various pecentages of corn starch after exposure to 98% R.H. at room temperature.

Time	3%			6%			9%			12%		
(hrs)	W	D	H	W	D	H	W	D	H	W	D	H
0	0	1.00	7.10 (0.40)	0	1.00	5.73 (0.77)	0	1.00	4.96 (0.65)	0	1.00	4.94 (0.66)
6	0.184	0.99	4.28 (0.25)	0.321	0.98	2.92 (0.51)	0.393	0.99	2.10 (0.62)	0.446	0.97	2.76 (0.68)
24	0.316	0.99	3.60 (0.38)	0.506	0.97	2.45 (0.22)	0.786	0.96	—	1.131	0.94	—
48	0.342	0.98	2.83 (0.53)	0.532	0.96	1.90 (0.32)	0.967	0.95	—	1.339	0.92	—
72	0.369	0.98	2.83 (0.45)	0.689	0.95	1.41 (0.58)	0.914	0.94	1.40 (0.09)	1.339	0.91	—

Table 4 The percent increase in weight, W, ratio of tablet density, D, and hardness, H, of dibasic calcium phosphate dihydrate tablets containing various percentages of cross-linked polyvinyl pyrrlidone after exposure to 98% R.H. at room temperature.

Time	1%			3%			5%			7%		
(hrs)	W	D	H	W	D	H	W	D	H	W	D	H
0	0	1.00	5.67 (0.54)	0	1.00	4.41 (0.62)	0	1.00	2.59 (0.27)	0	1.00	—
6	0.209	0.97	1.81 (1.12)	0.393	0.90	—	0.655	0.83	—	0.704	0.88	—
24	0.394	0.93	—	0.765	—	—	1.509	—	—	1.655	—	—
48	0.395	0.93	—	0.944	—	—	1.637	—	—	2.345	—	—
72	0.421	0.91	—	0.996	—	—	1.719	—	—	1.895	—	—

Table 5 The percent increase in weight, W, ratio of tablet density, D, and hardness, H, of dibasic calcium phosphate dihydrate tablets containing various percentages of microcrystalline cellulose after exposure to 98% R.H. at room temperature.

Time	20%			30%			40%			50%		
(hrs)	W	D	H	W	D	H	W	D	H	W	D	H
0	0	1.00	6.82 (0.34)	0	1.00	8.01 (0.38)	0	1.00	10.20 (0.45)	0	1.00	15.05 (0.83)
6	0.618	0.98	4.21 (0.45)	0.602	0.99	6.14 (0.38)	0.628	0.99	8.41 (0.38)	0.733	0.99	11.41 (0.92)
24	0.895	0.97	3.56 (0.18)	1.207	0.97	4.78 (0.28)	1.398	0.97	6.36 (0.34)	1.585	0.97	9.30 (0.37)
48	1.174	0.96	2.50 (0.33)	1.752	0.95	43.10 (0.92)	2.088	0.96	4.69 (0.35)	2.459	0.95	6.61 (0.18)
72	1.007	0.97	2.93 (0.40)	1.393	0.96	4.01 (0.34)	1.594	0.95	5.62 (0.36)	3.189	0.94	5.40 (0.13)

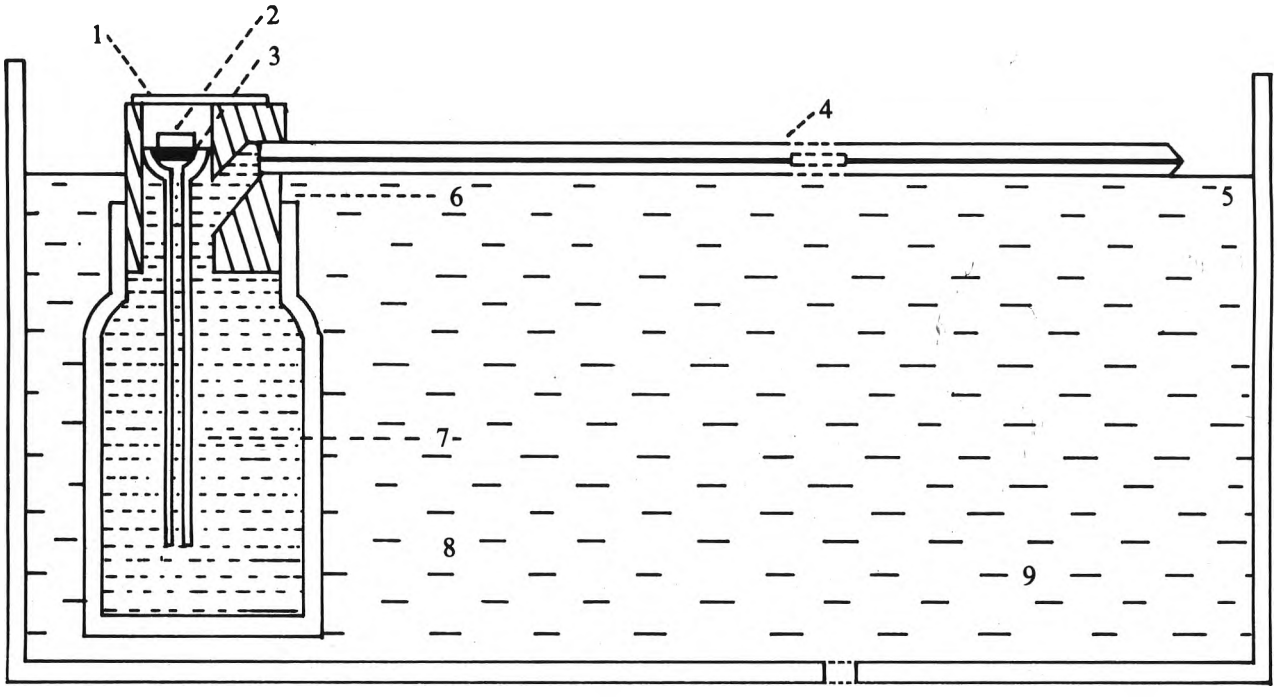

Figure 1 Apparatus for determination of water penetration into tablets. 1. cover slide 2. tablet 3. filter paper 4. pipette 5. water level 6. rubber bung 7. filter stick 8. glass bottle 9. thermostated at 37° C

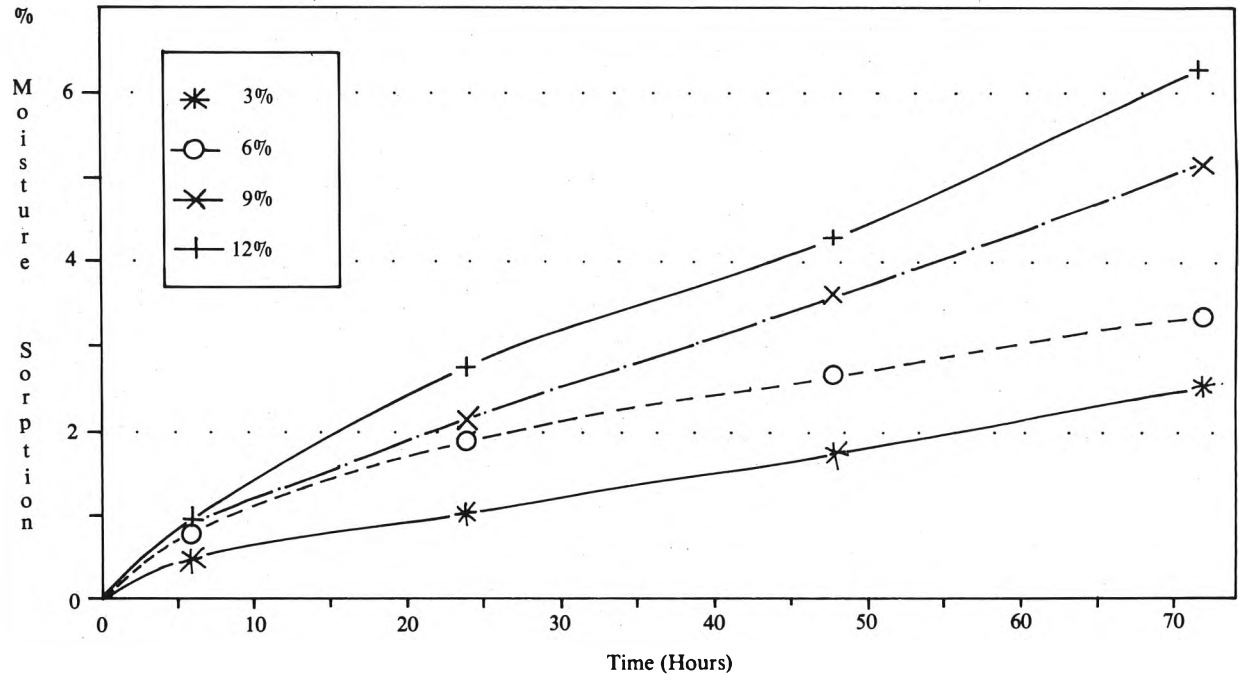

Figure 2 Moisture sorption profiles of dibasiccalcium phosphate dihydrate tablets containing different levels of sodium starch glycolate after exposure to 98% R.H.

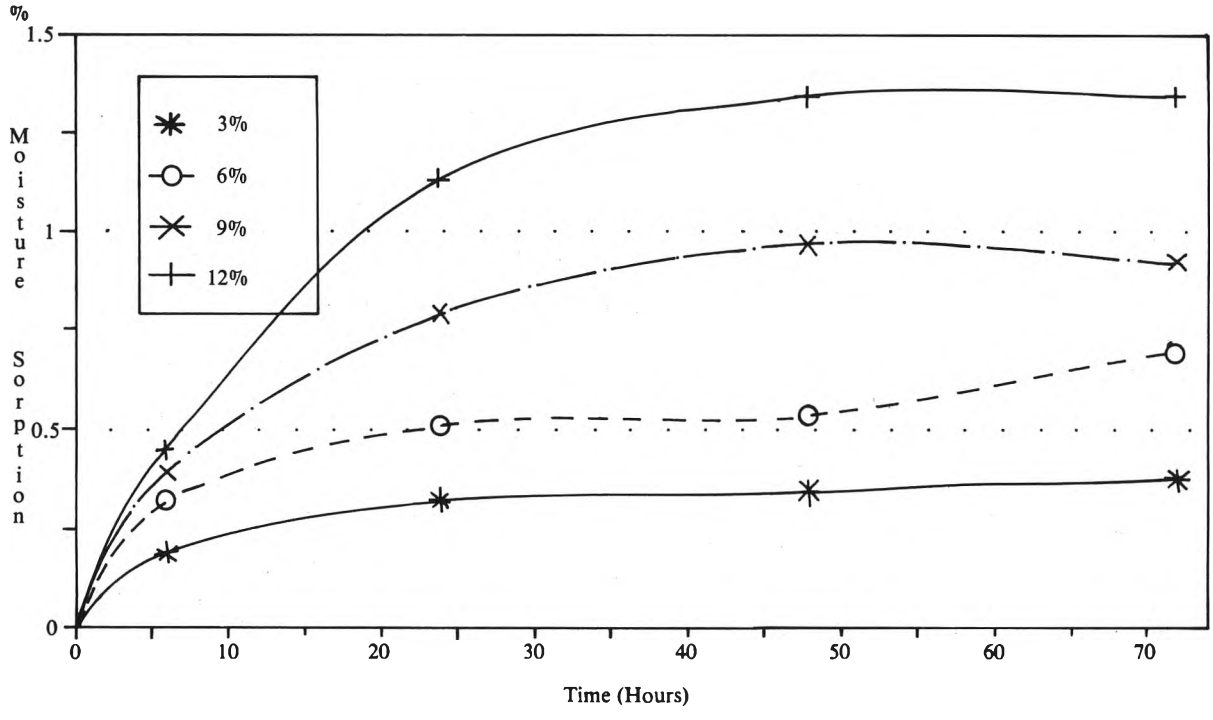

Figure 3 Moisture sorption profiles of dibasiccalcium phosphate dihydrate tablets containing different levels of corn starch after exposure to 98% R.H.

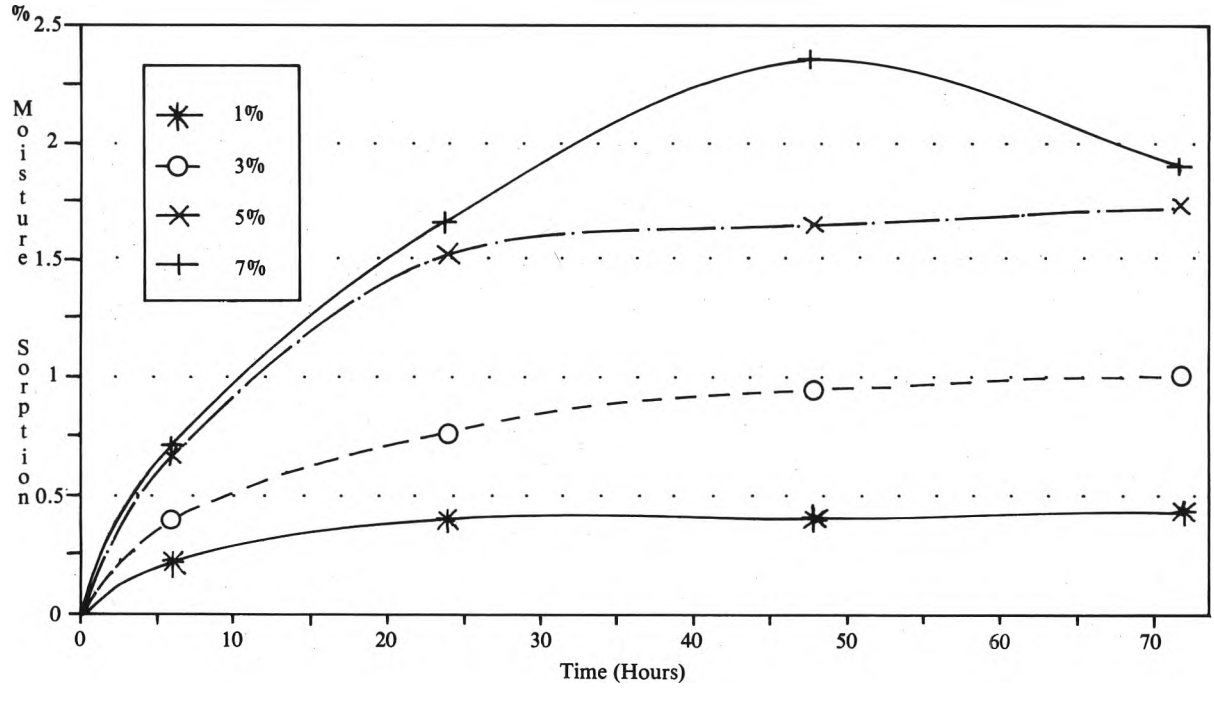

Figure 4 Moisture sorption profiles of dibasiccalcium phosphate dihydrate tablets containin different levels of cross-linked polyvinylpyrrolidone after exposure to 98% R.H.

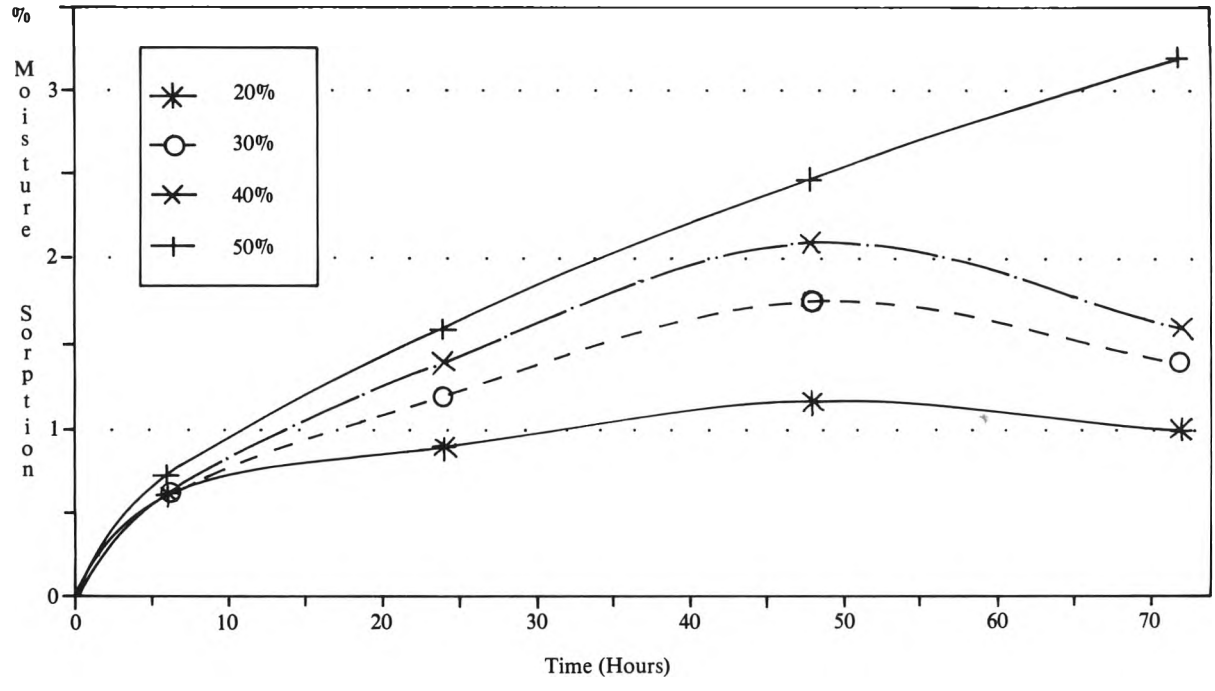

Figure 5 Moisture sorption profiles of dibasiccacium phosphate dihydrate tablets containing different levels of microcrystalline cellulose after exposure to 98% R.H.

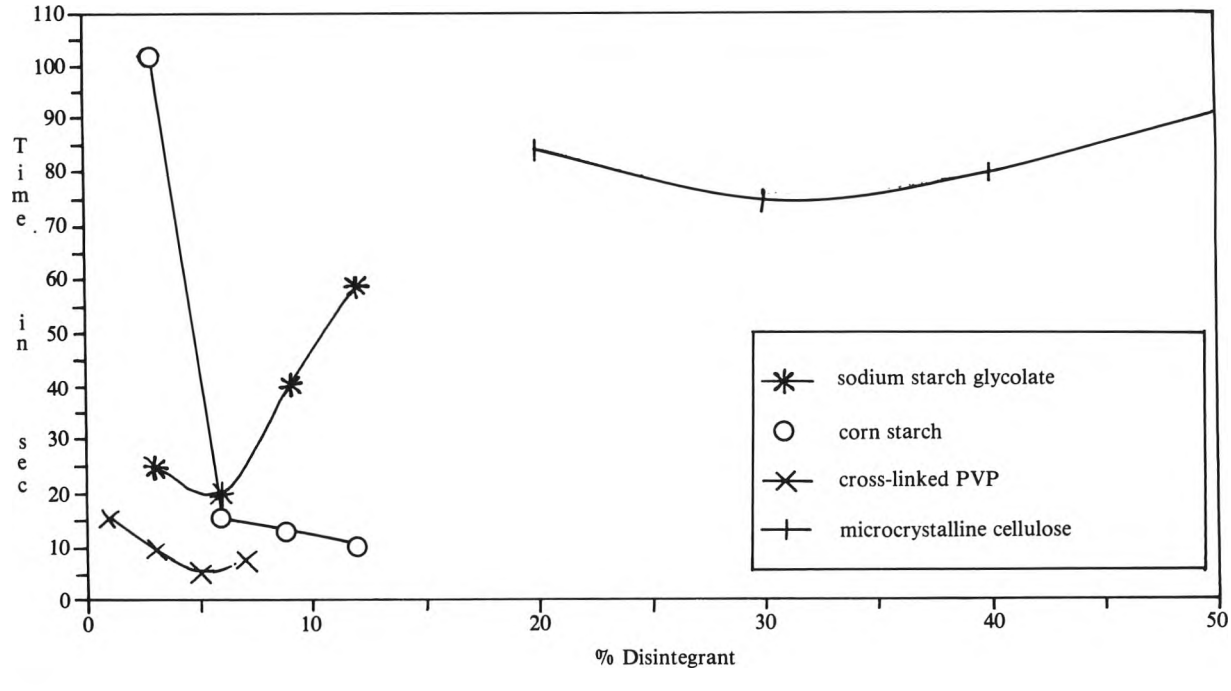

Figure 6 The effect of concentration and type of disintegrant on the disintegration time of dicalcium phosphate dihydrate tablets.

1.1 percent moisture sorption The percent moisture sorption of tablets containing sodium starch glycolate, corn starch, cross-linked polyvinylpyrrolidone and microcrystalline cellulose, determined as the percent weight gain after exposure to 98% relative humidity was plotted against time as shown in Figure 2-5, respectively. It could be seen that the percent moisture sorption gradually increassed until the twenty-fourth hour for tablets containing corn starch, cross-linked polyvinylpyrrolidone and 20 to 40% of microcrystalline cellulose. These tablets showed maximum or equilibrium moisture sorption after 24-hour exposure. The moisture sorption rate was then determined by using the equation,

$$\log \left[1 - \frac{mt}{m\infty} \right] = a.t \qquad \text{.....(eq. 1)}$$

where : mt is the percent moisture sorption at time t,
$m\infty$ is the percent maximum or equilibrium moisture sorption,
a is the moisture sorption rate constant.

When plotting log [1-(mt/m∞)] against t, the moisture sorption rate of these tablets appeared to follow first order rate model ($r^2 > 0.7983$). On the contrary, the tablets containing sodium starch glycolate and 50% of microcrystalline cellulose continued to adsorb moisture throughout the experiment for 72 hours.

As the level of disintegrants increased, the mean percent moisture sorption increased. A linear relationship between the percent moisture sorption and the amount of disintegrant was observed and the regressions were 0.9878, 0.9962, 0.9830, and polyvinylpyrrolidone, and microcrystalline cellulose, respectively. Among these disintegrants, sodium starch glycolate showed the largest moisture sorption, followed by microcrystalline cellulose and cross-linked polyvinylpyrrolidone. Corn starch showed the least.

1.2 volume change The volume changes of these tablets were expressed as the ratio of the apparent tablet density at time interval and the initial tablet density. The ratio of tablet density gradually decreased as the concentration of disintegrant increased and as a function of time. Tablets containing high amount of sodium starch glycolate and cross-linked polyvinylpyrrolidone were unable to handle after 48- and 24-hour exposure to high humidity, respectively. Thus, their densities were unmeasurable. Tablets containing cross-linked polyvinylpyrrolidone showed the highest density change, orderly followed by tablets containing sodium starch glycolate, corn starch and microcrystalline cellulose. All tablets exhibited significantly decreased in density ($\alpha = 0.05$) except those containing 3% corn starch.

1.3 hardness The hardness of tablets decreased as the amount of disintegrant increased except tablets containing microcrystalline cellulose that exhibited the opposite result. All tablets showed a decrease in hardness after exposure to high humidity as a function of time, especially tablets containing sodium starch glycolate and cross-linked polyvinylpyrrolidone. They were unmeasurable after 24-hour exposure. The hardness of tablets containing microcrystalline cellulose was the highest, orderly followed by that of tablets containing corn starch, sodium starch glycolate and cross-linked polyvinylpyrrolidone.

2. Water Penetration The water penetration rates of tablets containing different amount and type of disintegrants were listed in Table 6-9. It could be seen that all tablets except tablets containing sodium starch glycolate exhibited the maximum water penetration rate at the first 5 seconds and the rate then decreased against time. Tablets containing sodium starch glycolate showed a gradual increase in water penetration rate. The maximum rates were observed at 30 seconds for tablets containing low amount of disintegrant, and 60 seconds for high amount of disintegrant. Then the penetration rates decreased. Comparison of the maximum rates of the four disintegrants, cross-linked polyvinylpyrrolidone produced the highest rate, followed by sodium starch glycolate, corn starch and microcrystalline cellulose, respectively.

Higher amount of corn starch produced higher water penetration rate. However, optimum concentrations ofr the other disintegrants were observed. For sodium starch glycolate, the optimum concentration was 6%, for cross-linked polyvinylpyrrolidone, 5%, and for microcrystalline cellulose, 40%.

3. Disintegration Time The effect of type and amount of disintegrants on the disintegration times of tablets was illustrated in Figure 6. An optimum concentration of disintegrant to produce the fastest disintegration time was exhibited except corn starch. Higher amount of corn starch produced faster disintegration. Comparison of the four disintegrants, cross-linked polyvinylpyrrolidone produced the fastest disintegration, orderly followed by corn starch, sodium starch glycolate and microcrystalline cellulose.

DISCUSSION AND CONCLUSION

The disintegration behaviors of tablets depend upon various factors. One of the more important factors is the disintegrant itself, both type and amount incroporated. Different disintegrants exert various mechanisms of action. From the experiment, the rates of water penetration into tablets could be used to elucidate the disintegration behaviors of all tablets except those containing microcrystalline cellulose. They were correlated to the disintegration time of tablets. The relationship between the initial rate of water penetration and the disintegration time was illustrated in Figure 7. Tablets with the greater initial

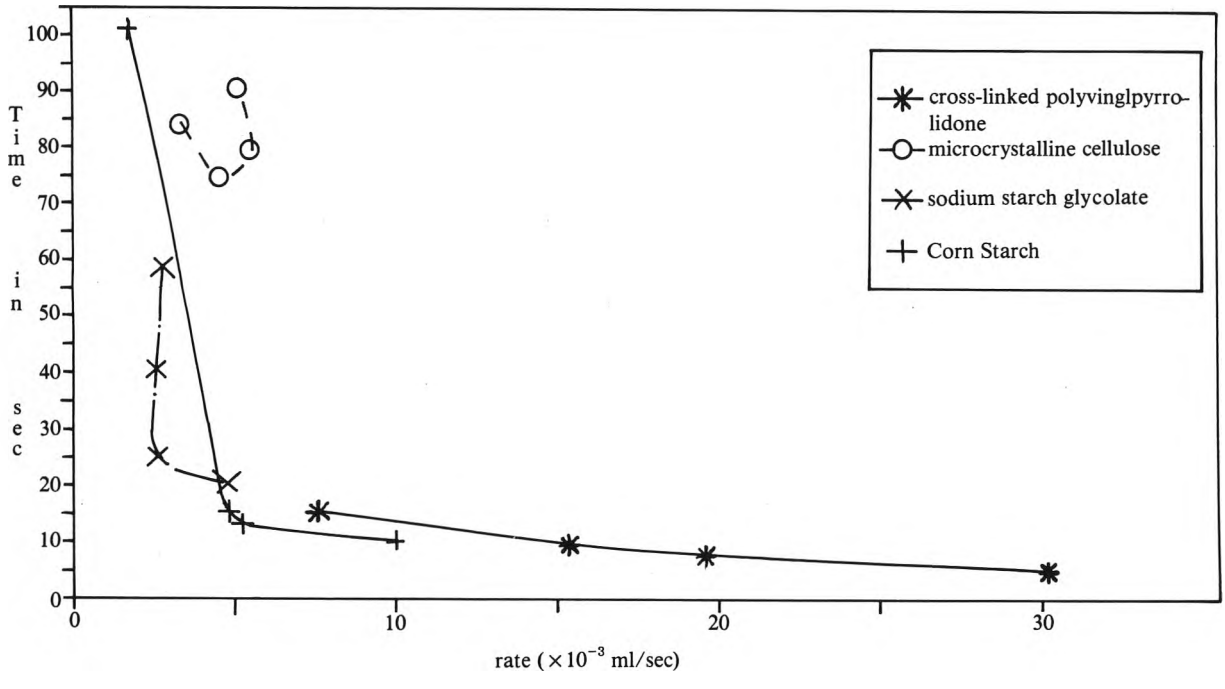

Figure 7 The relationship between the disintegration time and the initial rate of water penetration into dibasiccalcium phosphate dihydrate tablets containing various disintegrants.

rate of water penetration exhibited the faster disintegration time. The initial rate of water penetration of tablets containing cross-linked polyvinylpyrrolidone exhibited a linear relationship with the disintegration time (r^2 = 0.9035). For tablets containing corn starch, a significant correlation was also found (r^2 = 0.9387) on a log-log scale, between the initial rate of water penetration and the disintegration time.

The initial rate of water penetration of tablets containing sodium starch glycolate showed poor correlation, whether on normal scale (r^2 = 0.2960) and log-log scale (r^2 = 0.3716) with the disintegration time. Nevertheless, this initial rate was not the highest rate of water penetration. The latter occurred between 15 and 30 seconds and between 45 and 60 seconds for the two low and two high concentrations of sodium starch glycolate. The initial obstacle was more prominent in tablets containing higher concentrations of the disintegrant. Sodium starch glycolate is insoluble in water but becomes viscous dispersion. According to Washburn's equation (10-12), the volume of water uptake depended upon the viscosity of

Table 6 The Rate of Water Penetration of Dibasic Calcium Phosphate Dihydrate Tablets Containing Different Levels of Sodium Starch Glycolate Determined at Different Time Intervals.

	rate (x 10^{-3} ml/sec)			
Time (sec)	**3%**	**5%**	**7%**	**10%**
0 - 5	2.6	4.8	2.6	2.8
5 - 10	4.0	7.8	5.0	4.8
10 - 15	4.0	8.8	5.8	5.0
15 - 30	7.5	11.6	6.3	4.6
30 - 45	6.8	8.6	7.1	5.9
45 - 60	1.7	4.7	7.2	7.1
60 - 90	0	0.16	5.3	6.6
90 - 120	0	0	2.2	4.9

Table 7 The Rate of Water Penetration of Dibasic Calcium Phosphate Dihydrate Tablets Containing Different Levels of Corn Starch Determined at Different Time Intervals.

	rate (x 10^{-3} ml/sec)			
Time (sec)	**3%**	**5%**	**7%**	**10%**
0 - 5	1.8	4.6	5.2	10.0
5 - 10	1.2	4.0	1.0	6.0
10 - 15	1.0	1.1	1.0	3.0
15 - 30	2.1	1.2	1.4	0.4
30 - 45	0.54	0.13	0.066	0.066
45 - 60	0.16	0.1	0.066	0.13
60 - 90	0.066	0.1	0	0.033
90 - 120	0.083	0.16	0.066	0.033

Table 8 The Rate of Water Penetration of Dibasic Calcium Phosphate Dihydrate Tablets Containing Different Levels of Cross-linked polyvinylpyrrolidone Determined at Different Time Intervals.

	rate (x 10^{-3} ml/sec)			
Time (sec)	**1%**	**3%**	**5%**	**7%**
0 - 5	7.6	15.4	30.2	19.6
5 - 10	7.4	13.0	3.8	3.8
10 - 15	6.8	1.0	0.8	2.2
15 - 30	3.2	0.8	0.3	1.6
30 - 45	0.6	0.6	0.066	0.8
45 - 60	0.13	0.13	0.2	0.33
60 - 90	0.1	0.11	0.066	0.12
90 - 120	0.16	0	0	0.23

Table 9 The Rate of Water Penetration of Dibasic Calcium Phosphate Dihydrate Tablets Containing Different Levels of Microcrystalline Cellulose Determined at Different Time Intervals.

Time (sec)	rate (x 10^{-3} ml/sec)			
	20%	30%	40%	50%
0 - 5	3.4	4.6	5.6	5.2
5 - 10	1.8	2.0	2.8	2.8
10 - 15	2.2	2.2	2.0	1.8
15 - 30	2.0	2.0	1.6	1.4
30 - 45	1.4	1.7	1.8	1.4
45 - 60	0.4	1.1	1.4	1.5
60 - 90	0.1	0.23	0.53	1.1
90 - 120	0.16	0.13	0.16	1.7

the liquid and pore size within the tablet. Upon contact with water, sodium starch glycolate particles at the surface of the tablet formed viscous dispersion, thus the initial water penetration was interfered. After a period of time, the high wateruptaking property of the disintegrant increased the water penetration rate. A good correlation existed between the rate of water penetration at 30 seconds and the disintegrations time, on a normal scale (r^2 = 0.7645) and on a log-log scale (r^2 = 0.9118).

For tablets containing microcrystalline cellulose, no correlation existed between the initial rate of water penetration and the disintegration time on both normal and log-log scales (r^2 = 0.0040 and r^2 = 0.0154, respectively). The possible reason is that the mechanism of action of microcrystalline cellulose is different from the other disintegrants. It was reported that microcrystalline cellulose exhibited breaking H-bonding when contact with water (13). The more water was uptook by higher amount of the disintegrant, so did the breaking of H-bonding. However, higher amount of the disintegrant exhibited more H-bonding or stronger cohesive force resulting in harder tablets. Therefore, the higher rate of water uptake cause by a greater amount of microcrystalline cellulose may not produced a faster disintegration.

Increasing the amount of disintegrant should increase the ability to absorb water. Thus, the rate should be higher. This is true for corn starch. However, tablets of sodium starch glycolate and cross-linked polyvinylpyrrolidone exerted optimum concentrations. Higher concentration showed a slower rate of water penetration, and prolonged disintegration. This may due to the increase in the viscosity of the disintegration medium. These two disintegrants forms dispersion upon contact with water. At high concentration, they formed gel-like mass especially sodium starch glycolate, thus the viscosity tremendously increased. The increase in viscosity would therefore decrease the water uptake (10-12). Corn starch does not form dispersion with water. Thus the effect of viscosity was not exhibited.

Parameters obtained from moisture sorption resulted differently. It may not be used to evaluate the disintegration behaviors. Disintegrant with a greater amount of moisture absorbed did not produce the faster disintegration. Tablets containing sodium starch glycolate and microcrystalline cellulose adsorbed more moisture than tablets containing cross-linked polyvinylpyrrolidone and corn starch, but their disintegration times were less. This was in contrast with Khan et al (12) who concluded that disintegrants with the highest moisture sorption were generally the most effective in most tablets system. Moreover, the amount of moisture sorption was directly proportion to the amount of disintegrant, but the disintegration time was not, except for corn starch. For tablets containing the same disintegrant, a poor correlation was predicted between the amount of moisture sorption and the disintegration time.

The density change or the expansion per amount of moisture absorbed to be of some importance. Swelling or expansion of tablets somehow could elucidate the disintegration behaviors. Many investigators also reported its importance (12, 13). Disintegrant that produced more decrease in density seemed to

exhibit faster disintegration. Exception occured for sodium starch glycolate. It's density was more decrease than corn starch, but the disintegration was slower. In addition, for tablets containing the same disintegrant, the density change was directly related to the amount of disintegrant but the disintegration was not except for corn starch. Thus a poor correlation could be predicted between the desity change and the disintegration.

The hardness of tablets after exposure to high humidity was directly related to the density change. Thus its relationship with the disintegration was the same as in density change, except for tablets containing microcrystalline cellulose. The particles of this disintegrant hold together by H-bonding. The greater amount of microcrystalline cellulose the stronger the cohesive force, thus the hardness of tablets increased with the increasing amount of disintegrant.

It could be concluded that the disintegration behaviors of dibasic calcium phosphate dihydrate tablets were depended upon the type and amount of disintegrants. For sodium starch glycolate, cross-linked polyvinylpyrrolidone and corn starch, the highest or initial rate of water uptake could be used to elucidate the disintegration times but parameters from moisture sorption were of less importance. The type and amount of disintegrant that affected the initial or highest rate of water uptake would influence the disintegration time. For microcrystalline cellulose both water uptake and moisture sorption were not related to disintegration due to different mechanism of action. The other parameters were to be further investigated.

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พฤติกรรมการแตกตัวของยาเม็ดไม่ละลายน้ำที่ประกอบด้วยสารช่วยแตกตัวต่าง ๆ กัน

*กาญจน์พิมล ฤทธิเดช, Ph.D.**
*จักรี ทองเปล่งศรี, ภ.ม.***
*ศิริศักดิ์ ดำรงพิศุทธิกุล, ภ.ม.****

บทคัดย่อ

ยาเม็ด dibasiccalcium phosphate dihydrate ถูกตอกอัดโดยตรงพร้อมกับสารช่วยแตกตัวทั้งชนิดและเปอร์เซ็นต์ต่างกัน และศึกษากลไกการทำงานจากการดูดความชื้นและการแทรกซึมของน้ำเพื่ออธิบายพฤติกรรมการแตกตัวของยาเม็ด

ปริมาณความชื้นที่ถูกดูดซึมและการเปลี่ยนแปลงความหนาแน่นเพิ่มตามปริมาณของสารช่วยแตกตัวในทางตรงข้าม ความแข็งลดลงยกเว้นยาเม็ดที่ประกอบด้วย microcry-stalline cellulose อัตราการแทรกซึมของน้ำในระยะเริ่มแรกเป็นอัตราที่สูงสุดยกเว้นจากยาเม็ดที่ประกอบด้วย sodium starch glycolate มีการกีดขวางการแทรกซึมของน้ำในยาเม็ดที่ประกอบด้วยสารช่วยแตกตัวที่มีปริมาณสูง ยกเว้น corn starch เปอร์เซนต์ที่เหมาะสมของสารช่วยแตกตัวแต่ละชนิดใช้เวลาแตกตัวน้อยที่สุด ในสารช่วยแตกตัวทั้งสี่ชนิดที่ศึกษา cross-linked polyvinylpyrrolidone ให้การแตกตัวเร็วที่สุด พฤติกรรมการแตกตัวถูกอภิปรายให้มีความสัมพันธ์กับอัตราการแทรกซึมในระยะเริ่มแรกหรือสูงสุดของยาเม็ดที่ประกอบด้วยสารช่วยแตกตัวยกเว้น microcrystalline cellulose (ไทยเภสัชสาร ปีที่ 13 (2) : หน้า 141-154 (2531)).

* ผู้ช่วยศาสตราจารย์ ภาควิชาเภสัชอุตสาหกรรม คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย กทม.
** เภสัชกร บริษัท จิวบราเดอร์ส จำกัด กทม.
*** อาจารย์ ภาควิชาเภสัชอุตสาหกรรม คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย กทม.