Chapter III

Results

General Properties of Scaphium Powders

Scaphium powders were fine brown powders with a little characteristic odour. The treatments S_1 and S_2 behave like other natural hydrocolloids which swell on contact with water. It is possible that S_1 and S_2 would be polysaccharide possessing mucilage property. The chemical compositions of the treatment S_1 and S_2 were investigated and the results were shown in Table 4.

Physical Properties of Scaphium Powders

1. Morphology of Scaphium Powders

The photomicrographs of S_1 and S_2 are shown in Figures 6,7. It is apparent that the powders of S_1 and S_2 possess irregular shapes.

2. Size Distribution and Specific Surface Area

The particle size distribution of the powders (S_1,S_2) were analyzed by laser diffraction particle size analyzer. The histograms of particle size distribution and the cumulative percent undersize are presented in Appendix 1,2. The data for average particle size and specific surface area of S_1 and S_2 are shown in Table 5. The results showed that the particle size of S_2 was larger than of S_1 so that the specific surface area of S_1 was higher than of S_2.

Table 4 The Chemical Compositions[a] of S_1 and S_2

Chemical Compositions	Type	
	S_1	S_2
Heavy Metals		
-Lead (ppm)[b]	0.015	0.02
-Arsenic (ppm)	0.24	0.26
-Mercury (ppm)	-	4.28
Starch and Dextrin	negative	negative
Tannin	positive	positive
Amino Acid	positive	positive
Carbohydrate	positive	positive
-Reducing Sugar	negative	negative

a = The investigation was carried out according to the process in monograph under Acacia BP 1988 (75).

b = part per million

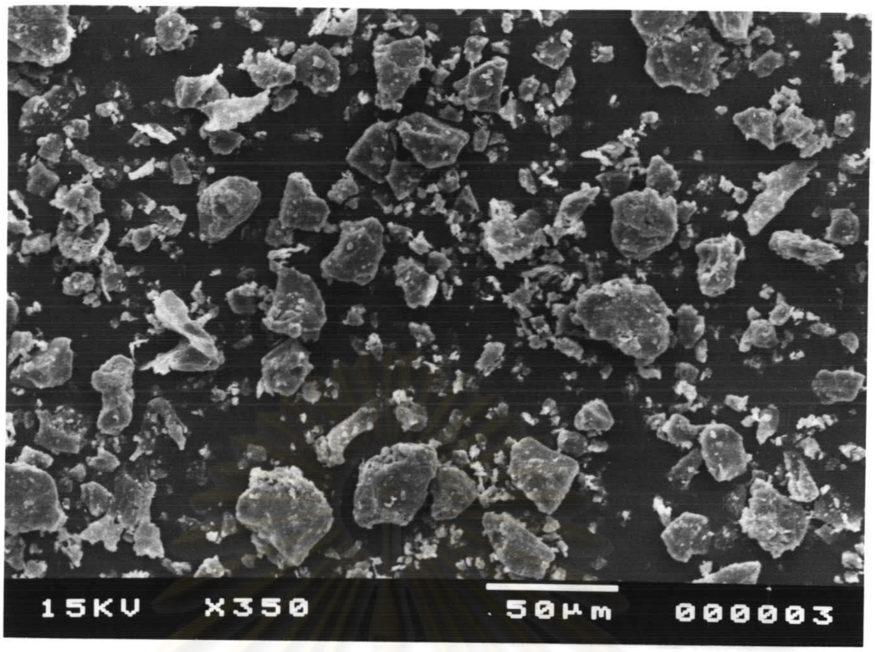

Figure 6 Electron Photomicrograph of S_1

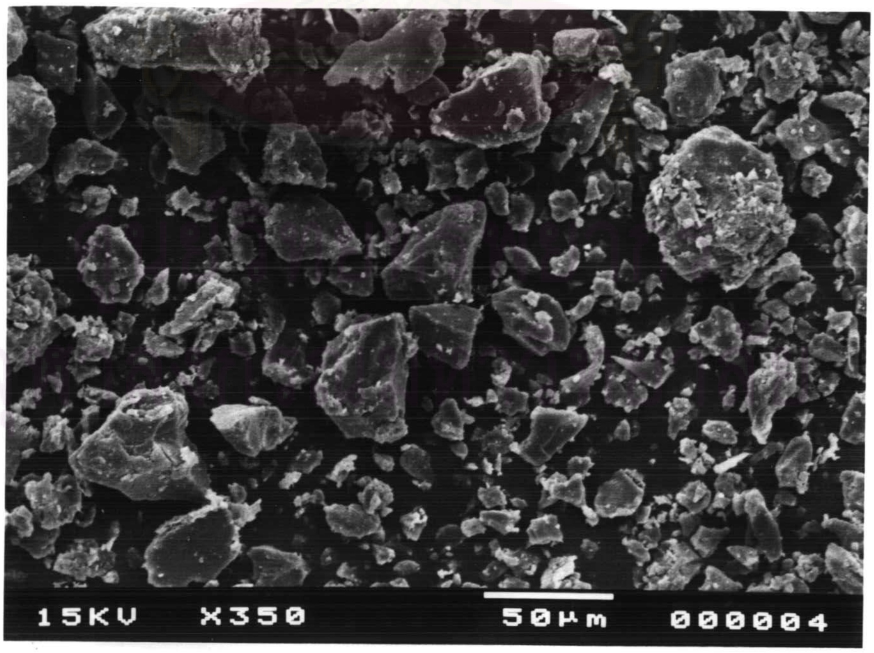

Figure 7 Electron Photomicrograph of S_2

Table 5 The Average Particle Size and Specific Surface Area of S_1 and S_2

Type	Average Particle Size (μm)		S.D.[c]	Specific Surface Area (m^2/sec)
	d_{vs}[a]	d_{wm}[b]		
S_1	8.7	22.18	2.57	0.6899
S_2	13.34	31.34	2.70	0.4498

a = volume surface mean diameter (nd^3/nd^2)

b = weight moment mean diameter (nd^4/nd^3)

c = standard deviation

3. Bulk Density, Tapped Density, Compressibility, True Density, Moisture Determination, Hydration Capacity and Ash Content

The results of bulk density, tapped density and percent compressibility are given in Table 6. From the data the bulk density of S_2 was more than of S_1, the tapped density of both powders were similar but percent compressibility of S_2 was more than of S_1. The true density of S_1 and S_2 were the same.

Moisture content of S_1 and S_2 were calculated as percent loss on drying (shown in Table 6). It was found that percent moisture content of S_2 was more than of S_1. The hydration capacity of S_2 was more than of S_1, but the ash content of S_1 was more than of S_2 (shown in Table 6).

4. Moisture Sorption Determination

The moisture sorption behaviors of S_1 and S_2 as a function of time are shown in Figure 8. The result from the data showed that the rate of moisture sorption of S_2 was more than of S_1.

5. Bulk Swelling Determination

The rates of bulk swelling of S_1 and S_2 could not be determined because they formed gelling barrier preventing water penetration into the particles.

Table 6 Physical Properties of S_1 and S_2

Physical Properties* of Powders	Type	
	S_1	S_2
Bulk Density (gm/ml)	0.421	0.525
Tapped Density (gm/ml)	0.725	0.752
Compressibility (%)	42.7	30.23
True Density (gm/ml)	1.42	1.41
Moisture Content (%)	7.23	7.64
Hydration Capacity (ml/gm)	59.35	87.10
Ash Content (%)	6.72	6.40

* average of two determinations

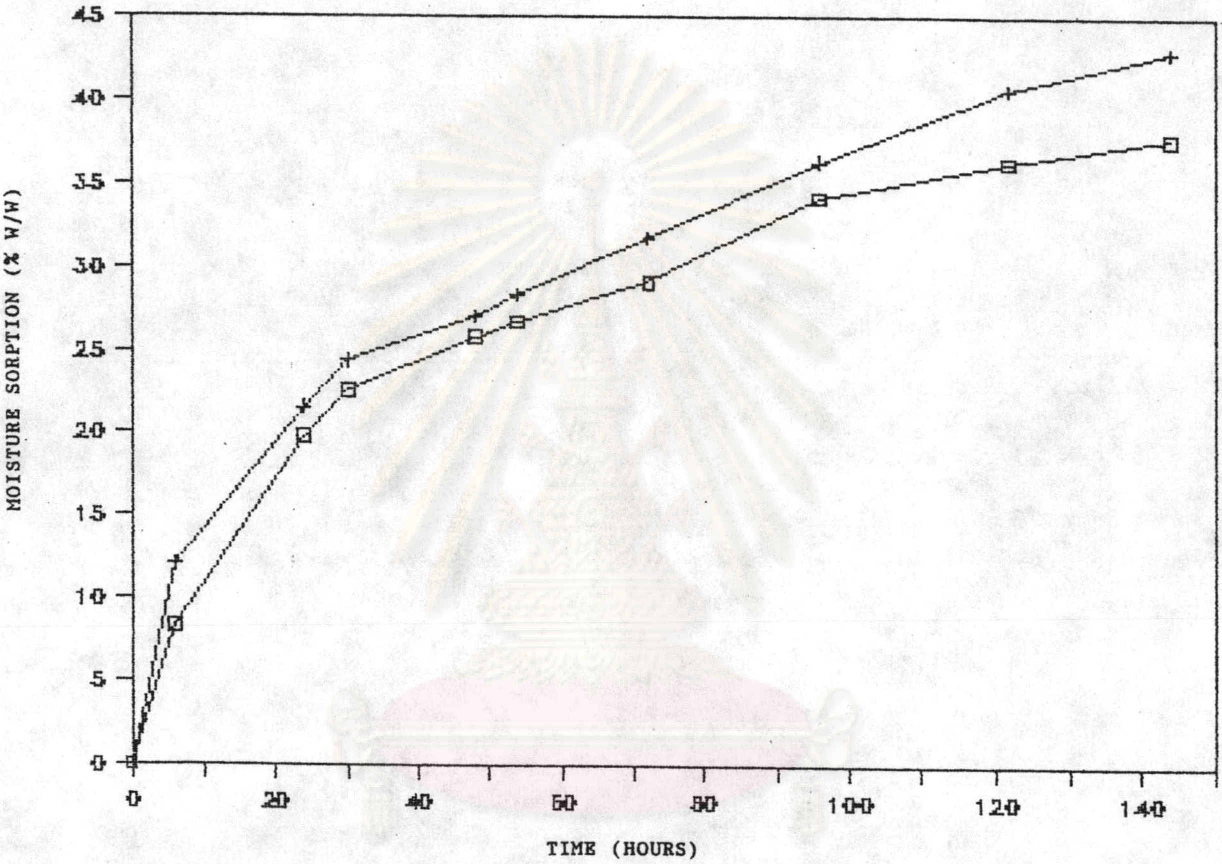

Figure 8 Moisture Sorption Profiles of S_1 and S_2
(Key : □ S_1 , + S_2)

Calibration of the Tablet Instrumentation

The strain gauges mounted on the upper punch holder were completely calibrated using hydraulic press over a range of applied force form 250 pounds upto 3750 pounds by measuring scope deflection. The linear relation between scope deflection (cm) and applied forces was found with correlation coefficient of 0.9998 as shown in Appendix 3,4. The compressional force could be determined by deflection signal which was calibrated from the standard curve. The tracing from the recorder was obtained at different compressional forces as shown in Appendix 5.

The Evaluation of Tablets without Active Ingredient

1. Weight Variation

The average weight, standard deviation and relative standard deviation of tablets for each formulation are given in Appendix 6-23. All tablet formulations exhibited within the USP requirement.

2. Tablet Thickness

The average thickness and standard deviation of tablets for each formulation are given in Appendix 6-23. The thickness standard deviations of dibasic calcium phosphate dihydrate system and α-lactose monohydrate system were not more than 0.015. Generally, it was found that the increase in compressional force caused decrease in thickness values.

3. Tablet Hardness

The average hardness and standard deviation of tablets are shown in Appendix 6-23. For all batches, the increase of hardness values were found with increasing compressional force but no significant change with the increased concentration of the disintegrants.

4. Tablet Friability

Friability of tablets for each formulations are presented in Appendix 6-23. Generally, the friability decreased with increasing compressional force for all formulations owing to the fact that the tablets became dense and less prone to break apart when the compression was increased.

5. Water Uptake of the Tablets

The rates of water uptake of various disintegrants with different concentrations compressed at four different compressional forces for dibasic calcium phosphate dihydrate system and α-lactose monohydrate system were investigated. A direct measuring method for the liquid penetration rate into tablets was determined by a relationship between the square of volumetric uptake (cm^6) and time t (second). The penetration of water into tablets was presented according to types of disintegrants and diluents as follows:

A. Blank Tablets

1. Water Insoluble Diluent

The water uptake curves of directly compressed dibasic calcium phosphate dihydrate without disintegrant are illustrated in Figure 9. It was shown that the amount volume of water uptake was very little and the increasing rate of water uptake was influenced by the compressional force. Slower water uptake was observed when the compressional force increased.

2. Water Soluble Diluent

In the case of directly compressed α-lactose monohydrate system, the water uptake curves are shown in Figure 10. The rate was similar to dibasic calcium phosphate system that an increase in compressional force produced decreasing in water uptake, but the higher amount of water uptake was attained.

B. S_1 Fraction

1. Water Insoluble Diluent

The water uptake curves of dibasic calcium phosphate dihydrate tablets containing various concentrations of S_1 when directly compressed at four compressional forces are given in Figures 11-14. The increasing in compressional force produced decreasing in penetration rate except at concentration of 3%. An increase in volume and rate of water uptake were also found when increased in concentrations of S_1 in the range of 0.5-3%.

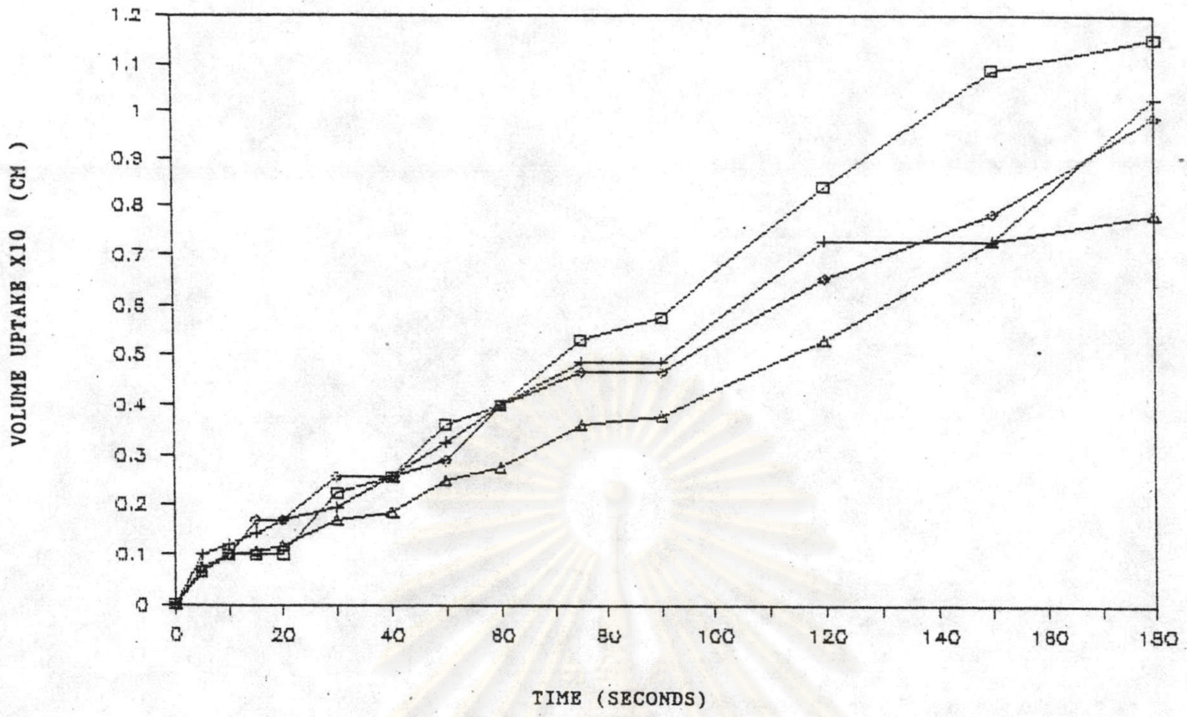

Figure 9 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate without Disintegrant at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

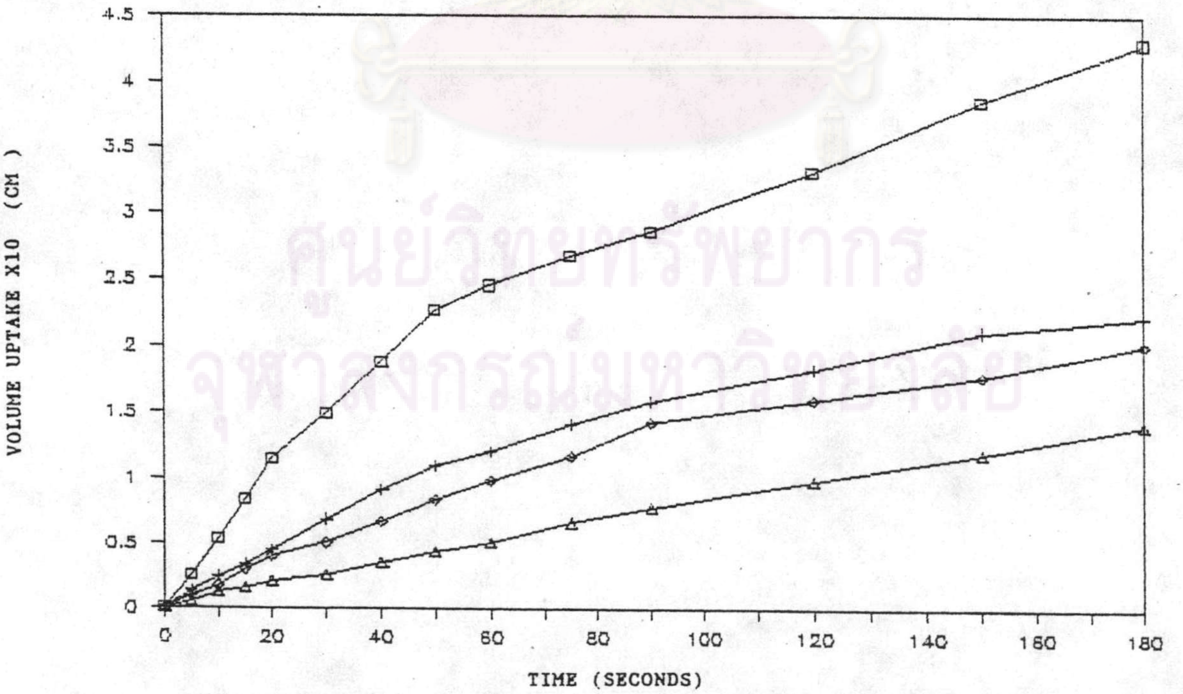

Figure 10 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate without Disintegrant at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

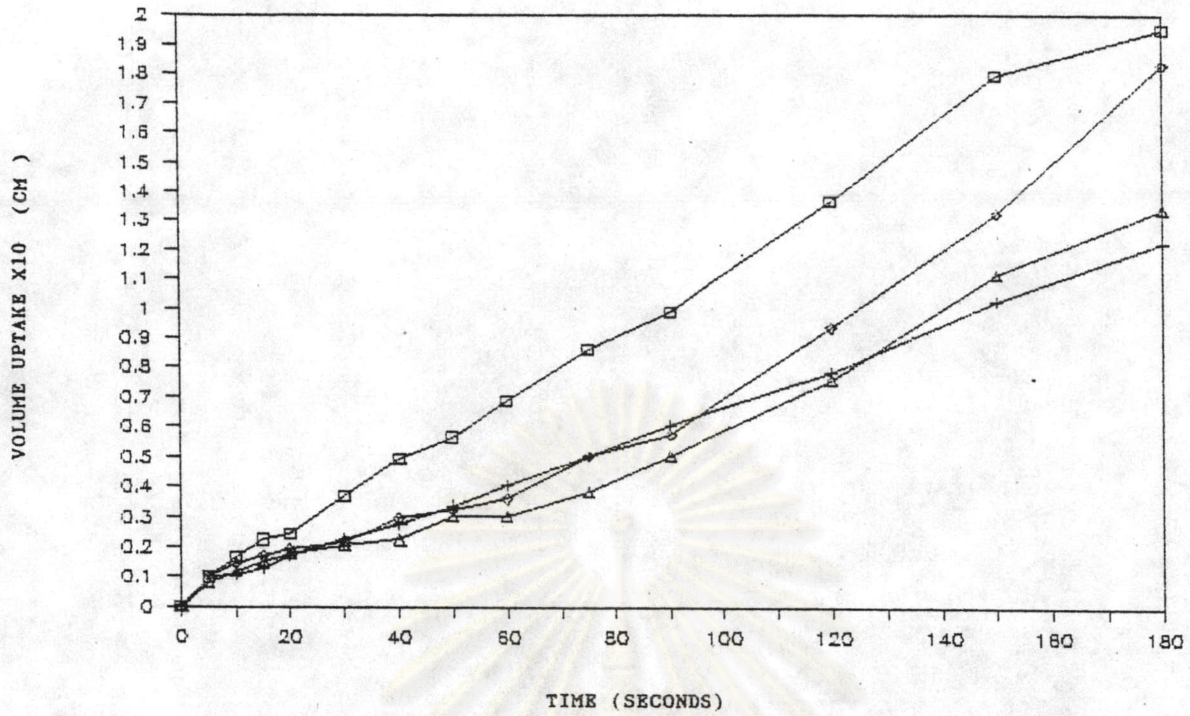

Figure 11 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

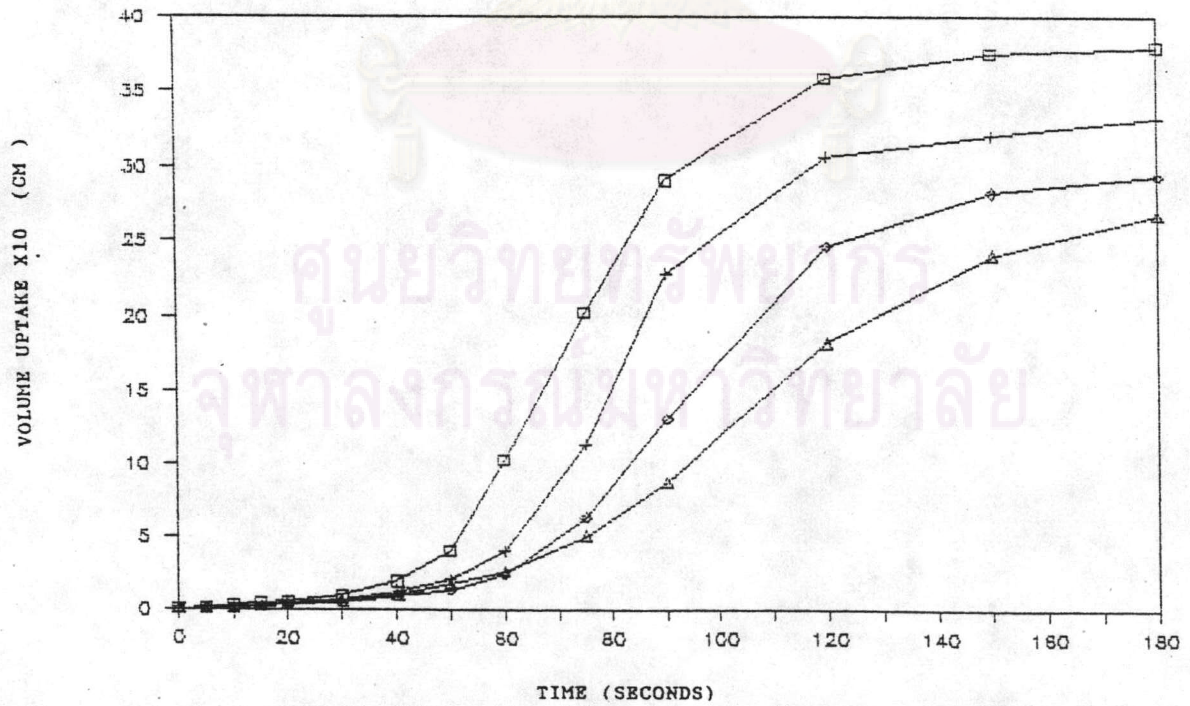

Figure 12 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

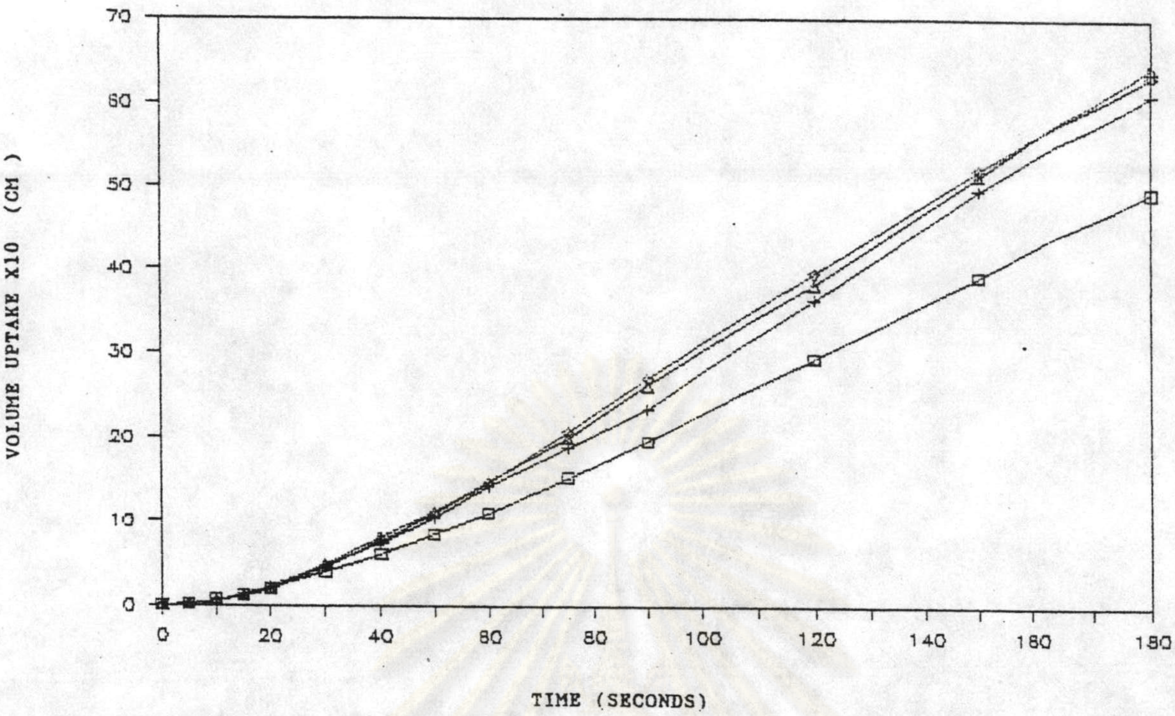

Figure 13 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

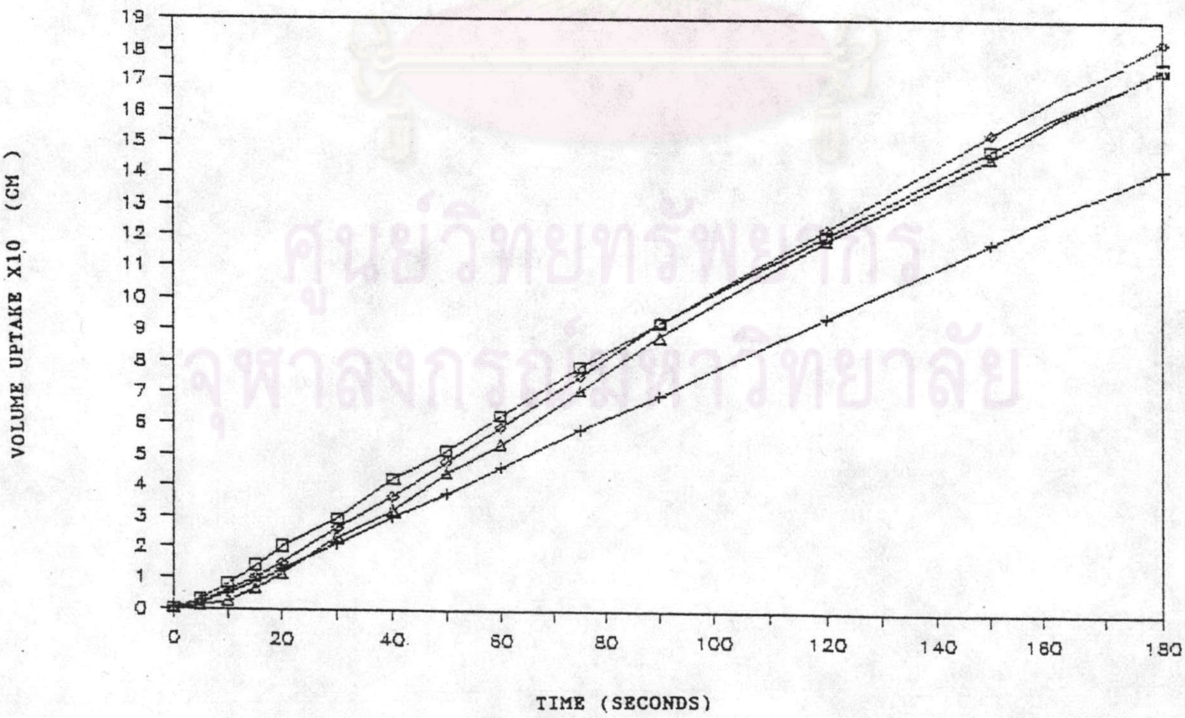

Figure 14 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

At 5% level, the volume and rate of water uptake became lower than of 1 and 3% levels.

2. **Water Soluble Diluent**

The effect of S_1 upon water uptake of directly compressed α-lactose monohydrate system at four compressional forces is presented in Figures 15-18. The curves showed that the penetration rate was clearly decreased with high compressional force. The rate and volume of water uptake were decreased with increasing in concentration of S_1. However, at concentration of 5%, the rate of water uptake appeared to increase at the higher compressional force.

C. S_2 Fraction

1. **Water Insoluble Diluent**

The water uptake of directly compressed dibasic calcium phosphate dihydrate tablets containing various concentrations of S_2 at four compressional forces are illustrated in Figures 19-22. The rate of water uptake was not dominantly influenced by the compressional forces. In the range of 0.5% and 1% levels, the volume and rate of water uptake increased with concentration of S_2. But at the concentration of S_2 higher than 3%, the volume and rate of water uptake (within 180 seconds) seemed to be decresed. The rate of water uptake was very slow when using concentration of S_2 5%.

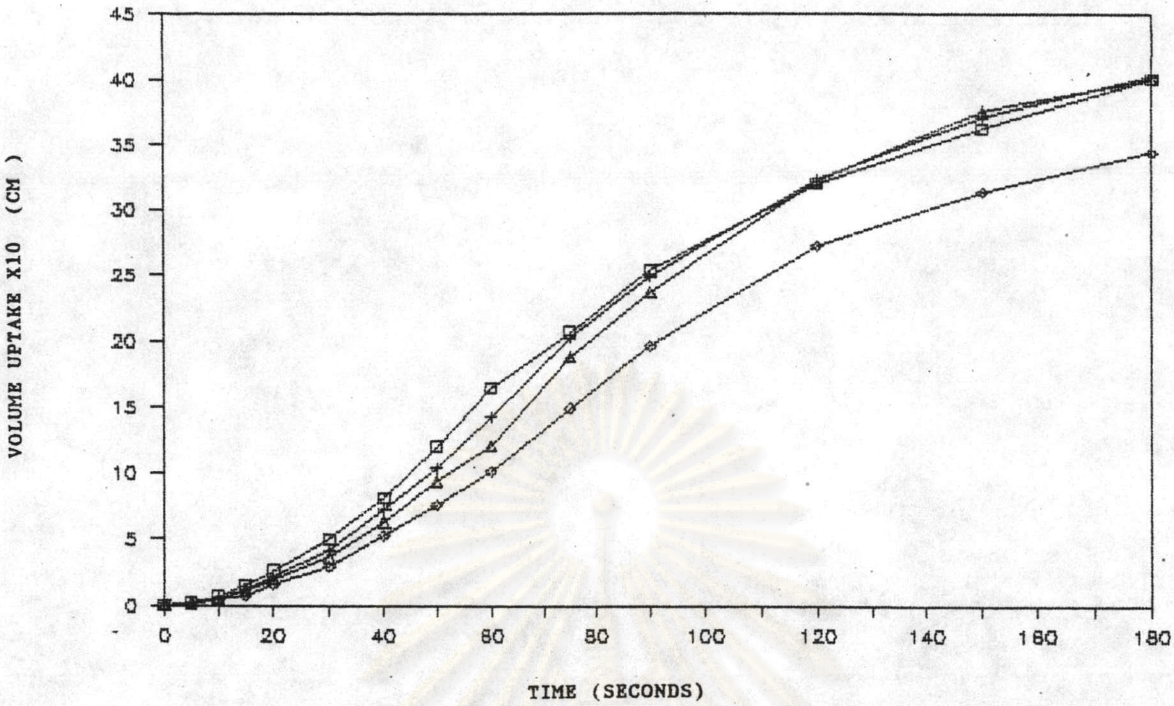

Figure 15 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

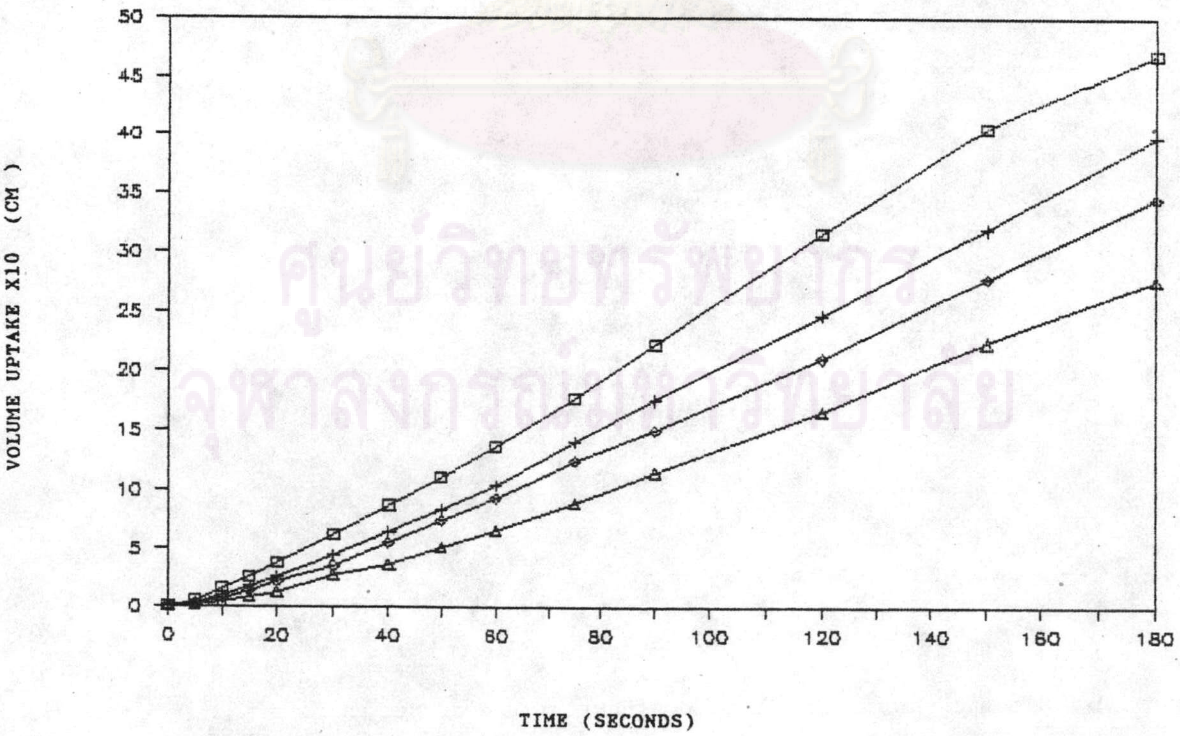

Figure 16 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

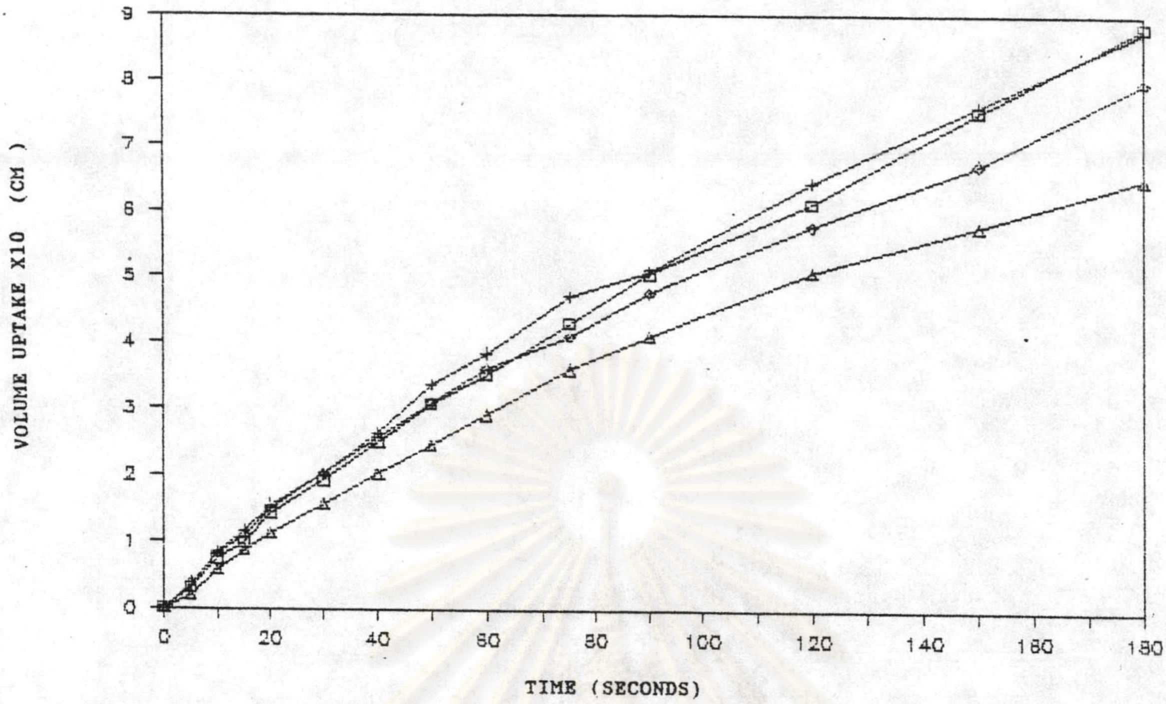

Figure 17 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

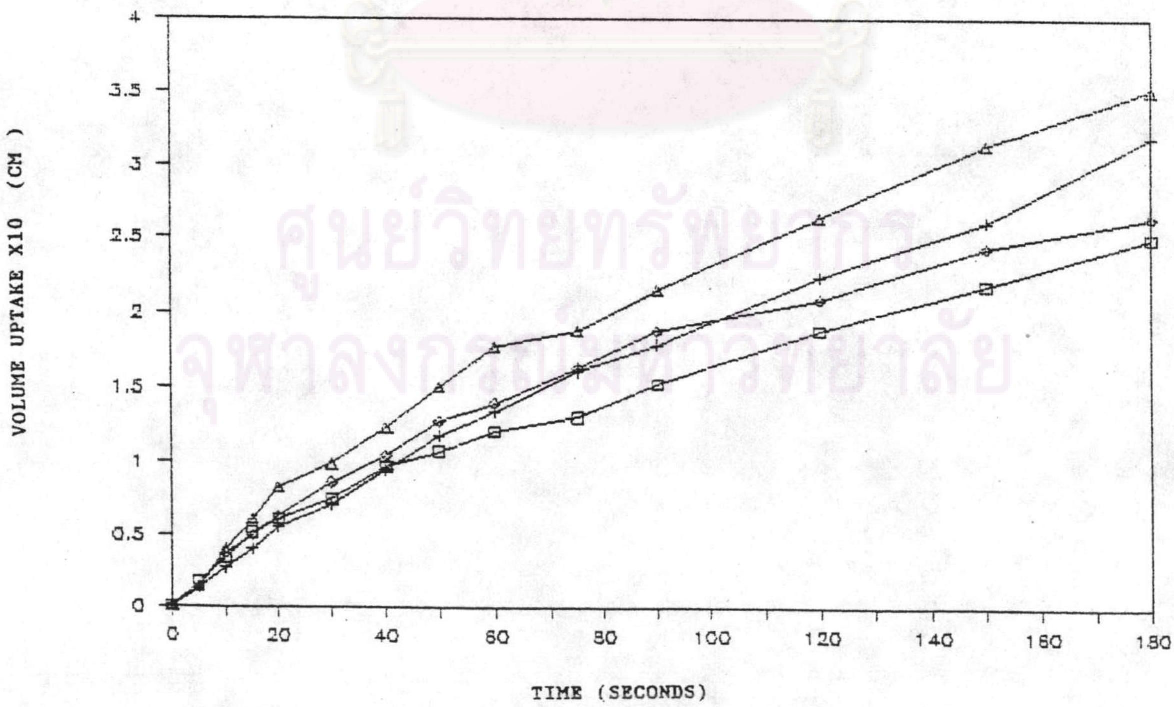

Figure 18 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of S_1 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

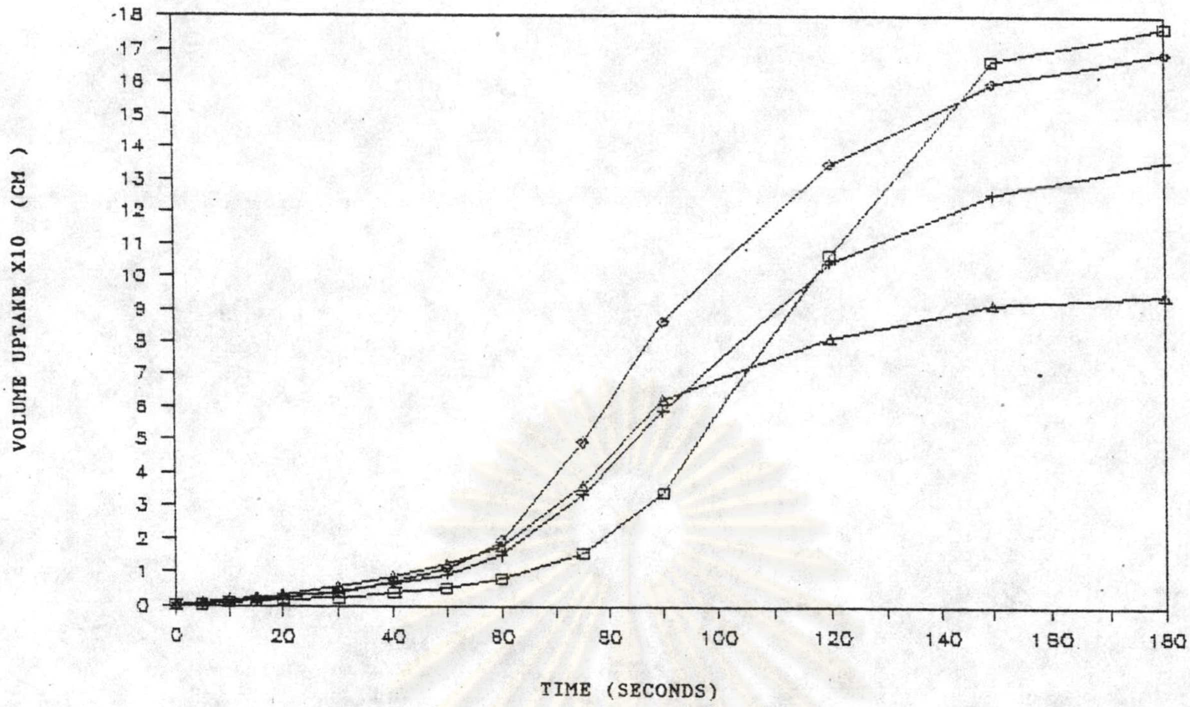

Figure 19 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

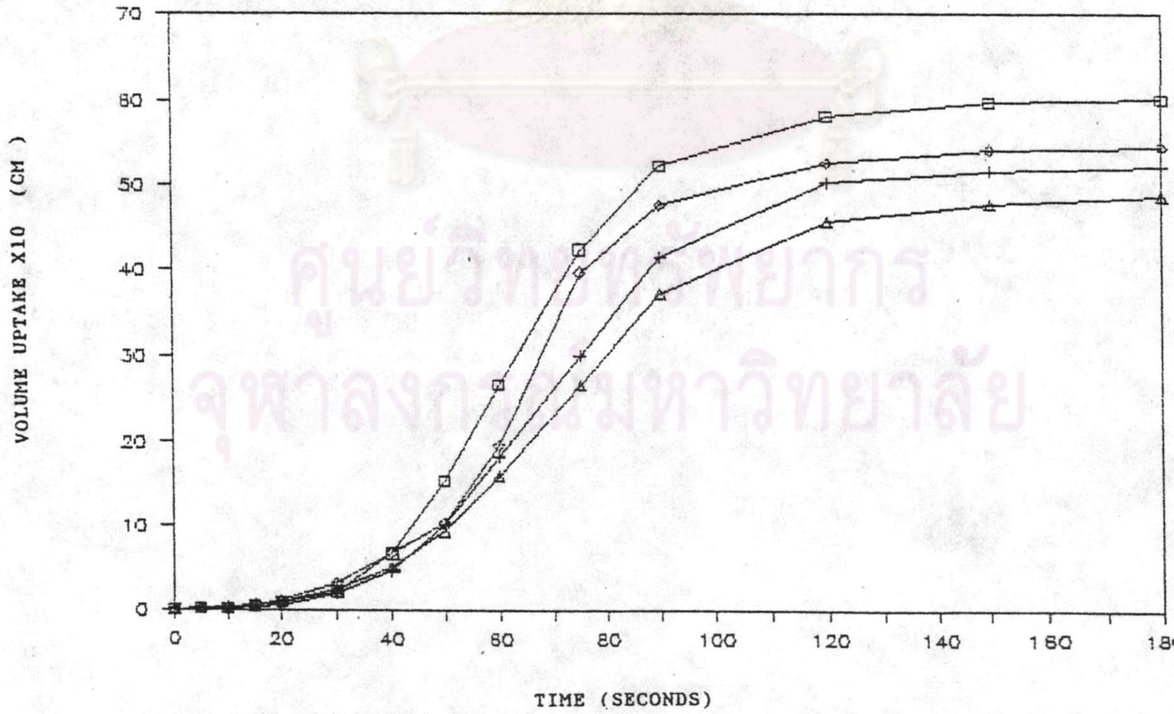

Figure 20 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

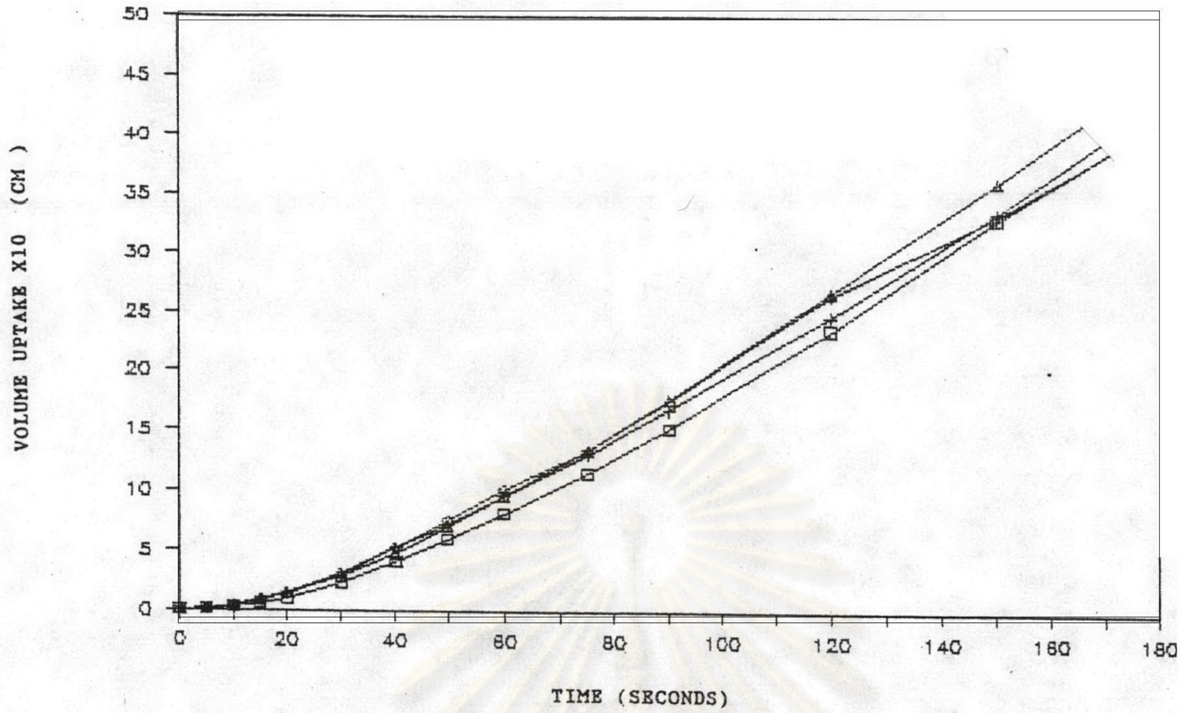

Figure 21 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

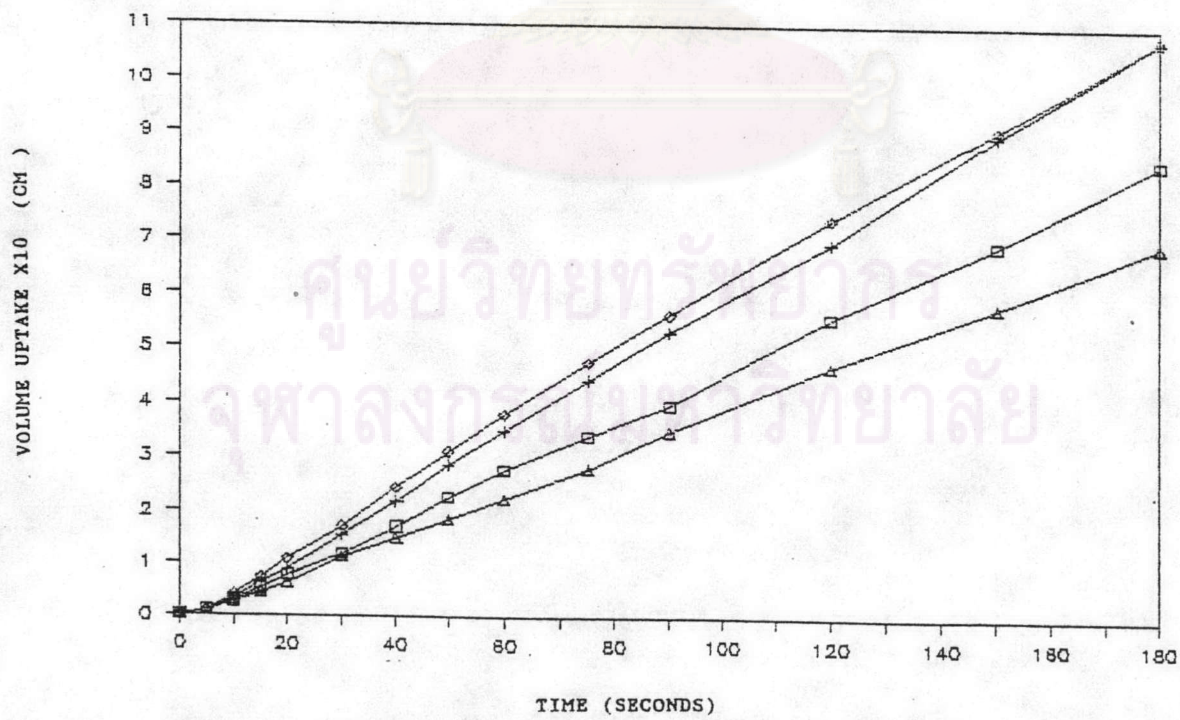

Figure 22 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

2. **Water Soluble Diluent**

In the case of directly compressed α-lactose monohydrate system containing S_2, the rate of water uptake was likely increased with decrease in compressional force as shown in Figures 23-26, except at the concentration of 1%, no effect of compressional force was observed. The amount and rate of water uptake were decreased when the amount of S_2 increased.

D. Ac-Di-Sol(R)

1. **Water Insoluble Diluent**

The effects of Ac-Di-Sol(R) upon water uptake into tablets prepared from dibasic calcium phosphate dihydrate compressed with various compressional forces are illustrated in Figures 27-30. Incorporation of high concentration of Ac-Di-Sol(R) resulted in a sudden increase in water penetration rate at the early stage while maximum water uptake was reached within 30 seconds. The water uptake rate increased with increase in compressional force.

2. **Water Soluble Diluent**

Water uptake behaviors of the tablets prepared from α-lactose monohydrate and Ac-Di-Sol(R) were illustrated in Figures 31-34. The compressional force was not influenced on water uptake rate except for the compressional force of 3000 pounds at disintegrant concentrations of 0.5 and 1% levels, the initial rates of water uptake were higher than of the others. The higher

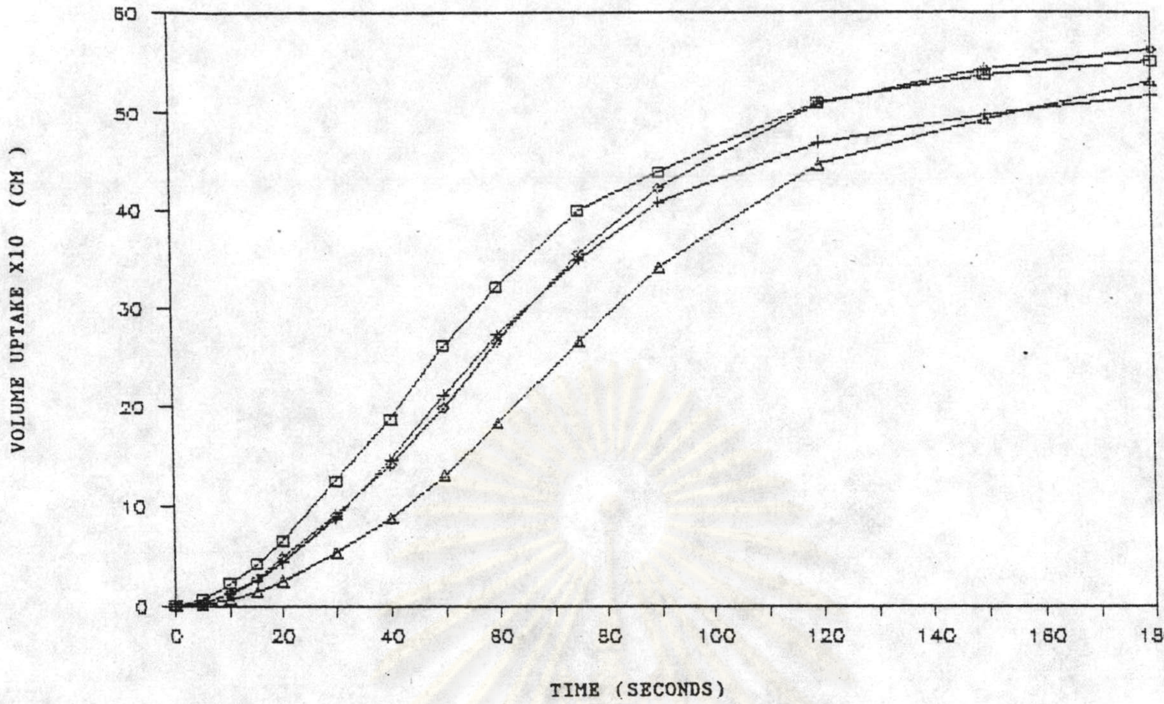

Figure 23 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

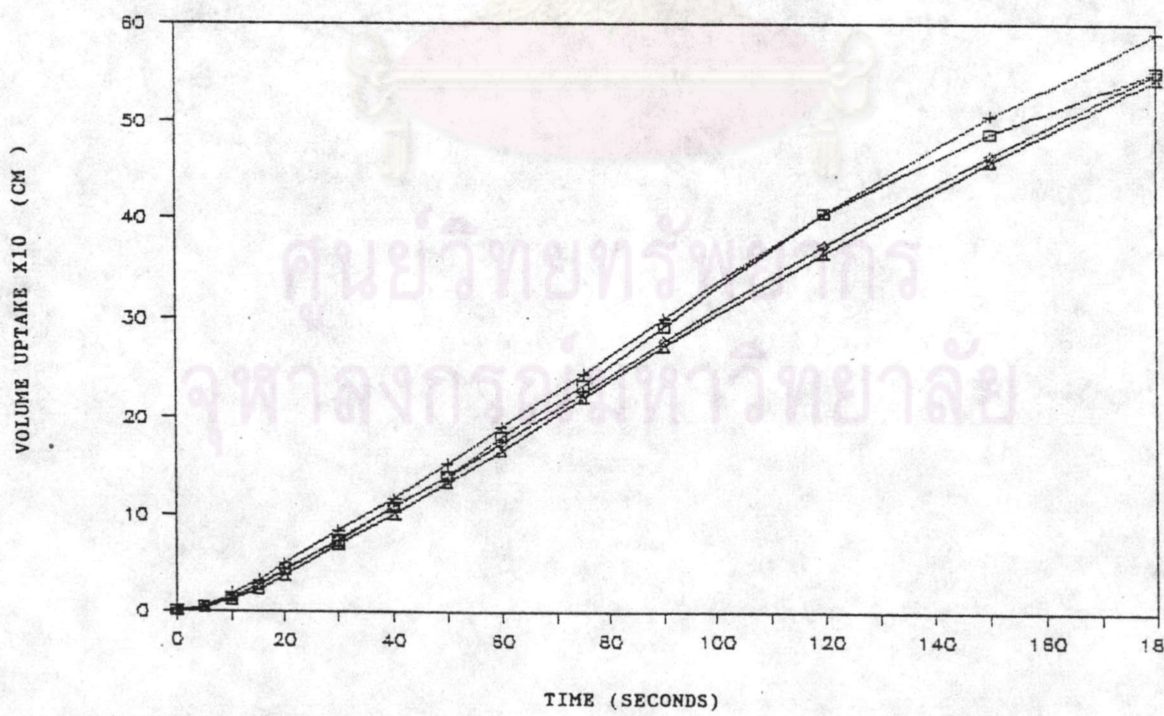

Figure 24 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

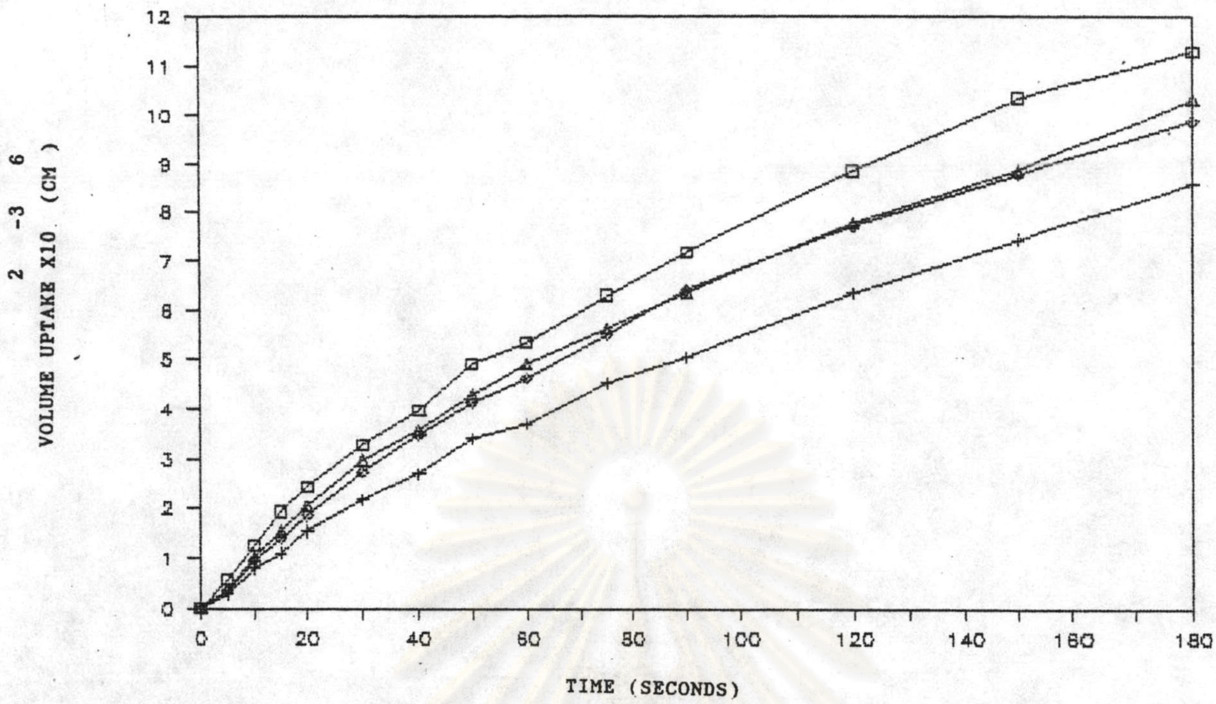

Figure 25 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

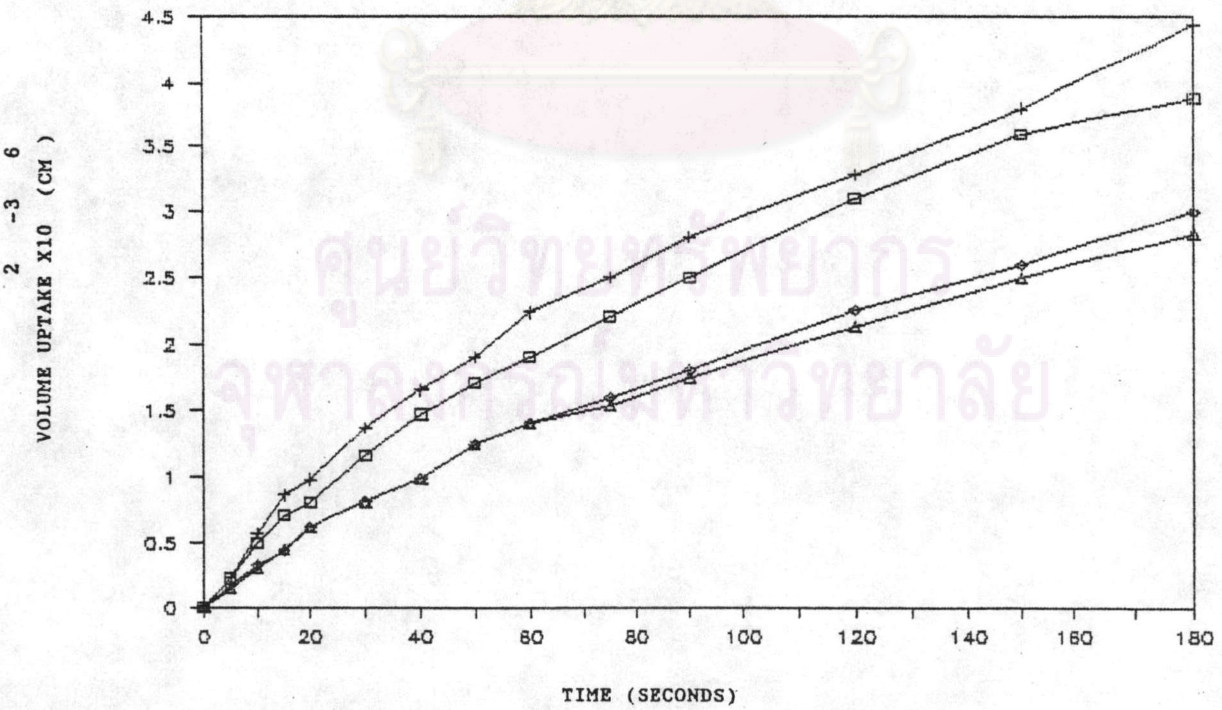

Figure 26 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of S_2 at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb

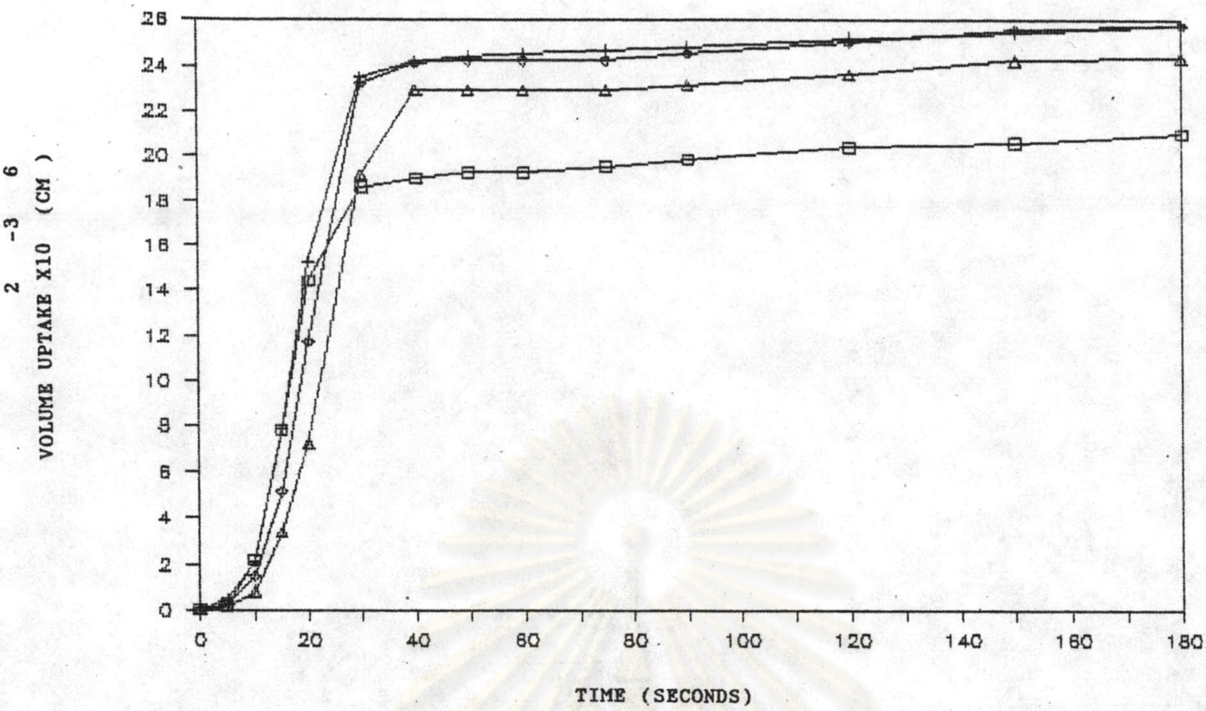

Figure 27 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of Ac-Di-Sol$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

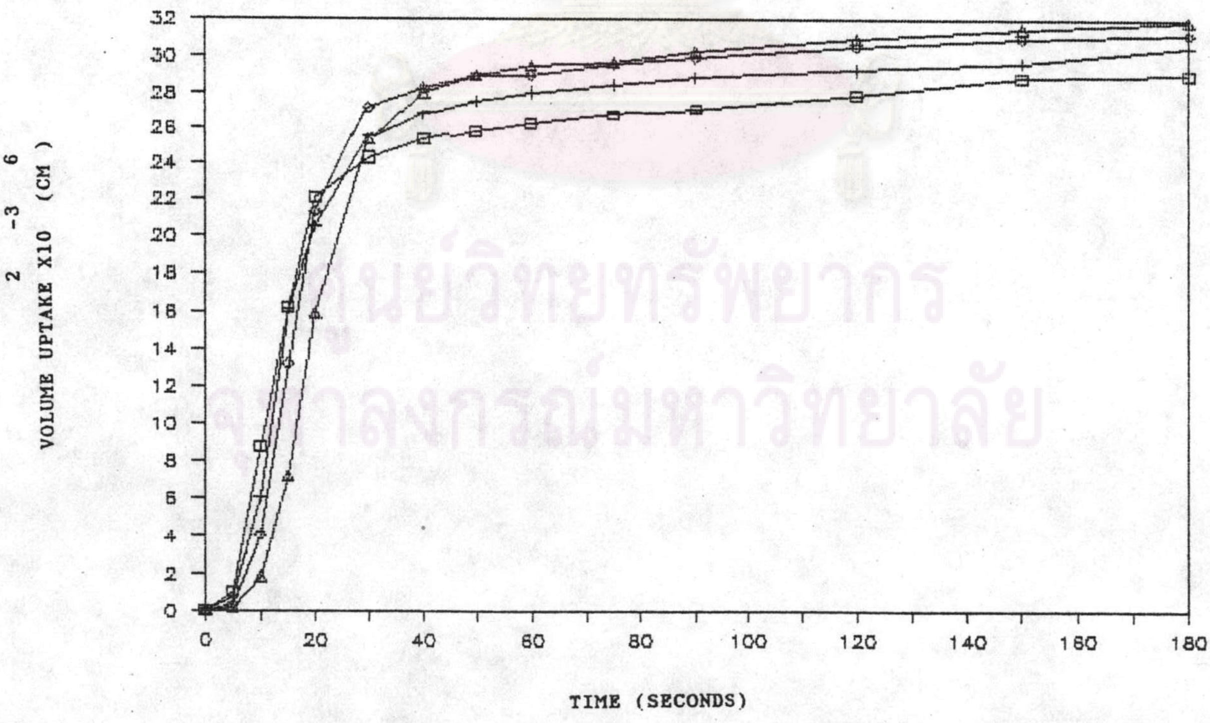

Figure 28 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of Ac-Di-Sol$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

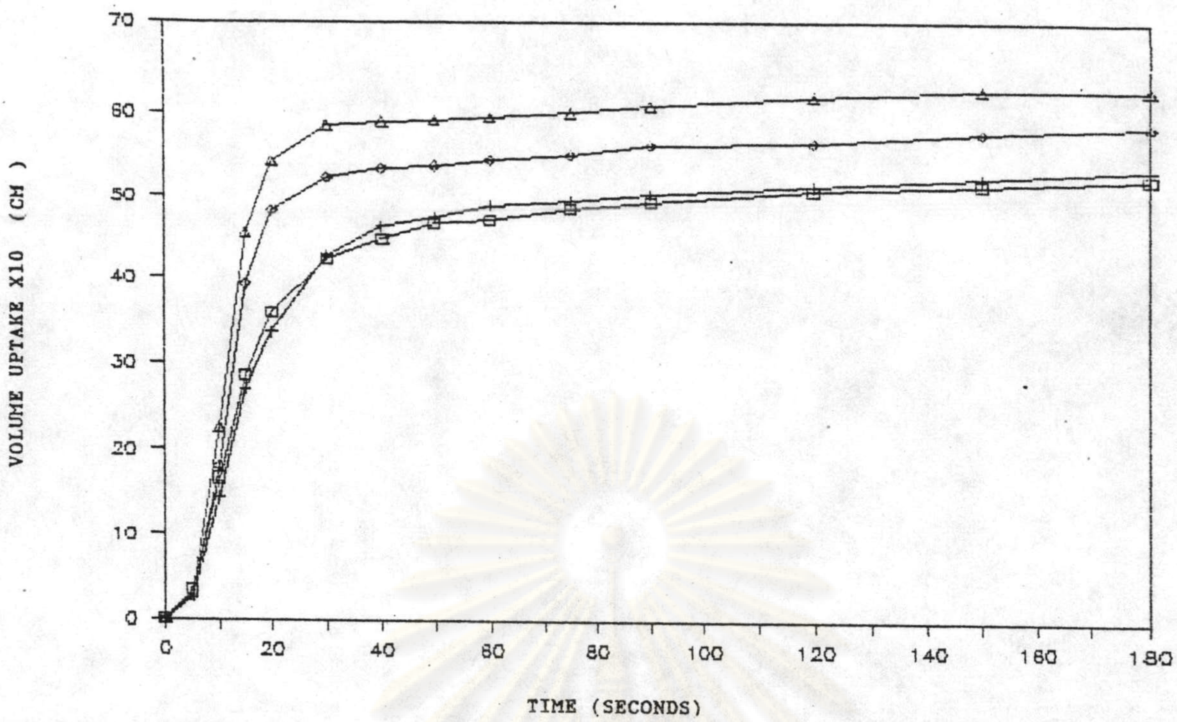

Figure 29 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of Ac-Di-Sol(R) at Different Compressional Forces (Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

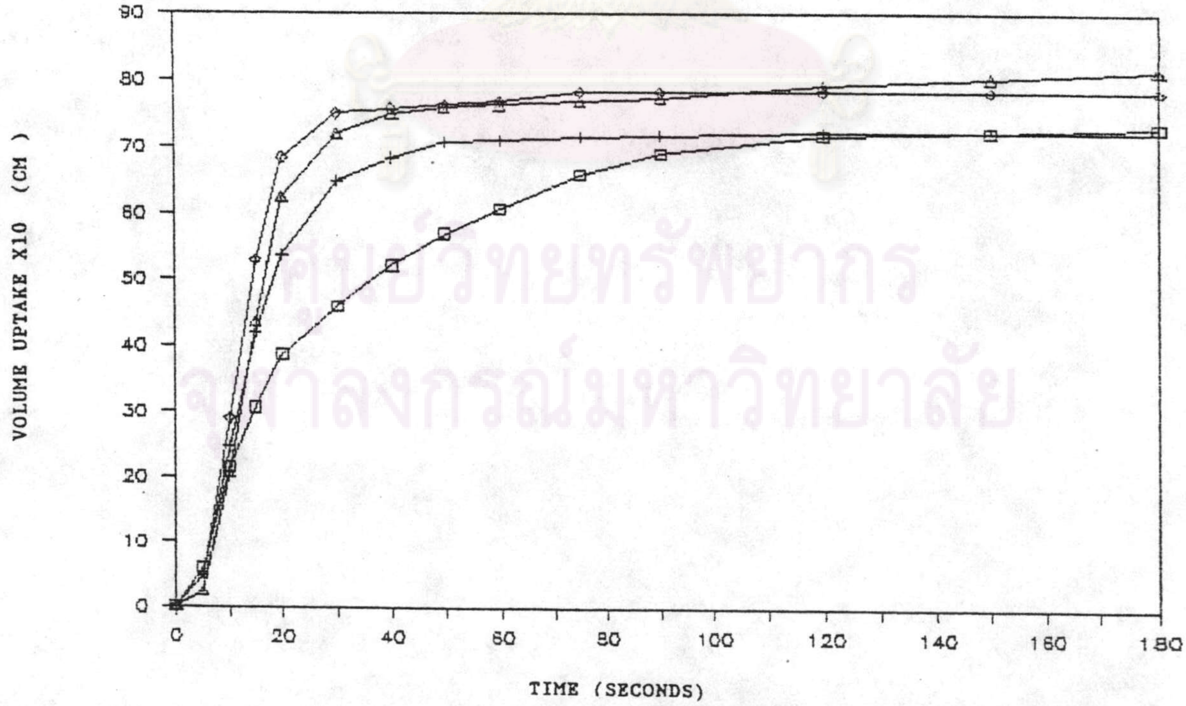

Figure 30 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of Ac-Di-Sol(R) at Different Compressional Forces (Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

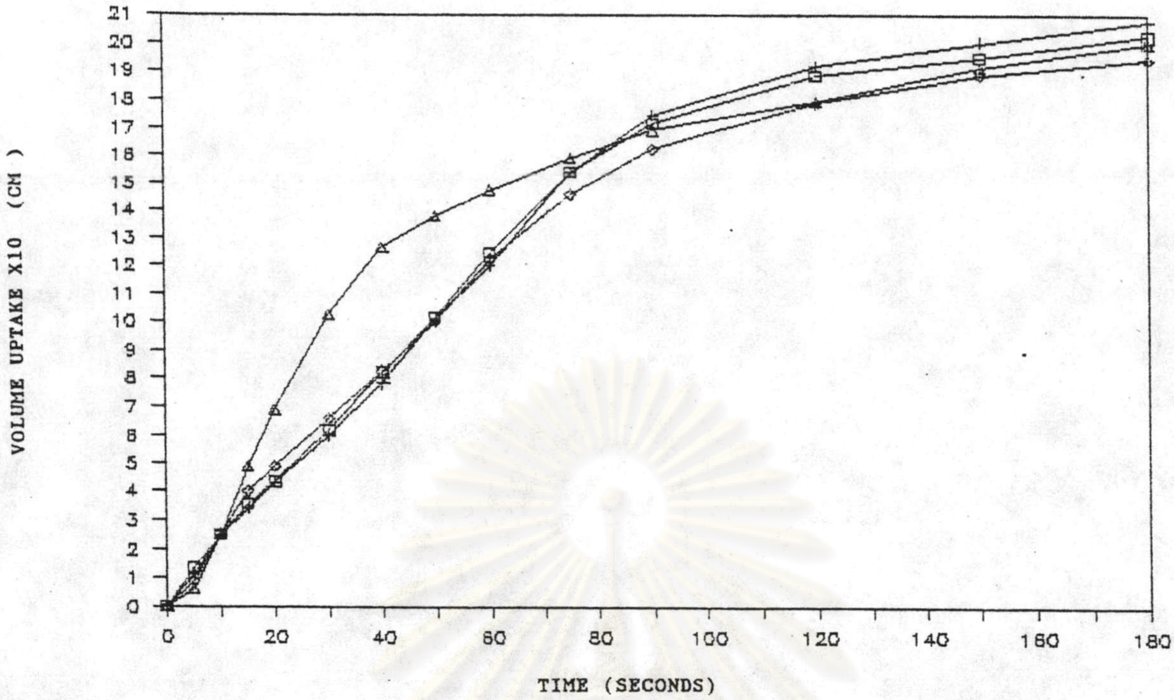

Figure 31 Water Uptake Profiles of Tablets Made from ∝-Lactose Monohydrate with 0.5% of Ac-Di-Sol(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

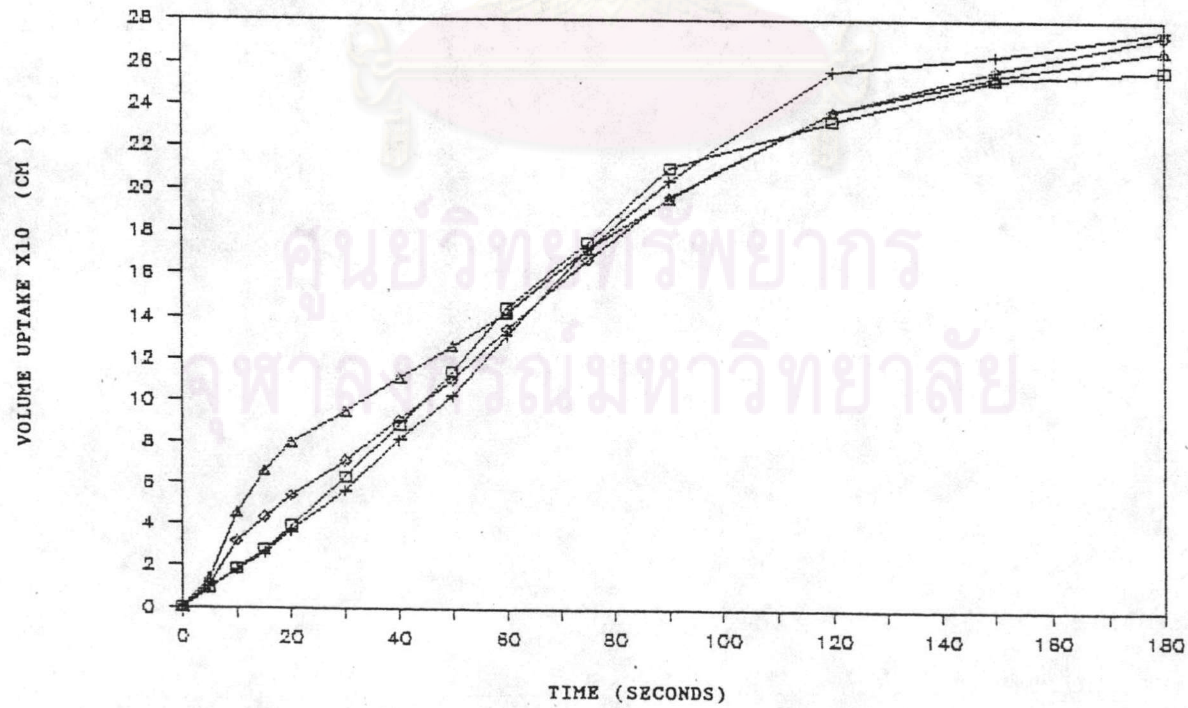

Figure 32 Water Uptake Profiles of Tablets Made from ∝-Lactose Monohydrate with 1% of Ac-Di-Sol(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

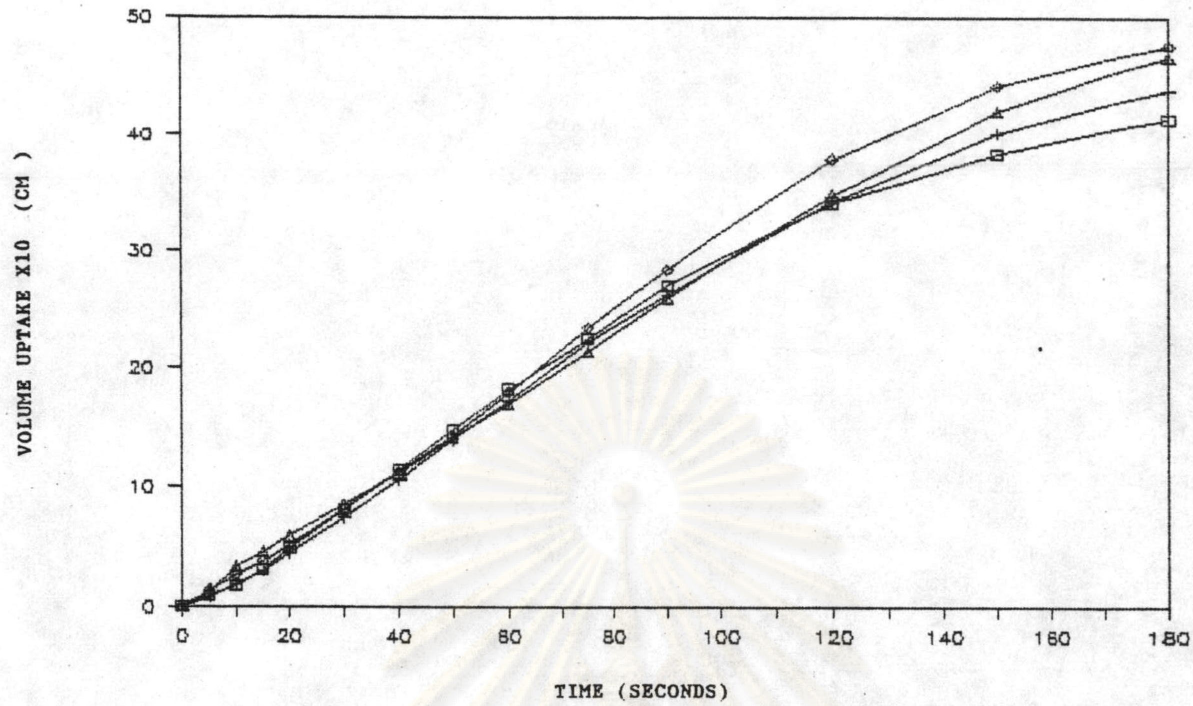

Figure 33 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of Ac-Di-Sol(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

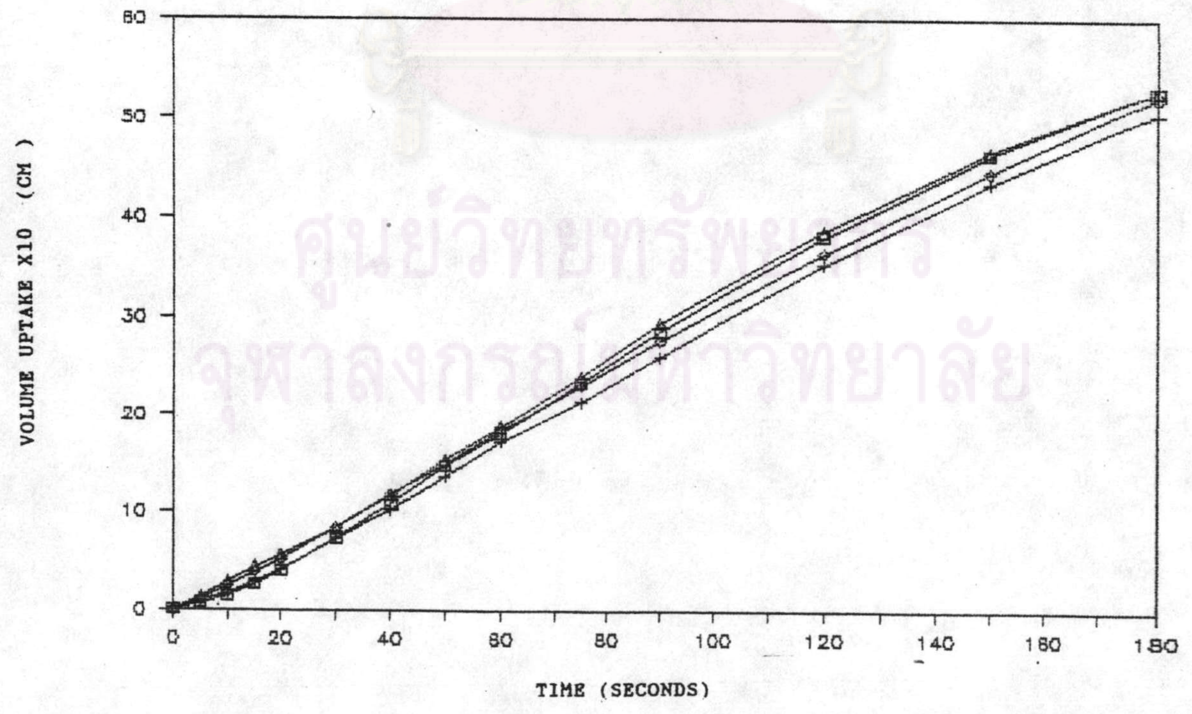

Figure 34 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of Ac-Di-Sol(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

the concentration of Ac-Di-Sol(R) was incorporated in formulation, the greater the rate of water uptake was obtained. In comparing with water insoluble system, the change in rate and extend of water uptake were smaller.

E. Corn Starch

1. Water Insoluble Diluent

The results of water uptake into dibasic calcium phosphate dihydrate tablets using corn starch as disintegrant at different compressional forces are presented in Figures 35-38. The water uptake rate increased with increase in compressional force at high concentration of corn starch in tablet. Higher concentration of corn starch obviously produced an increasing in penetration rate and shorter a lag time.

2. Water Soluble Diluent

The influences of corn starch on the water uptake into α-lactose monohydrate tablets directly compressed at various compressional forces are given in Figures 39-42. At 0.5 and 1% concentrations of corn starch, the rates of water uptake were increased with decrease in compressional forces, but at 3 and 5% concentrations the contrary results were observed. As concentration of corn starch increased the rate of water uptake also increased. On increasing concentration of corn starch resulted in increasing rate of water uptake and the reduction of the lag time.

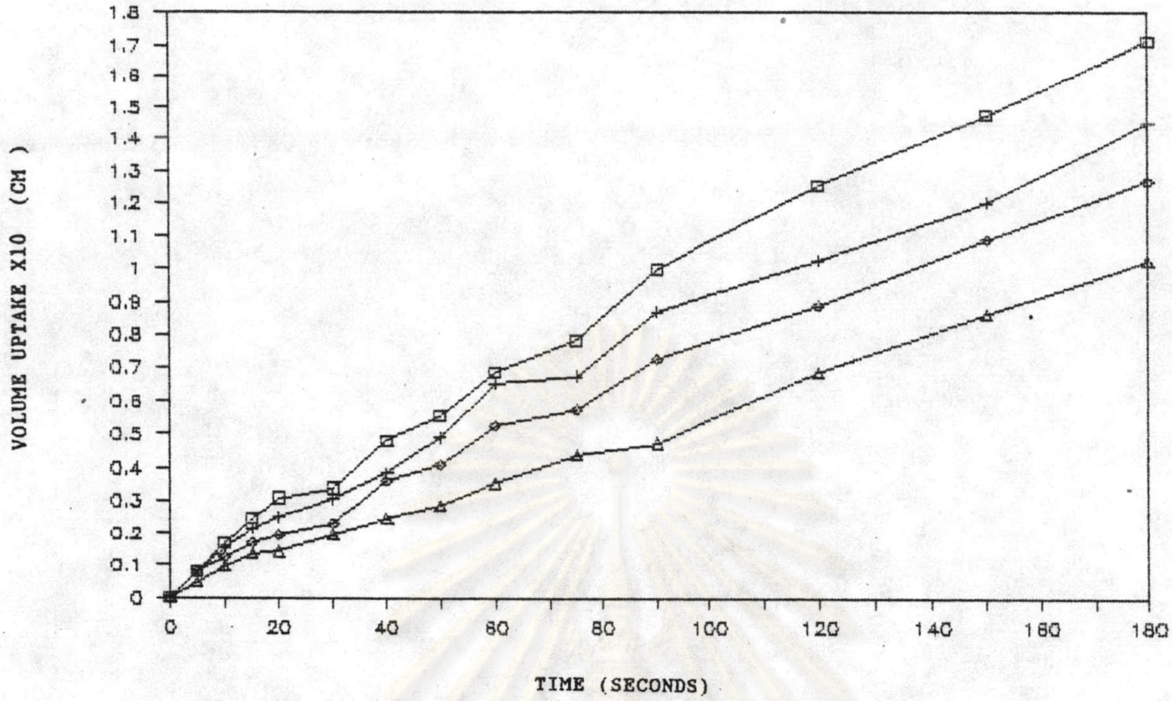

Figure 35 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

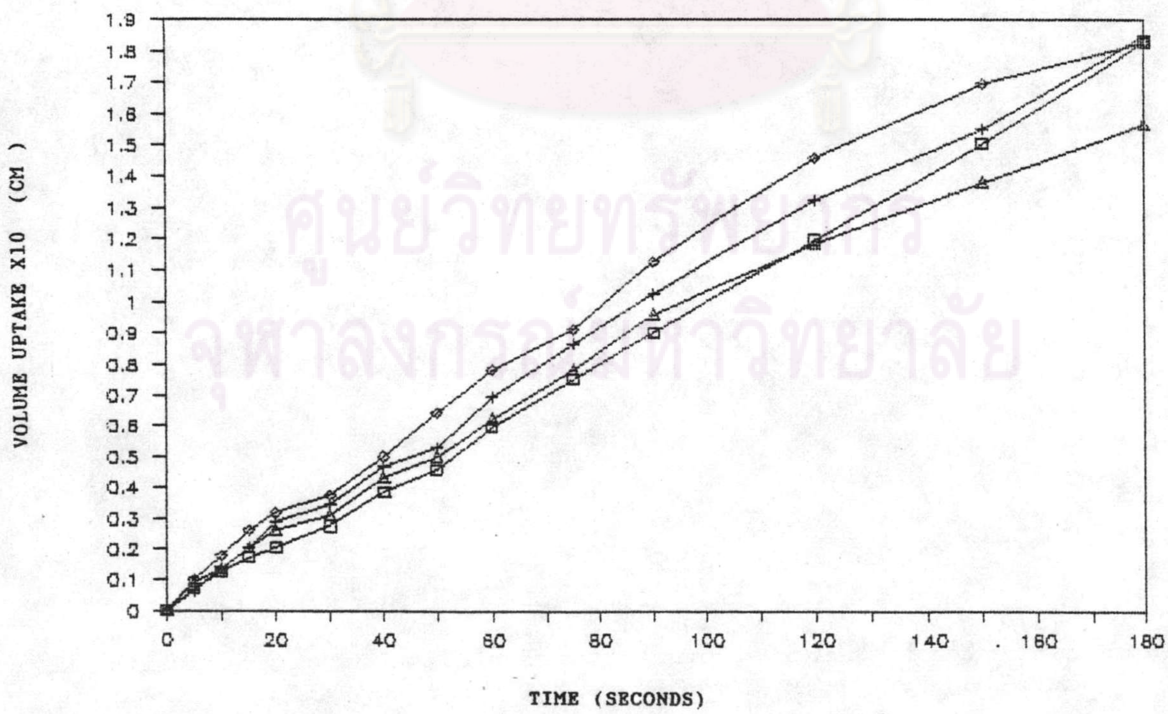

Figure 36 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

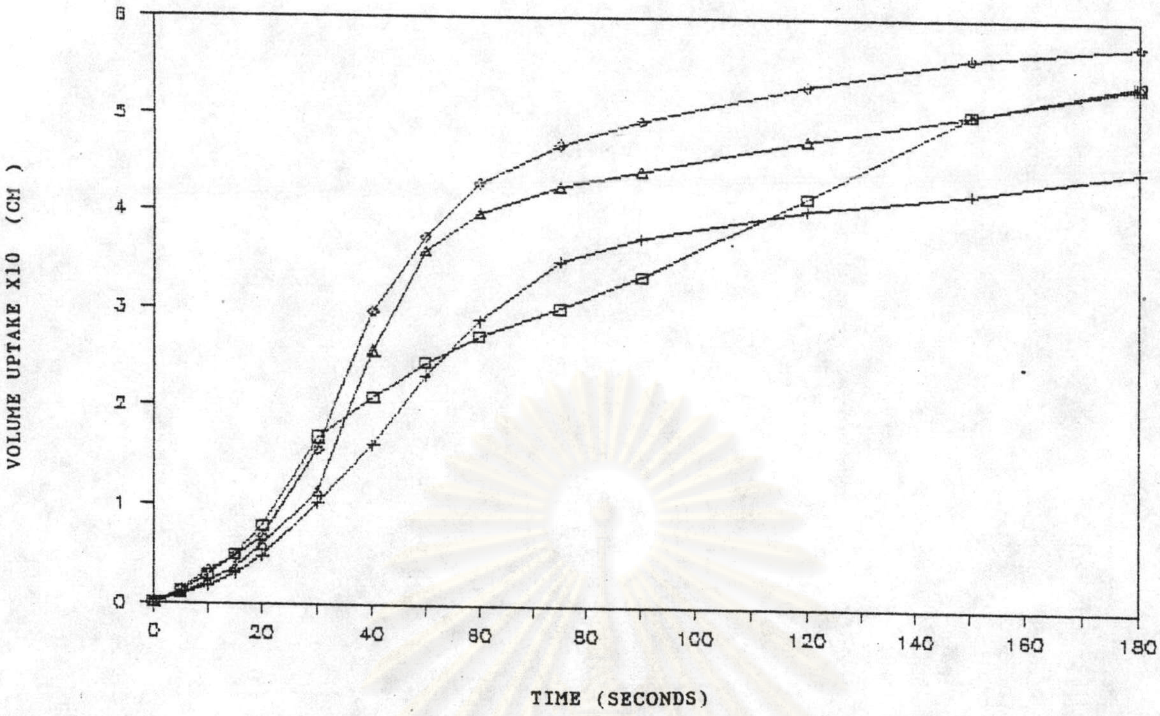

Figure 37 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

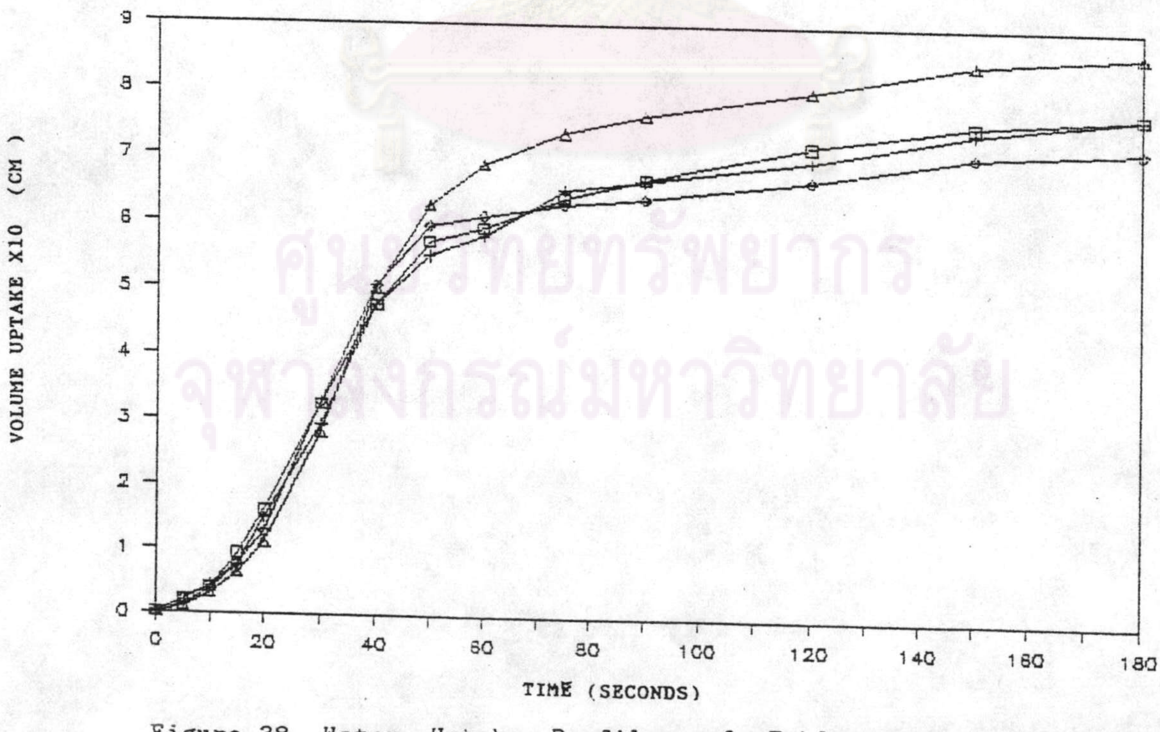

Figure 38 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

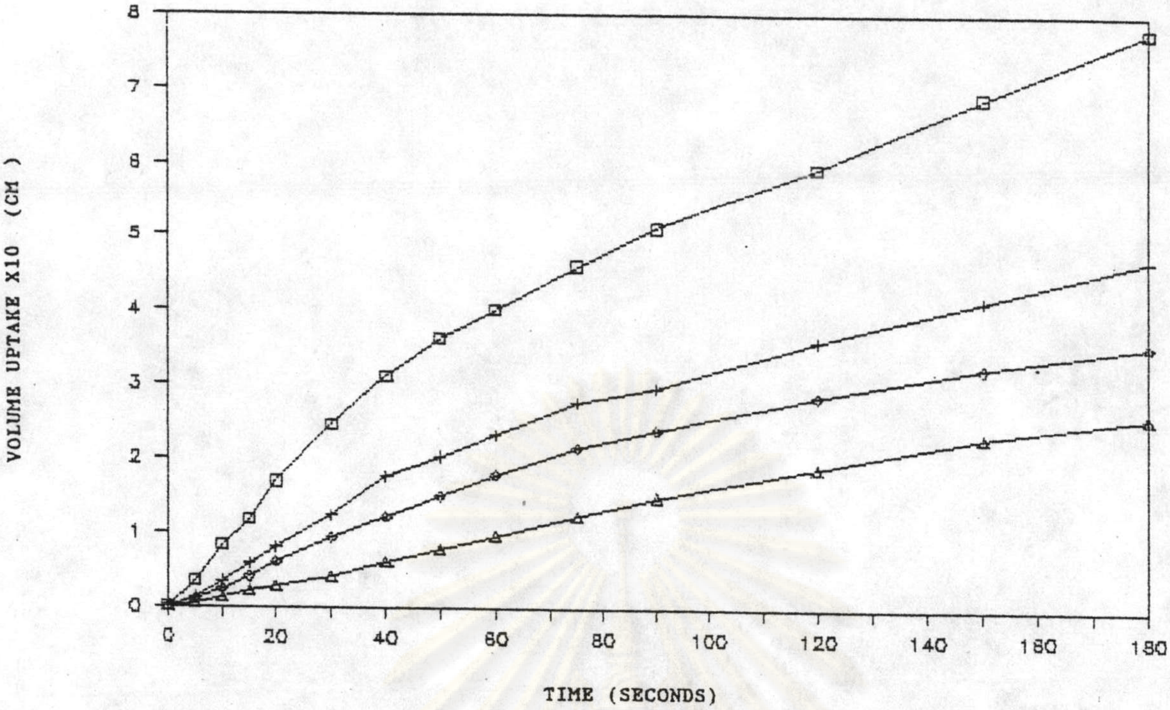

Figure 39 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

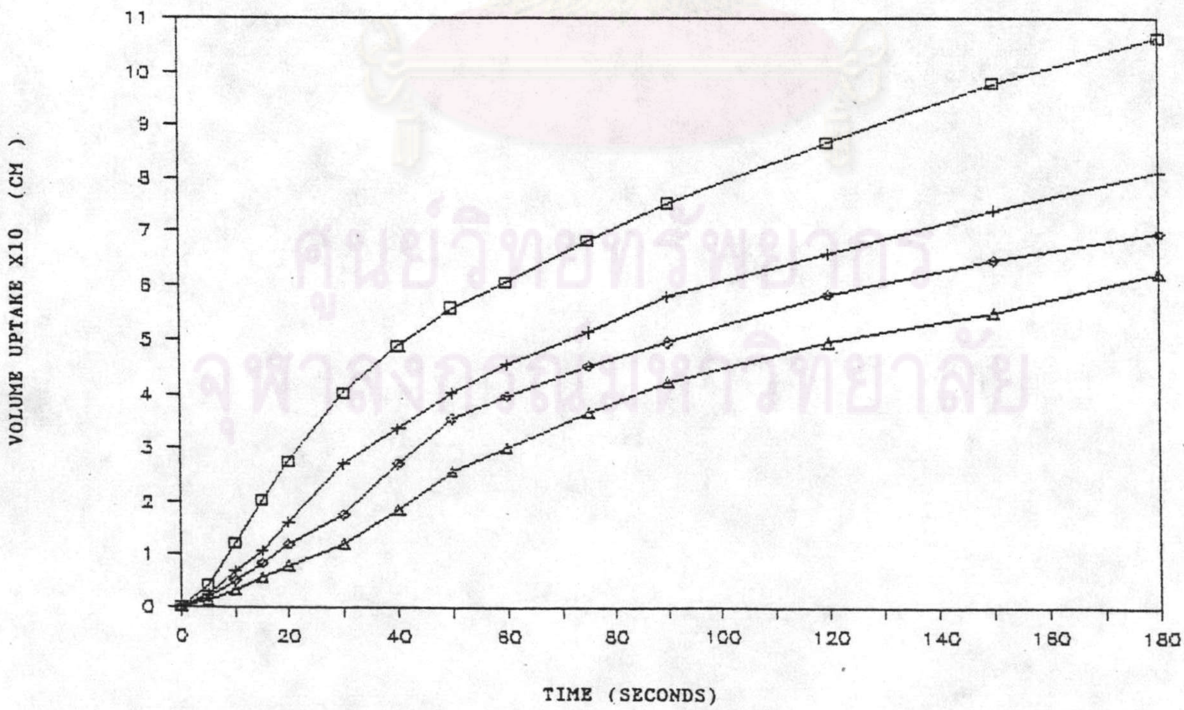

Figure 40 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrat with 1% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

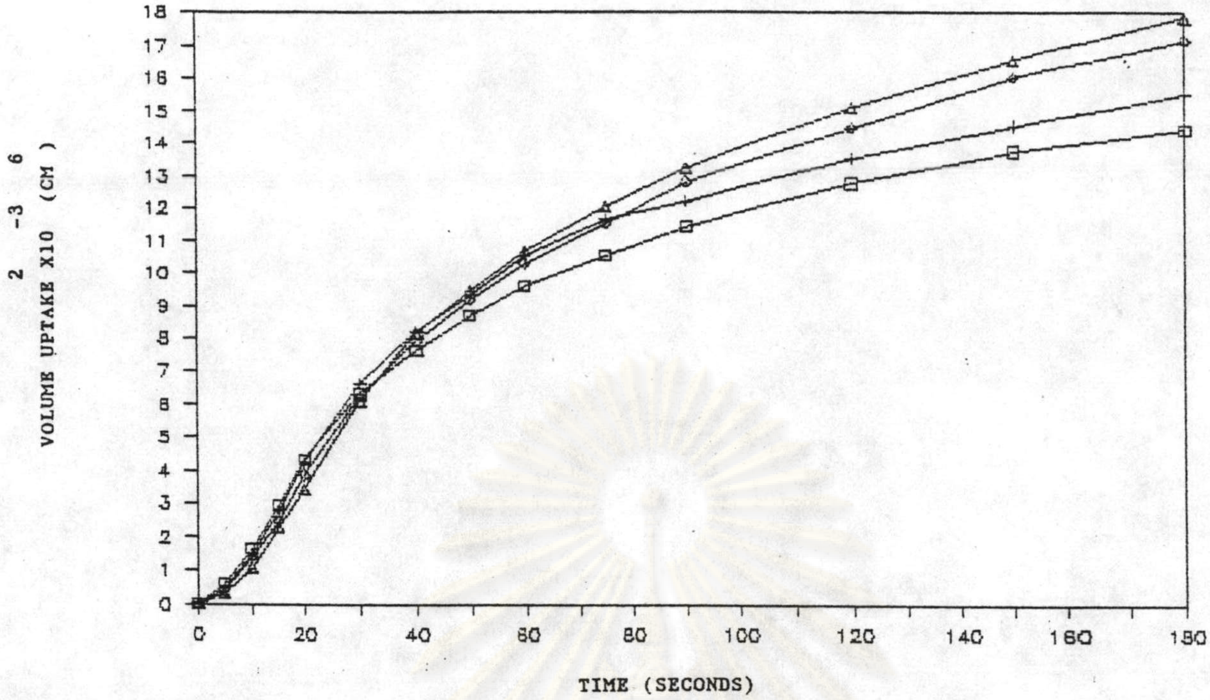

Figure 41 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

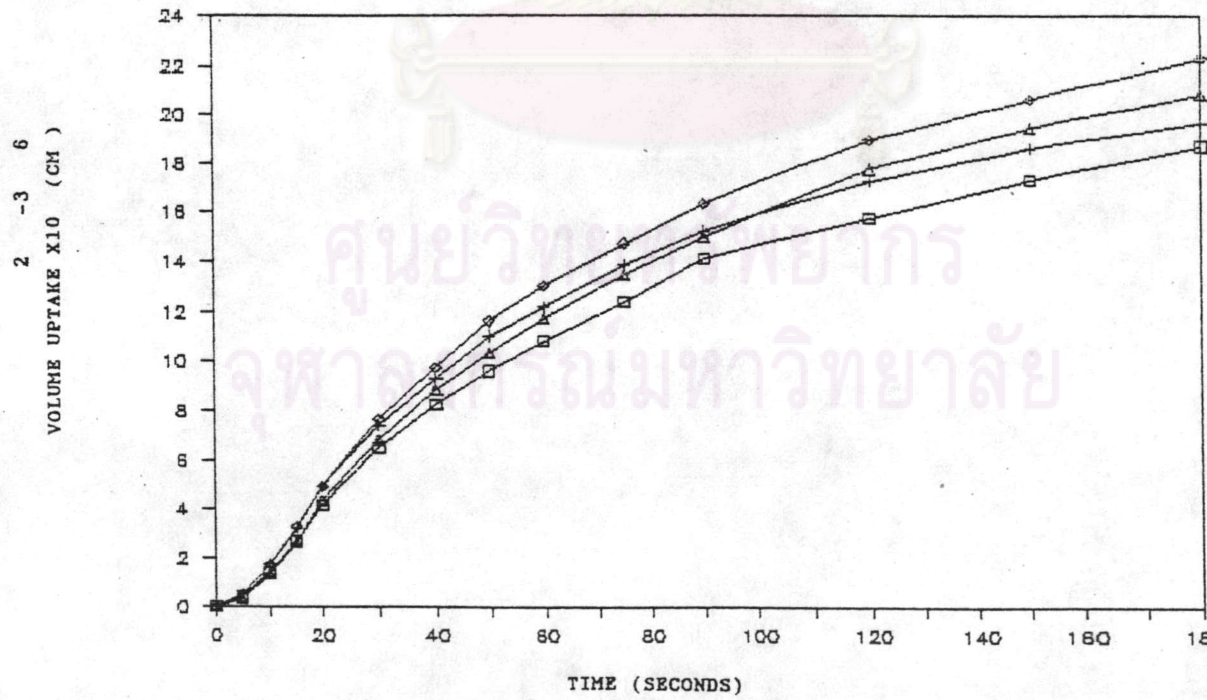

Figure 42 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of Corn Starch at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

F. ECG 505(R)

1. Water Insoluble Diluent

Water uptake rate behaviors of tablets prepared from dibasic calcium phosphate dihydrate and ECG 505(R) are illustrated in Figures 43-46. At concentrations of 0.5 and 1%, the rates of water uptake decreased with increasing in compressional forces. But at 3 and 5% levels, the rates of water uptake increased as compressional forces increased. It was noted that the rate and extent of water uptake were highly increased when increasing the amount of ECG 505(R). The lag time was also reduced when the larger amount of ECG 505(R) was added.

2. Water Soluble Diluent

In the case of directly compressed α-lactose monohydrate system, the compressional force exerted different influences on water uptake as shown in Figures 47-50. At 0.5% level, the rate of water uptake increased as compressional force decreased. For 1% level, the rate of water uptake increased as compressional forces decreased for the first 30 seconds. At the concentrations of 3 and 5%, the initial rates of water uptake within 40 seconds were not different. The dependence of water uptake rate on compressional force was observed when the saturation points were reached. Slight difference in lag time was shown when the concentration of ECG 505(R) increased, but the volume of water uptake became higher when the amount of disintegrant increased.

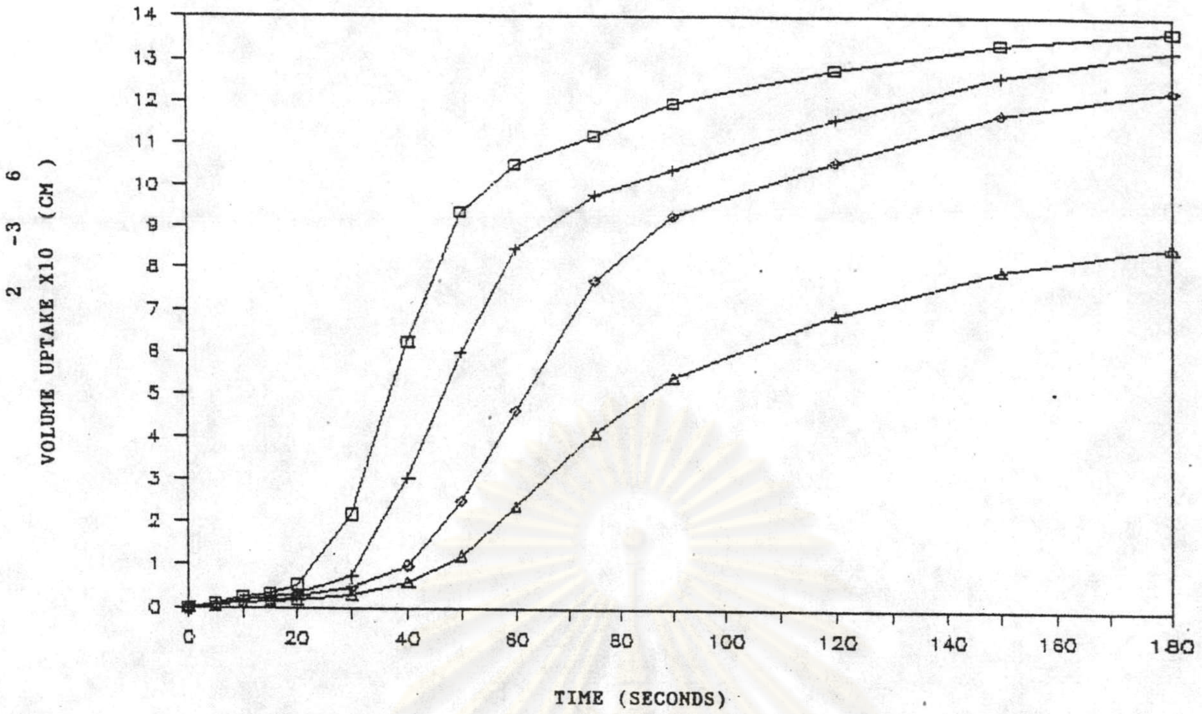

Figure 43 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

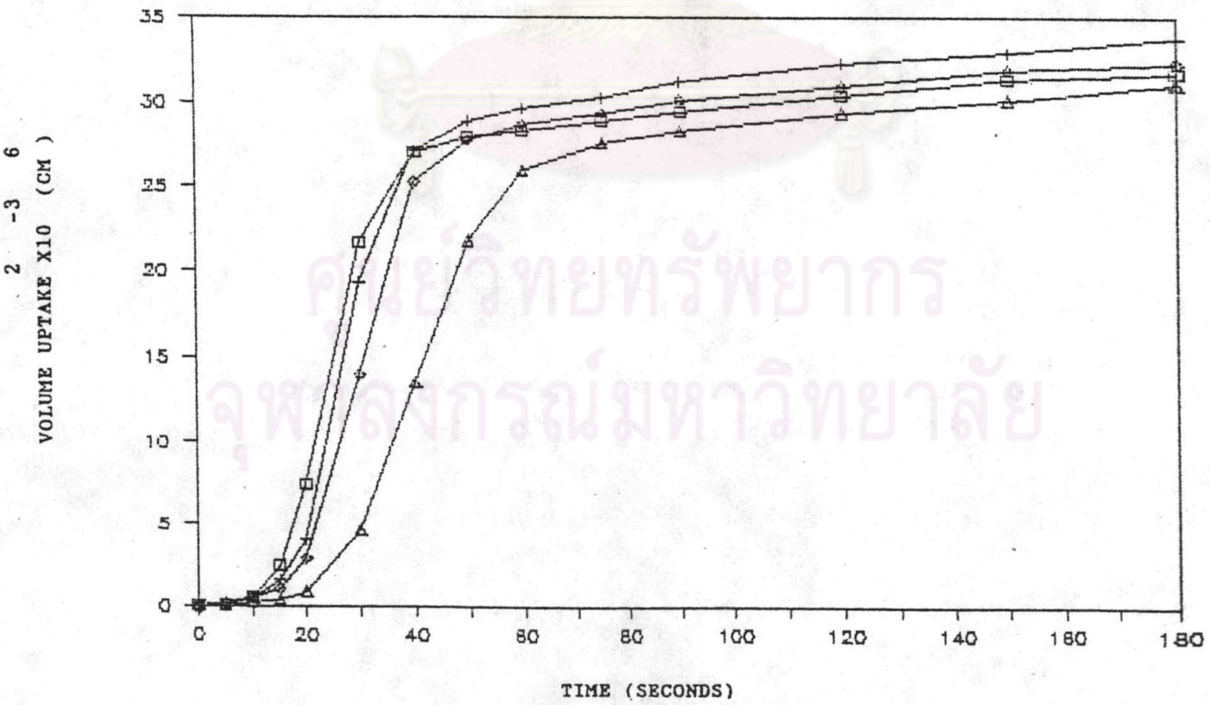

Figure 44 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

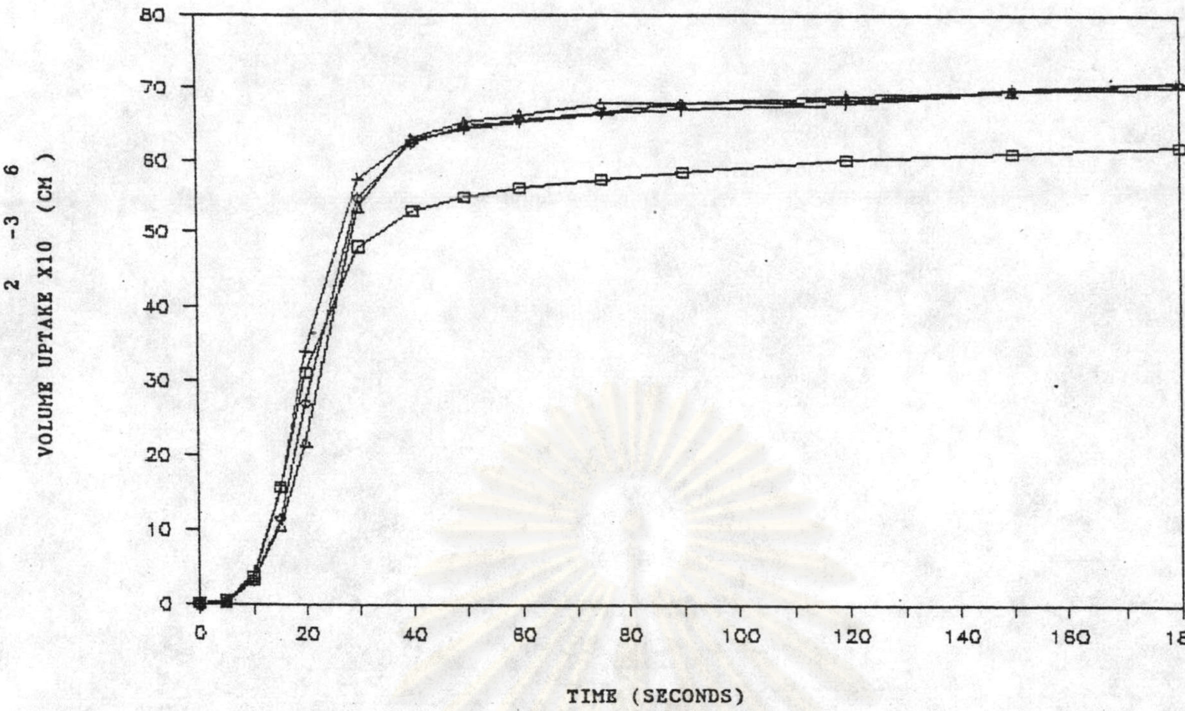

Figure 45 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

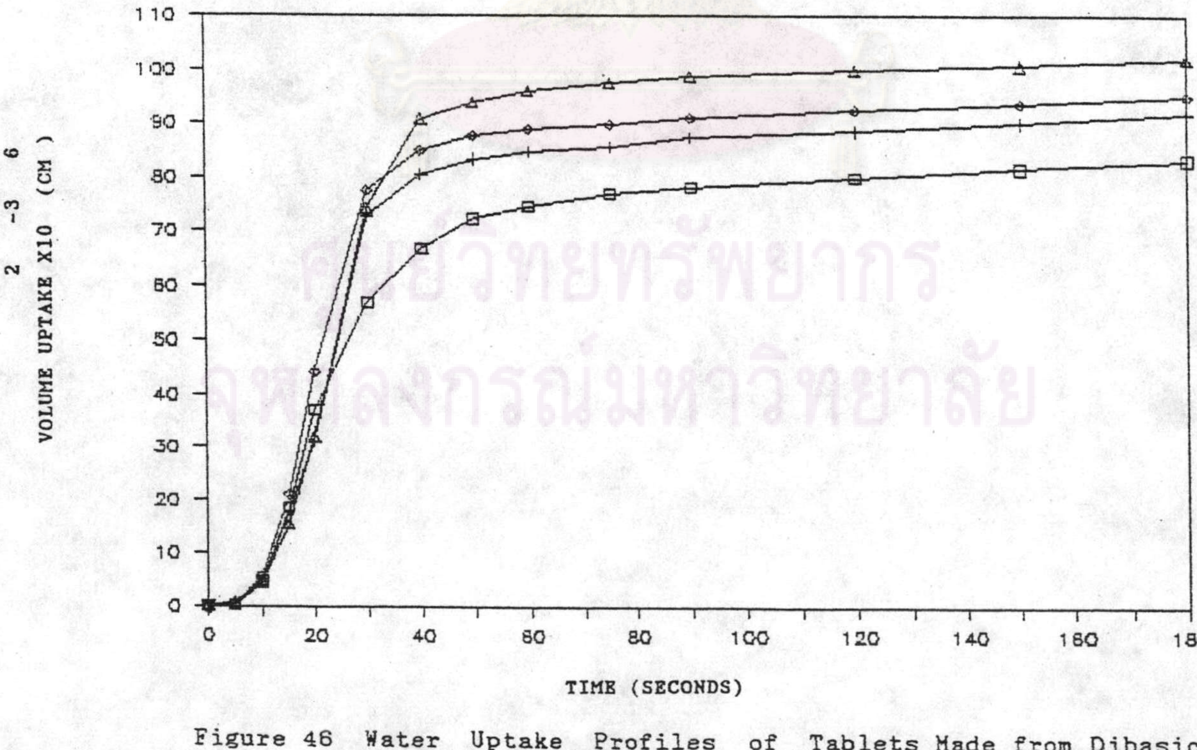

Figure 46 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

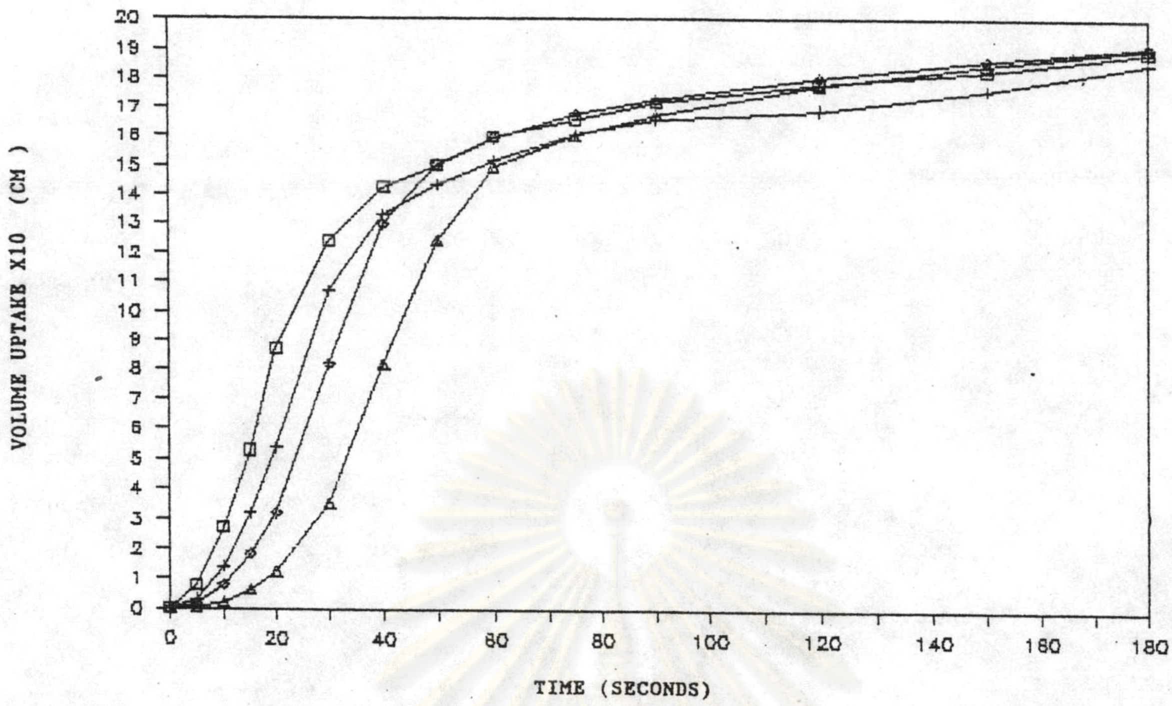

Figure 47 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

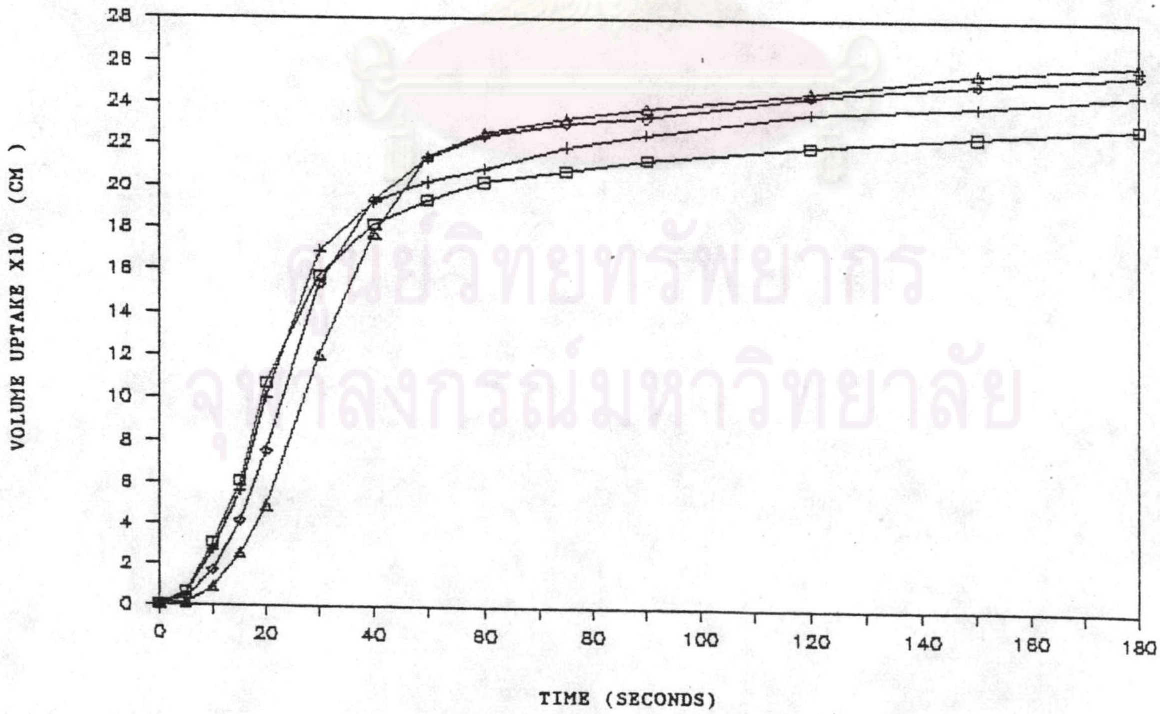

Figure 48 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

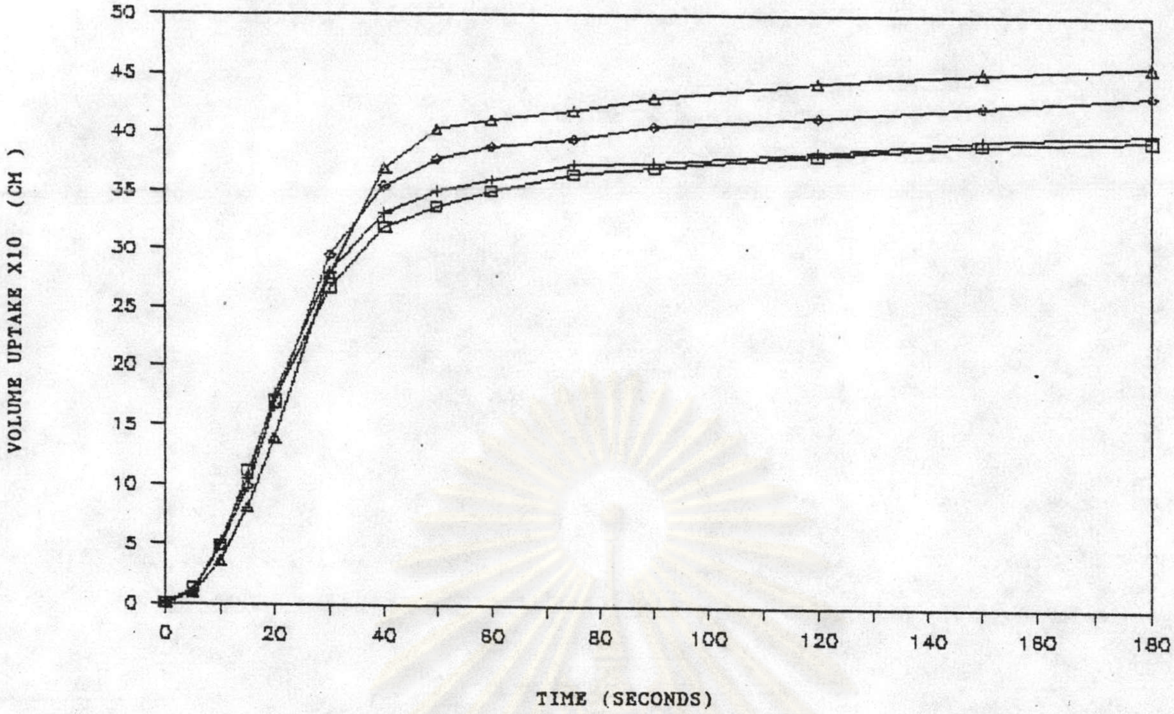

Figure 49 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

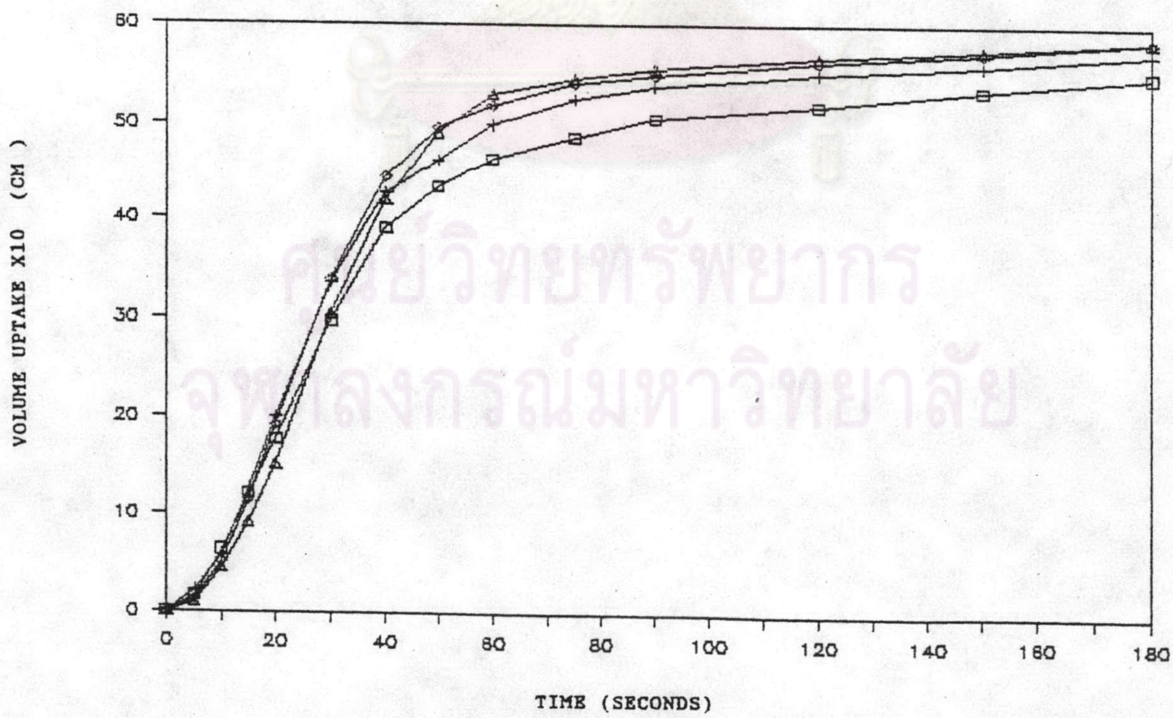

Figure 50 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of ECG 505$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

G. Explotab(R)

1. Water Insoluble Diluent

The influences of Explotab(R) on water uptake of directly compressed dibasic calcium phosphate dihydrate tablets at four compressional forces are illustrated in Figures 51-54. The rate of water uptake was not orderly related to the compressional force. It was noticed that the rate and extent of water uptake were sharply increased with increase in the amount of Explotab(R). The lag time became shorter when the amount of Explotab(R) increased.

2. Water Soluble Diluent

In the case of α-lactose monohydrate containing Explotab(R) directly compressed at various compressional forces, the profiles of water uptake were shown in Figures 55-58. At the concentrations of 0.5 and 1%, the rates of water uptake on the first 30 seconds were not affected by the compressional forces, but the rates of water uptake after 30 seconds appeared to increase in relation to the compressional forces. At the concentrations of 3 and 5%, the rates of water uptake increased as the compressional forces increased. The rate of water uptake increased in relation to the increase in concentration of Explotab(R) and the lag time was also reduced.

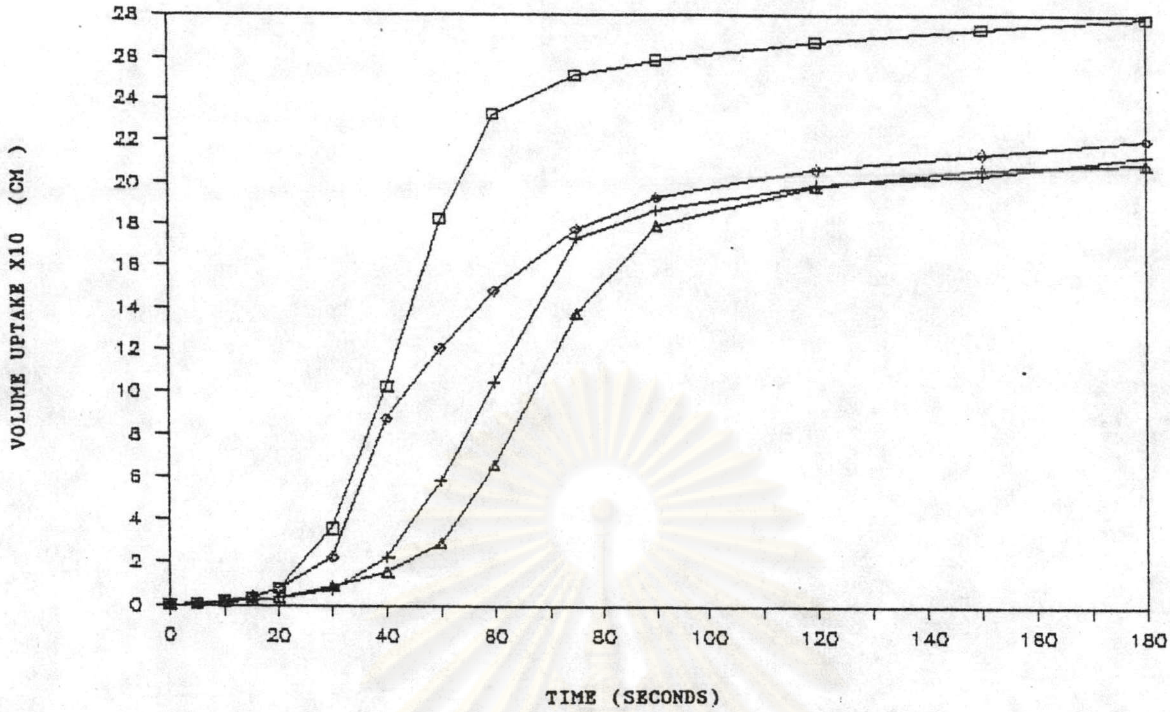

Figure 51 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

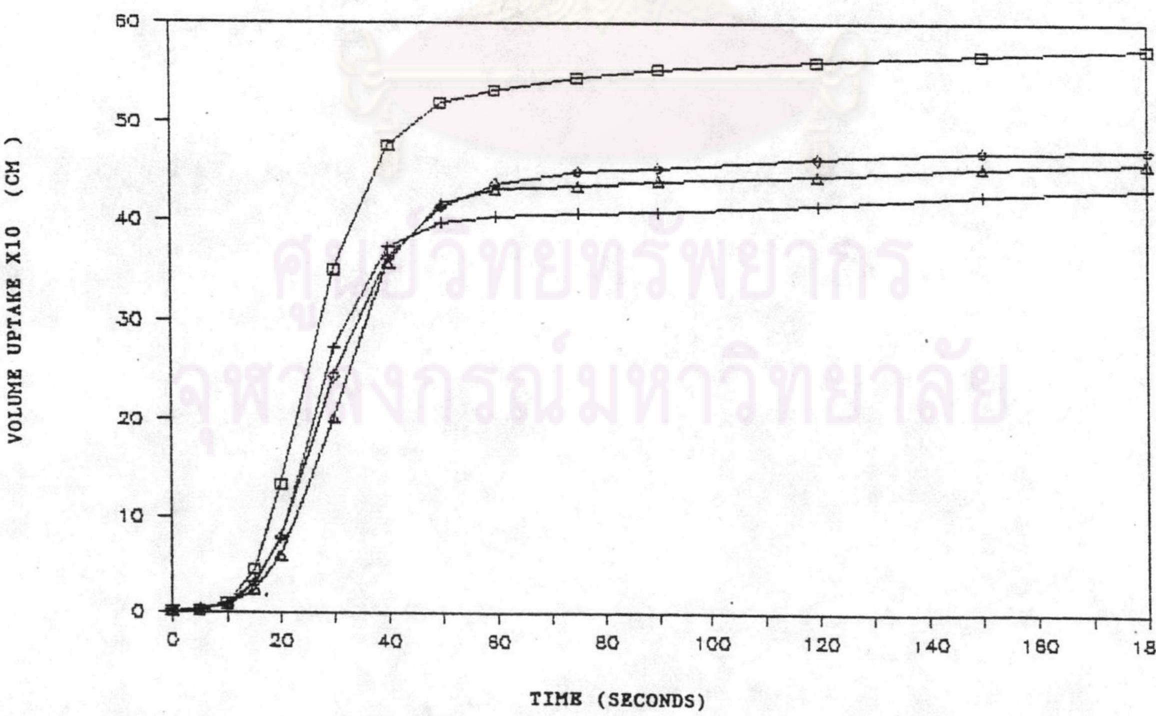

Figure 52 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

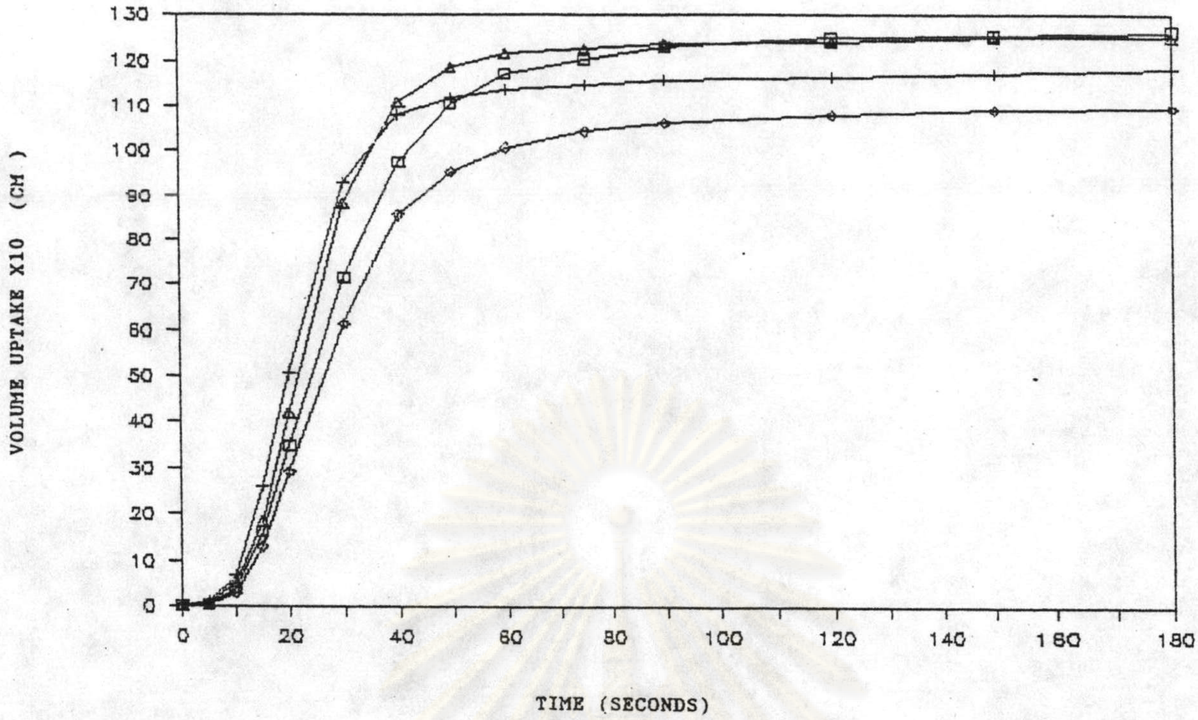

Figure 53 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of Explotab$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

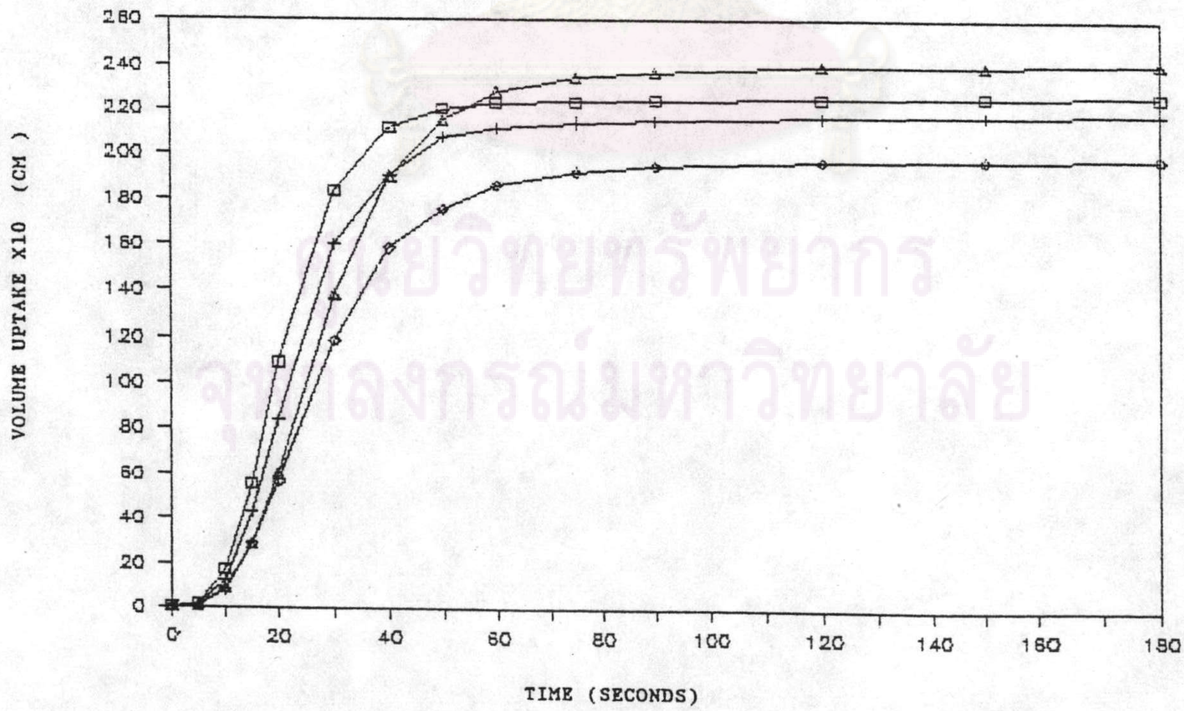

Figure 54 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of Explotab$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

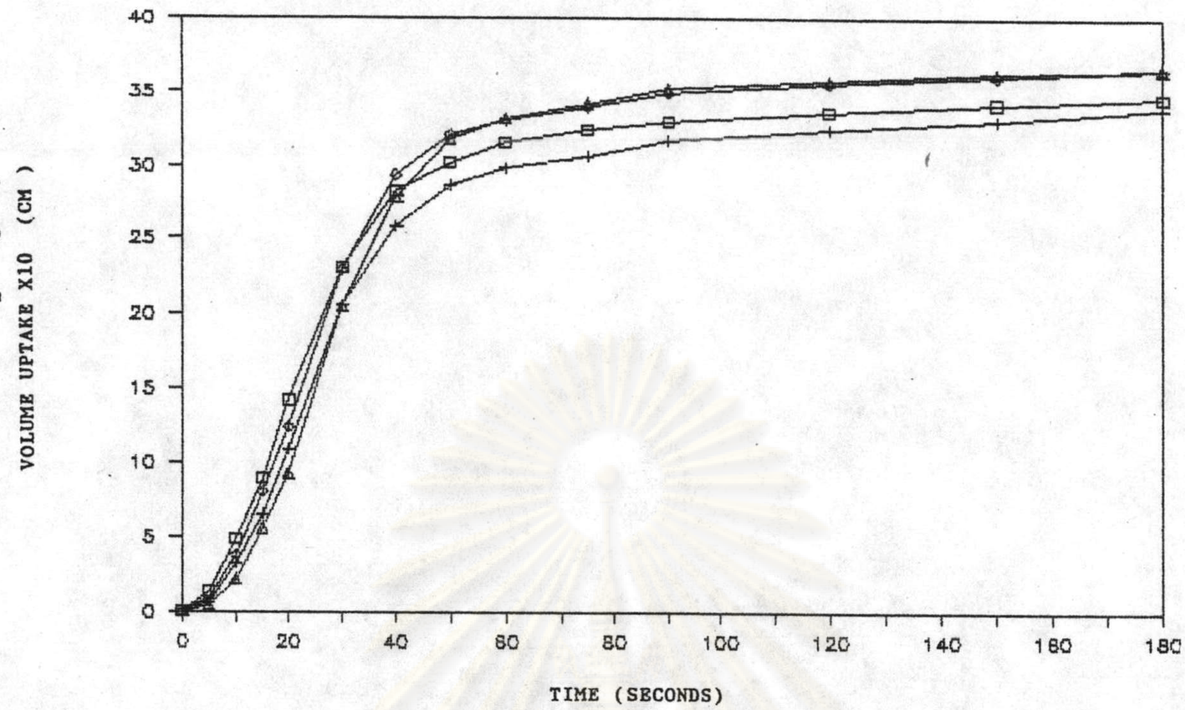

Figure 55 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

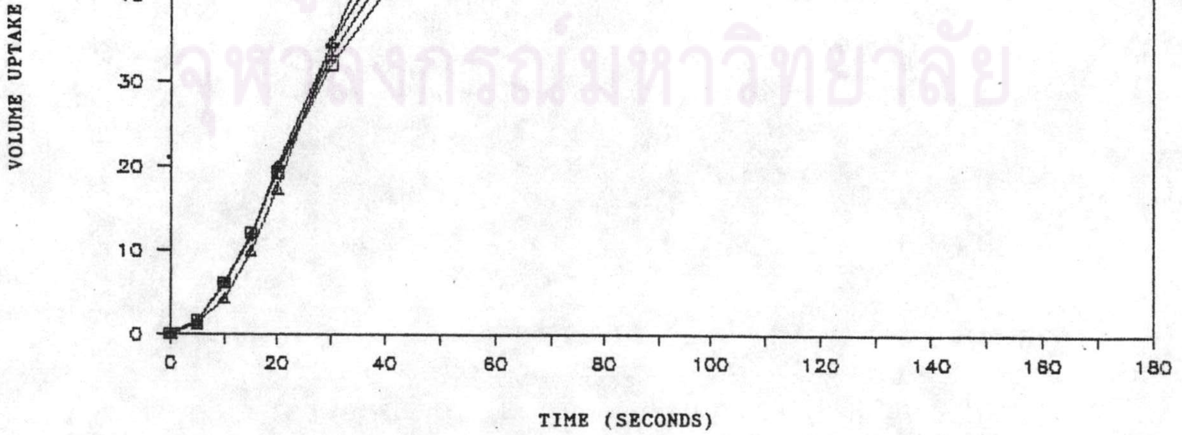

Figure 56 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

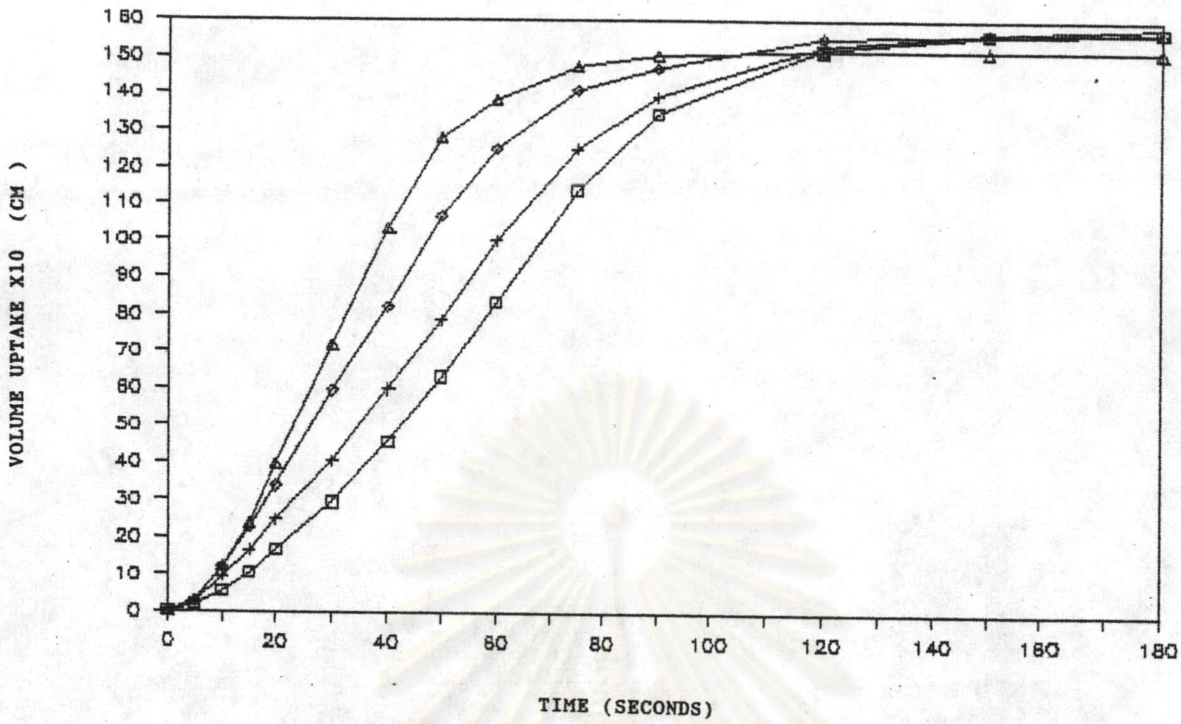

Figure 57 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

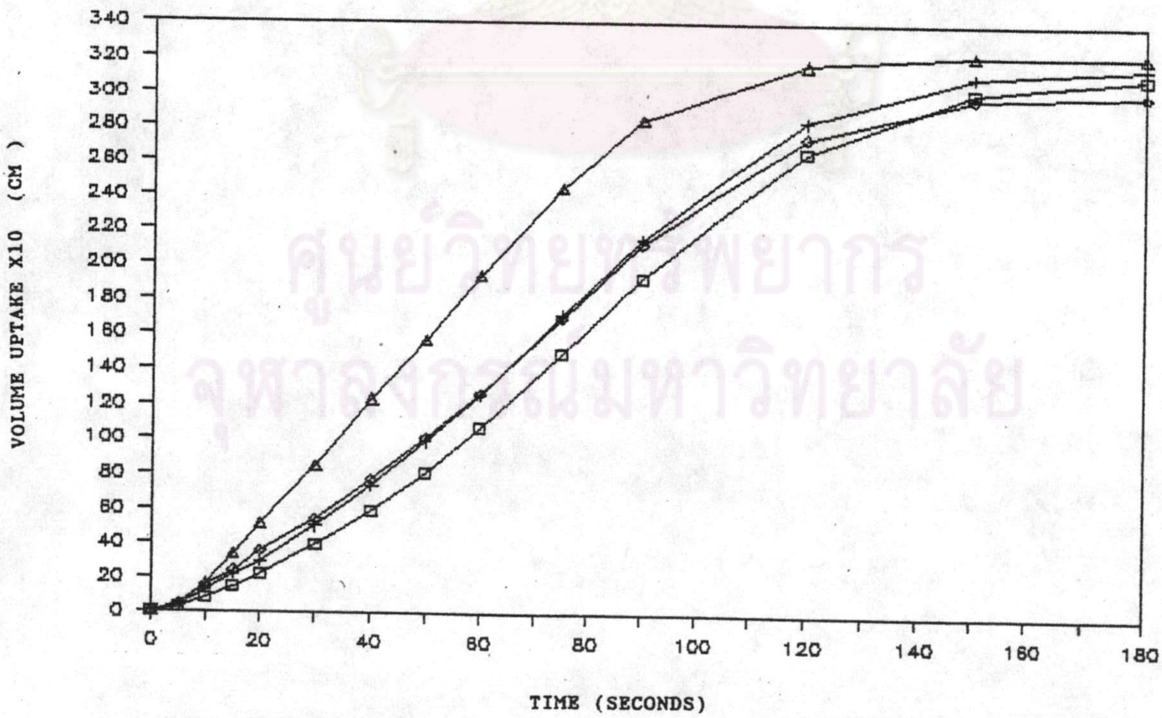

Figure 58 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of Explotab(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

H. Kollidon CL$^{(R)}$

1. Water Insoluble Diluent

The influences of Kollidon CL$^{(R)}$ on the water uptake into dibasic calcium phosphate dihydrate tablets directly compressed at various compressional forces are given in Figures 59-62. At 0.5% level, the tablets compressed at 1200 pounds exhibited the fastest rate of water uptake followed by the tablets compressed at 3000, 1800, 2400 pounds, respectively. For 1% level, the rate was contrary to the compressional force, but the water uptake of tablets containing 3 and 5% disintegrant seemed to be increased with the compressional force. An increase in the concentration of Kollidon CL$^{(R)}$ resulted in the increase of volume of water uptake. The lag time was also reduced as the concentration of Kollidon CL$^{(R)}$ was increased.

2. Water Soluble Diluent

The water uptake curves of α-lactose monohydrate compressible diluent containing Kollidon CL$^{(R)}$ directly compressed at four compressional forces were illustrated in Figures 63-66. At 0.5% level, the rate of water uptake decreased as the compressional force increased, but contrary results were observed at the concentration of 1%. However, at the concentrations of 3 and 5%, the rate did not depend on the compressional force. In comparing with the water insoluble system, the higher concentration of Kollidon CL$^{(R)}$ incorporated, the higher volume of water uptake was exhibited. The lag

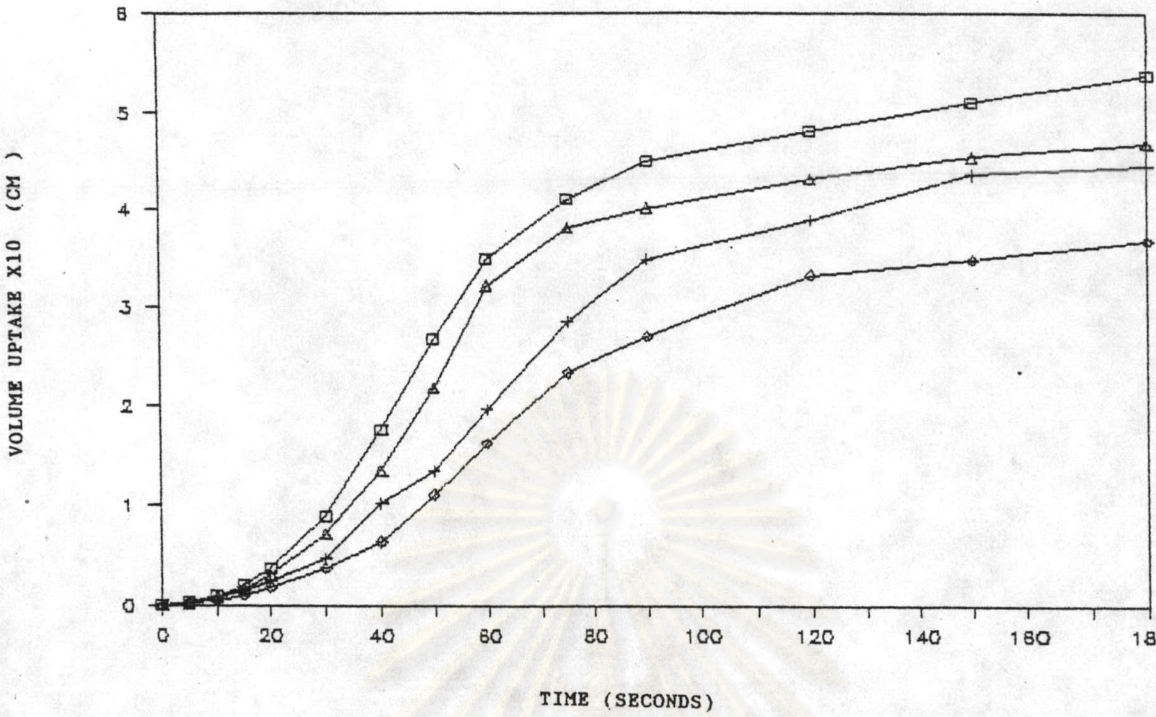

Figure 59 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

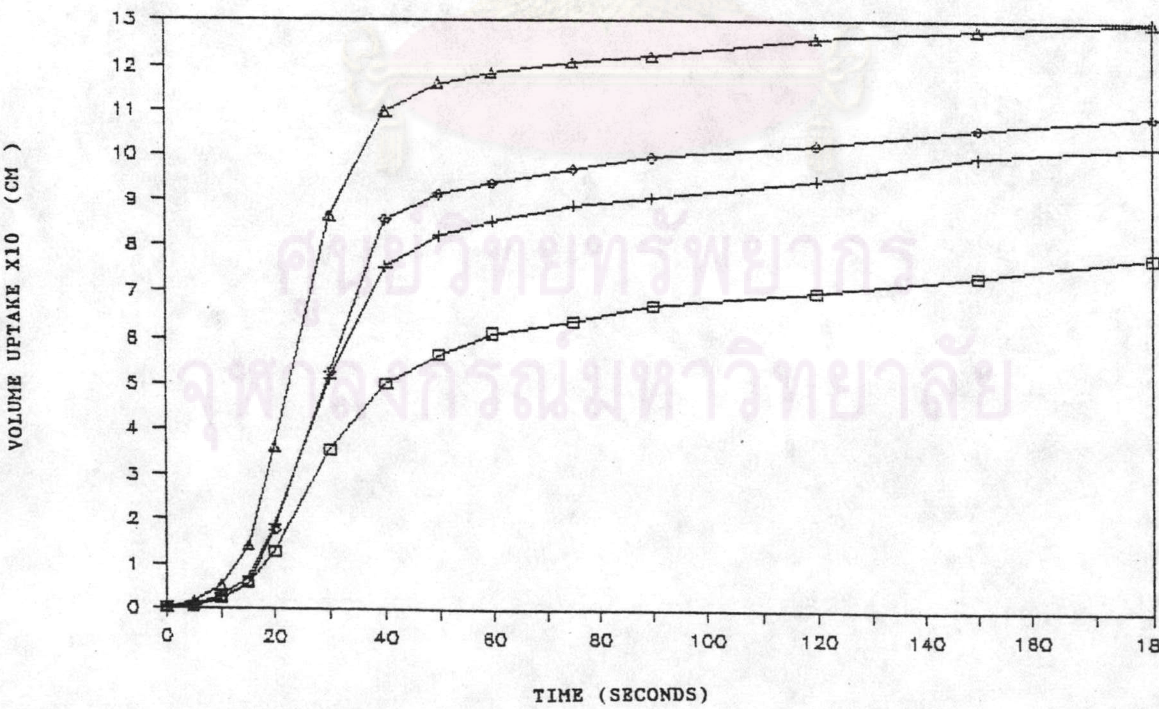

Figure 60 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

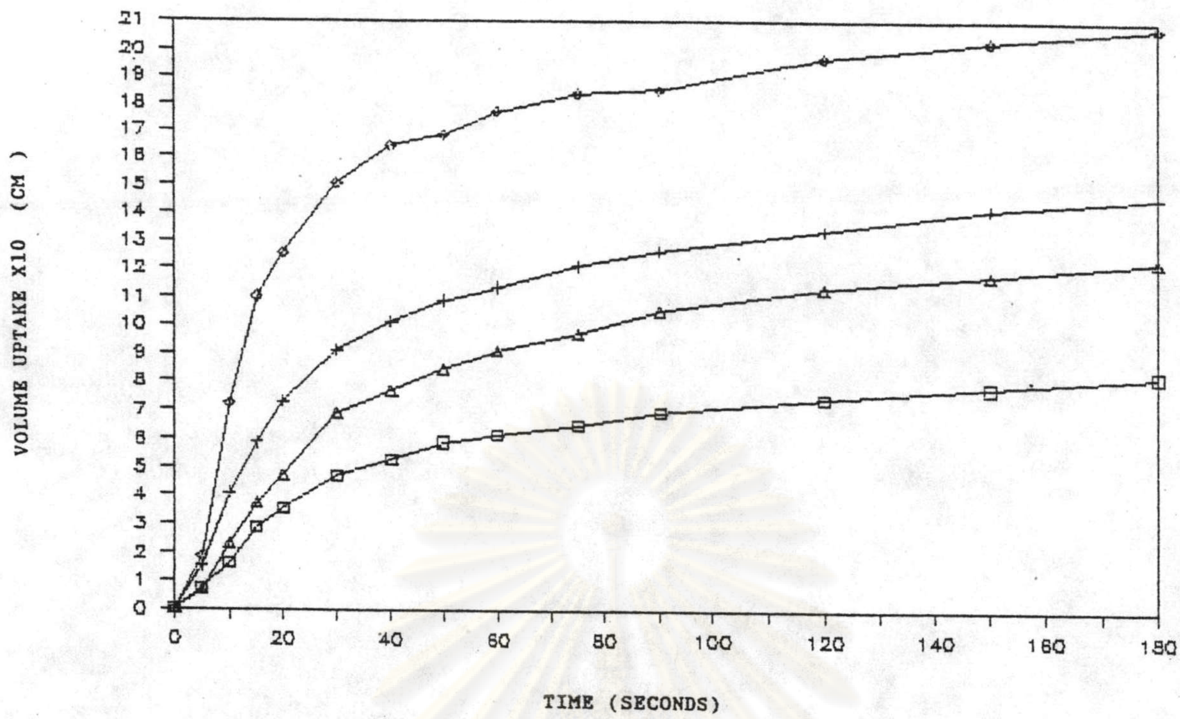

Figure 61 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

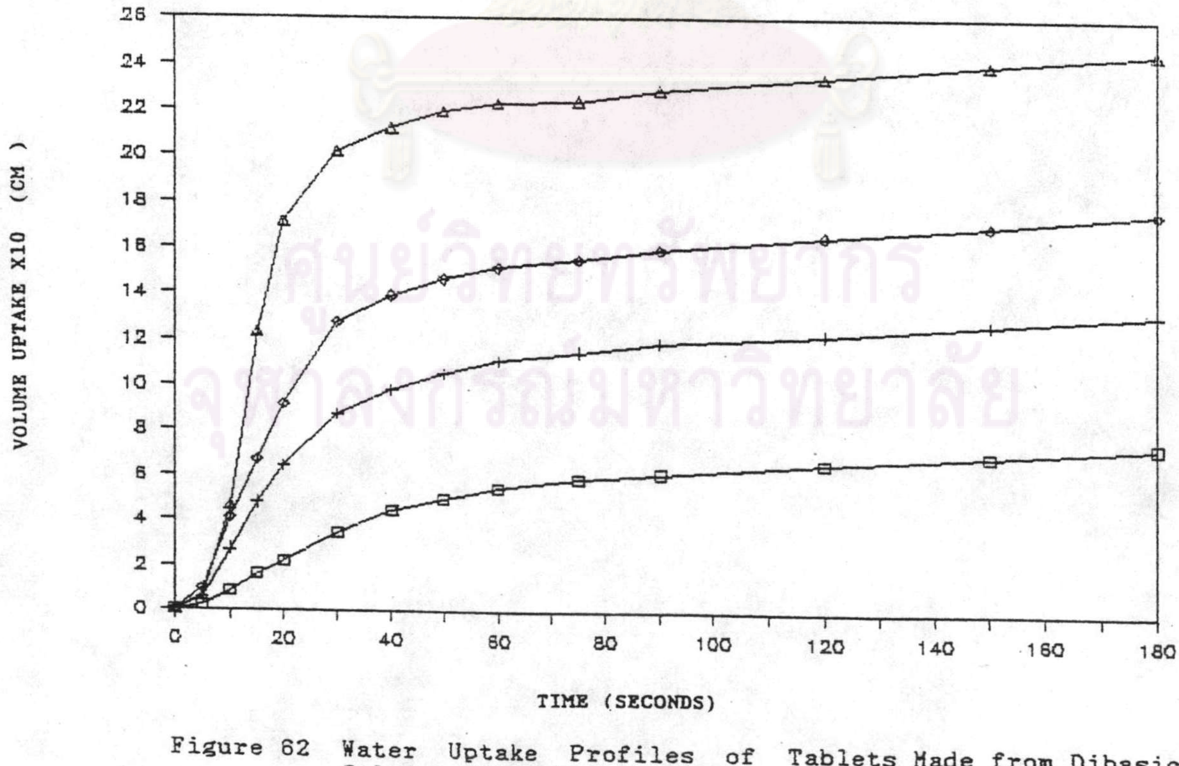

Figure 62 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

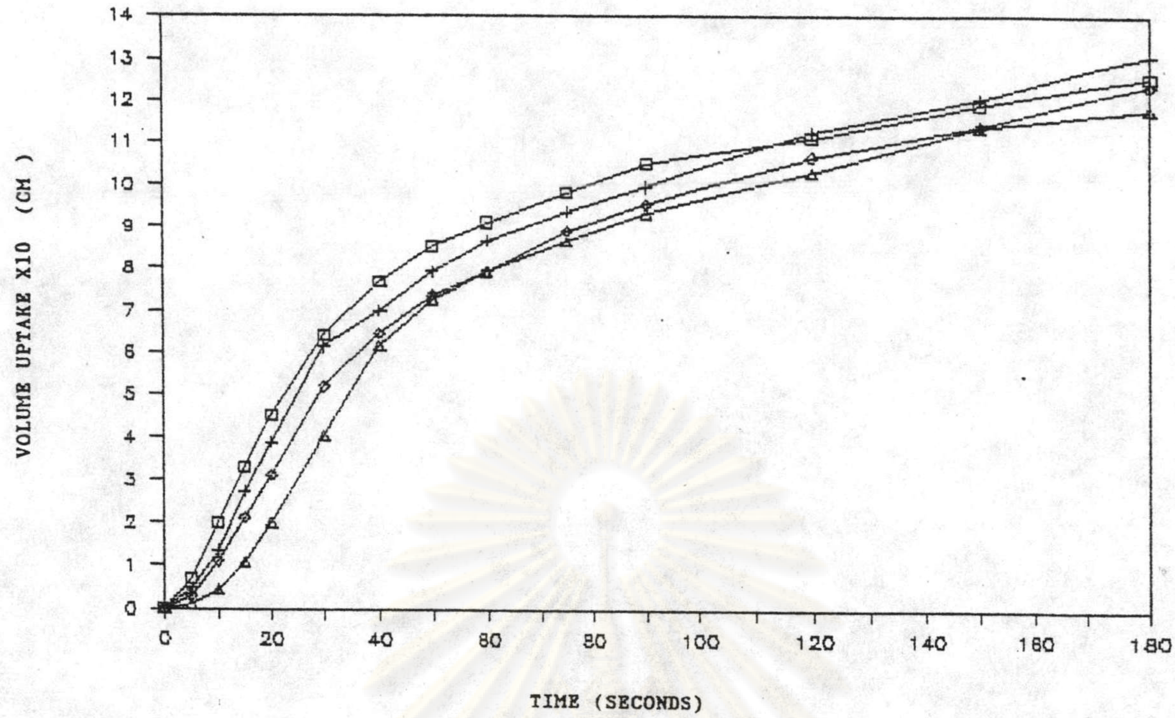

Figure 63 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

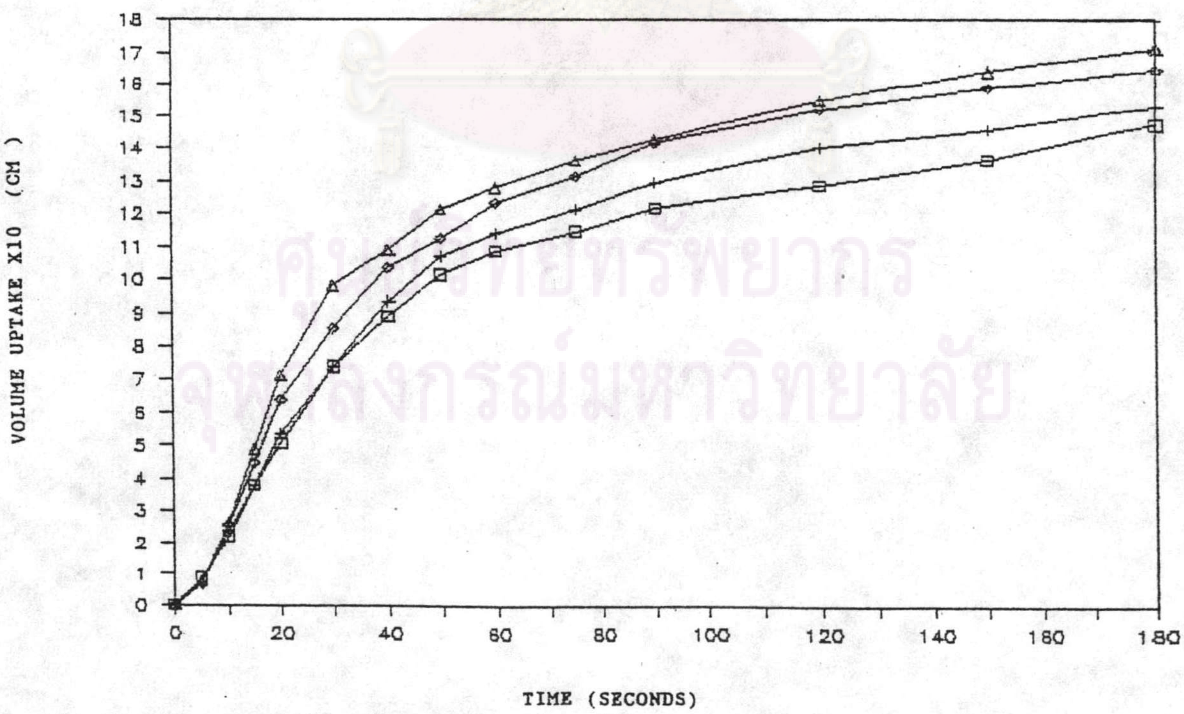

Figure 64 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of Kollidon CL(R) at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

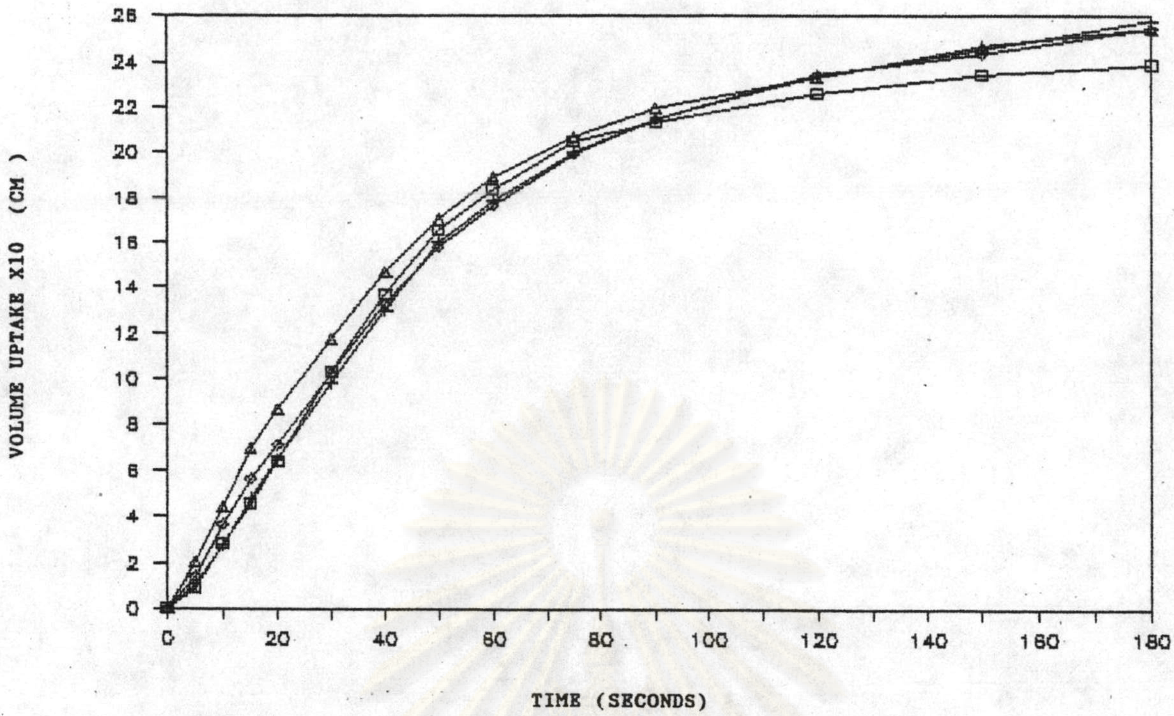

Figure 65 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of Kollidon CL$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

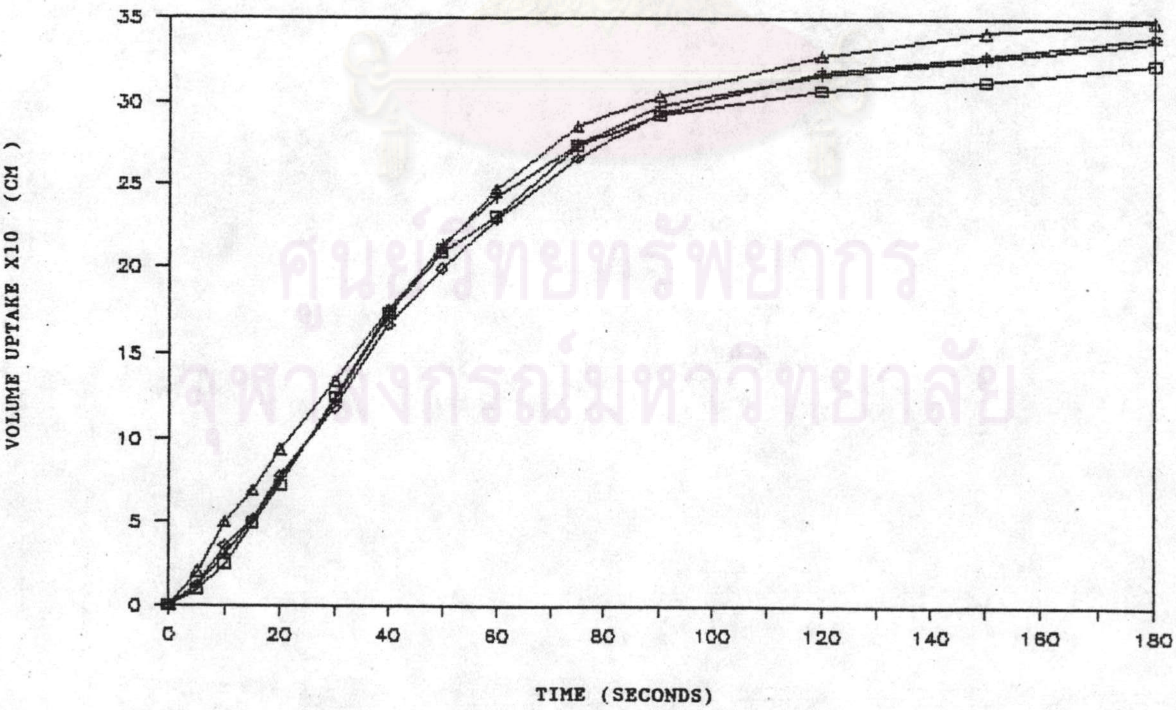

Figure 66 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of Kollidon CL$^{(R)}$ at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

time was also reduced with the increased concentration of Kollidon CL(R).

I. L-HPC

1. **Water Insoluble Diluent**

The influences of L-HPC on the water uptake into dibasic calcium phosphate dihydrate tablets directly compressed at various compressional forces were given in Figures 67-70. At 0.5 and 1% levels, the rates were increased with decreasing compressional forces while at the concentrations of 3 and 5%, the higher compressional forces caused increase in water uptake of the tablets. Incorporation of higher concentration of L-HPC into dibasic calcium phosphate dihydrate tablets showed greater effect on water uptake and reduction in lag time.

2. **Water Soluble Diluent**

For α-lactose monohydrate system with L-HPC, the water uptake curves of tablets are given in Figures 71-74. Generally, it seemed that water uptake was directly related to compressional force except at 0.5% level. As concentration of L-HPC increased, the rates of water uptake at all compressional forces were greatly increased and the lag time of tablets were reduced.

6. **Disintegration Time of Tablets**

The results of disintegration time of tablets containing various concentrations of disintegrants at different compressional forces are illustrated in Tables 7,8

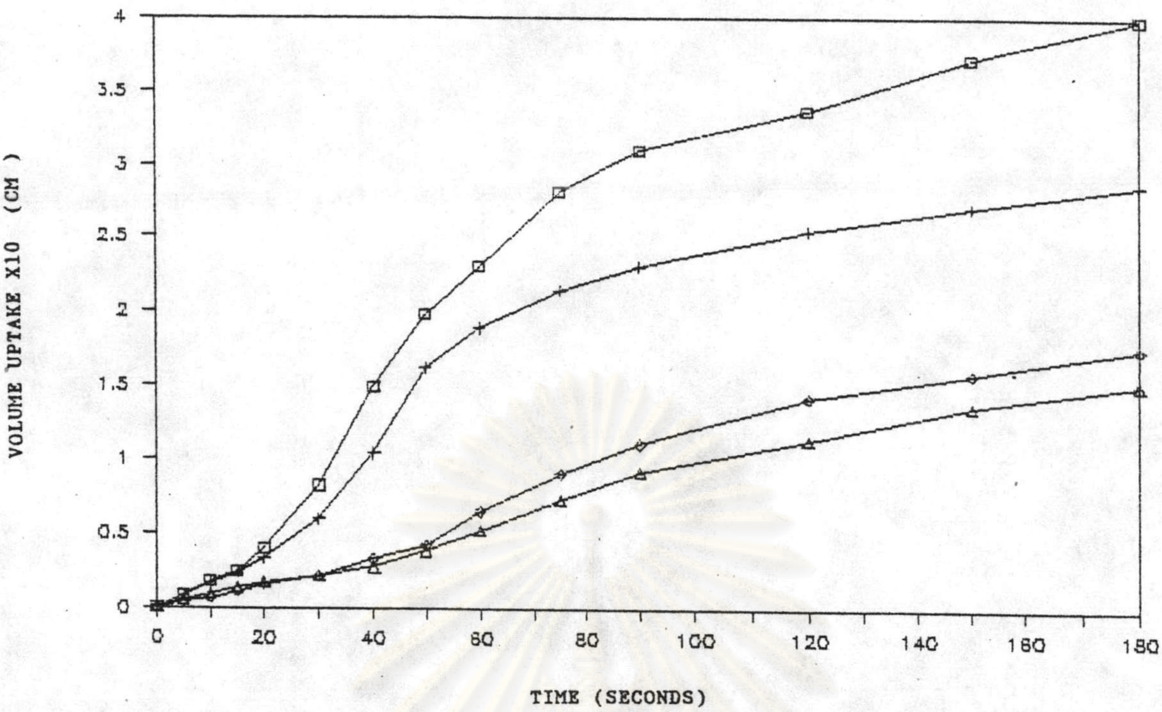

Figure 67 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 0.5% of L-HPC at Different Compressional Forces.
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

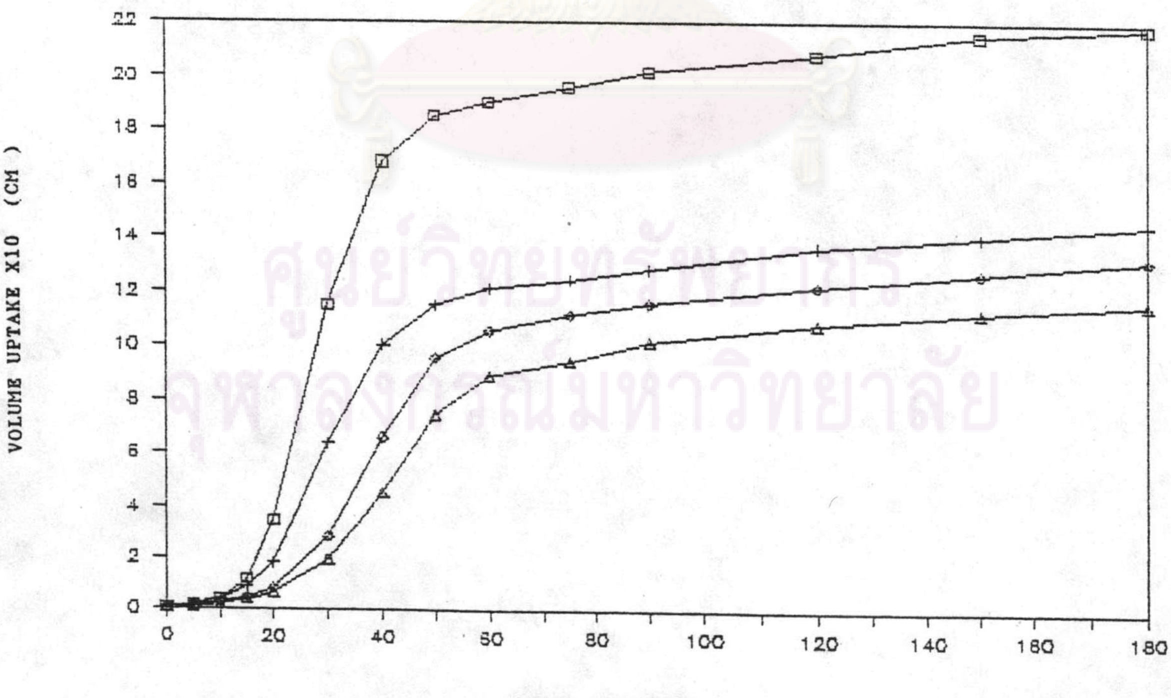

Figure 68 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 1% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

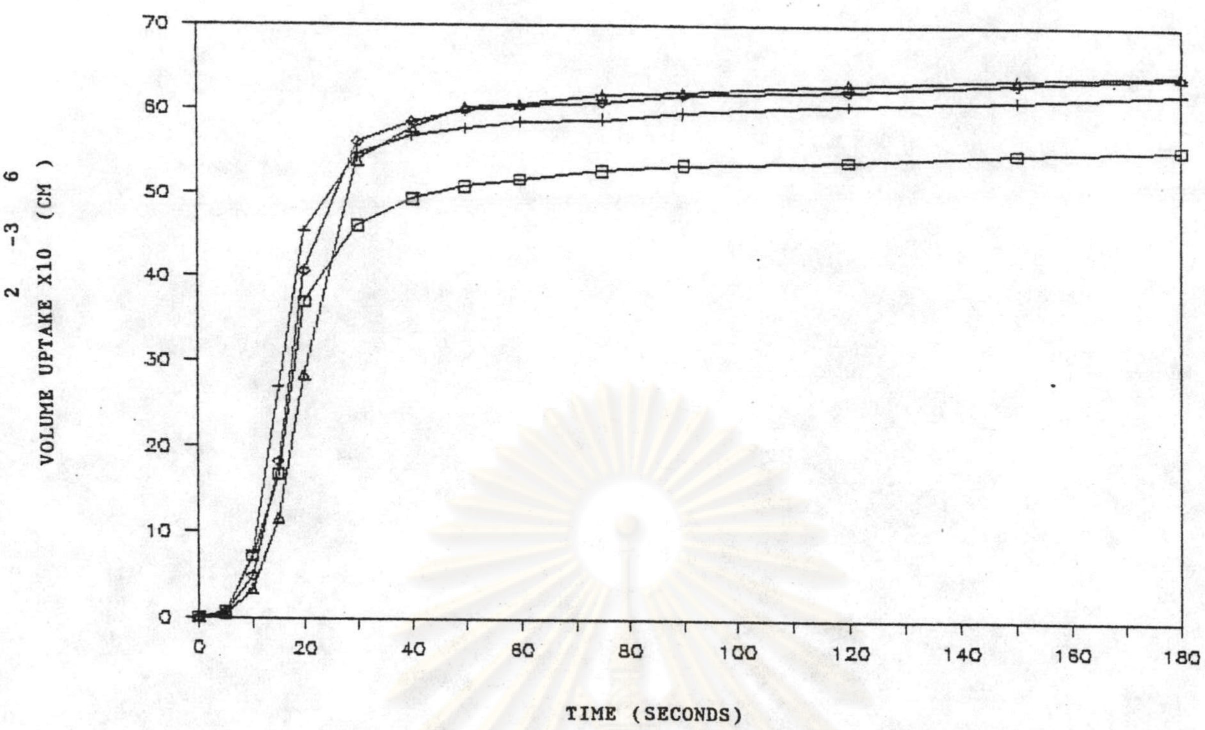

Figure 69 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 3% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

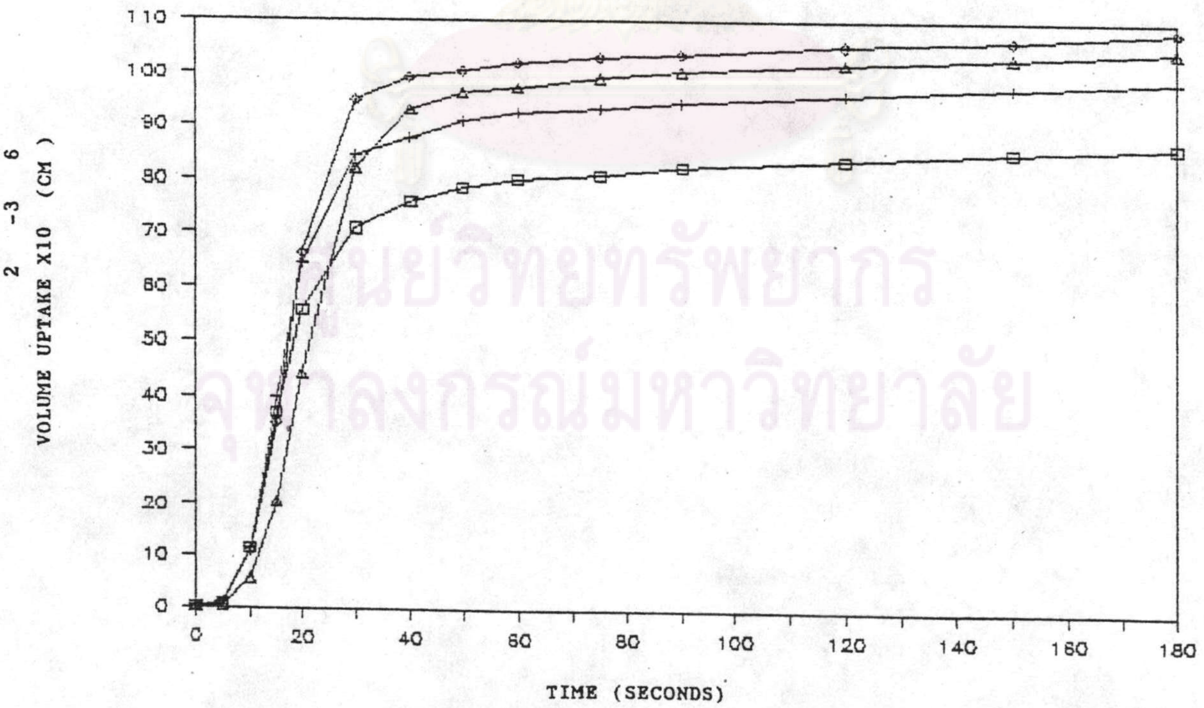

Figure 70 Water Uptake Profiles of Tablets Made from Dibasic Calcium Phosphate Dihydrate with 5% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

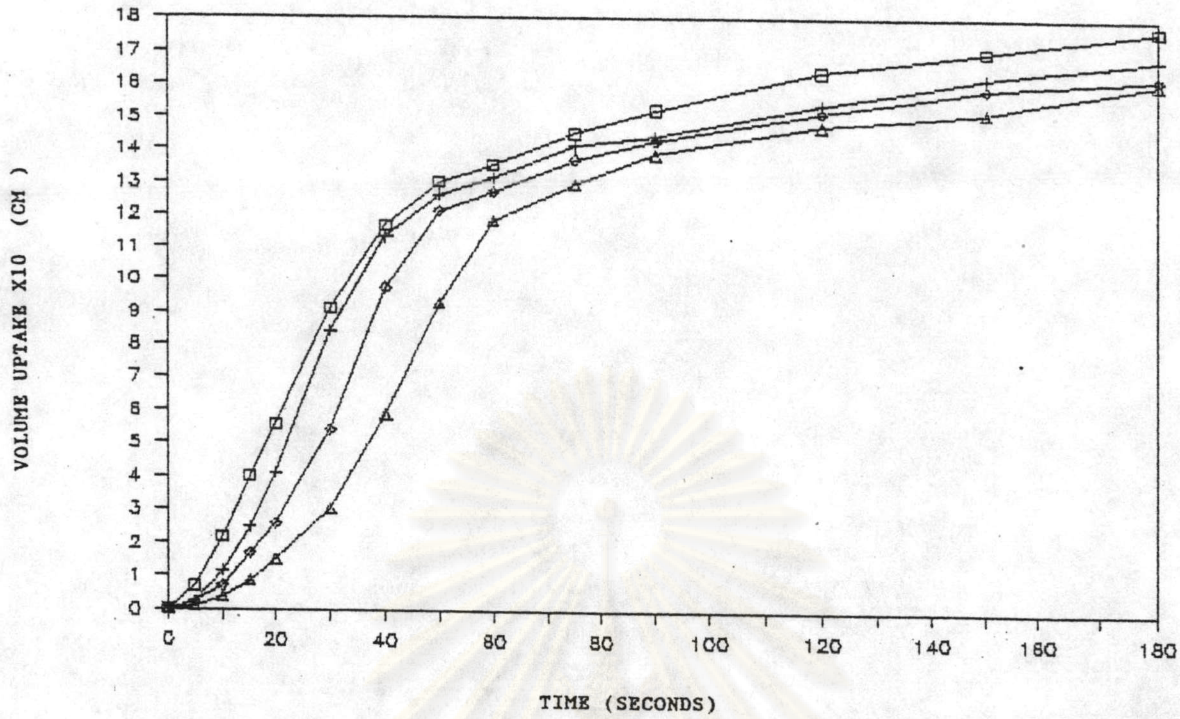

Figure 71 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 0.5% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

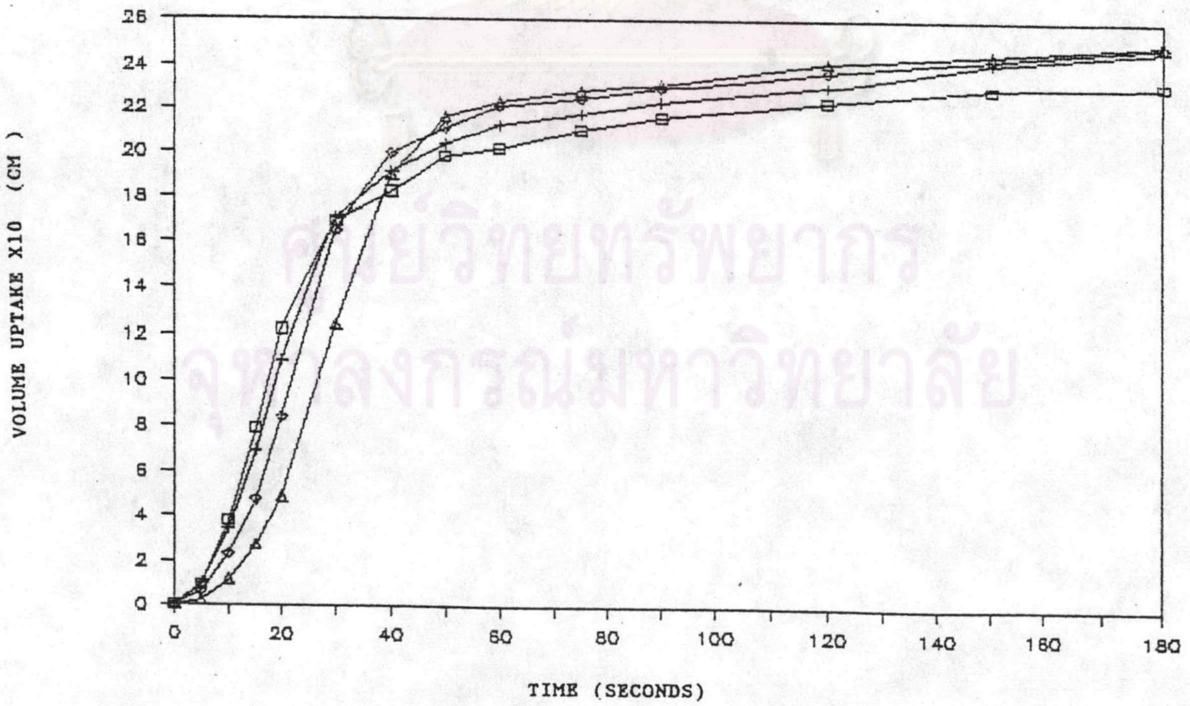

Figure 72 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 1% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

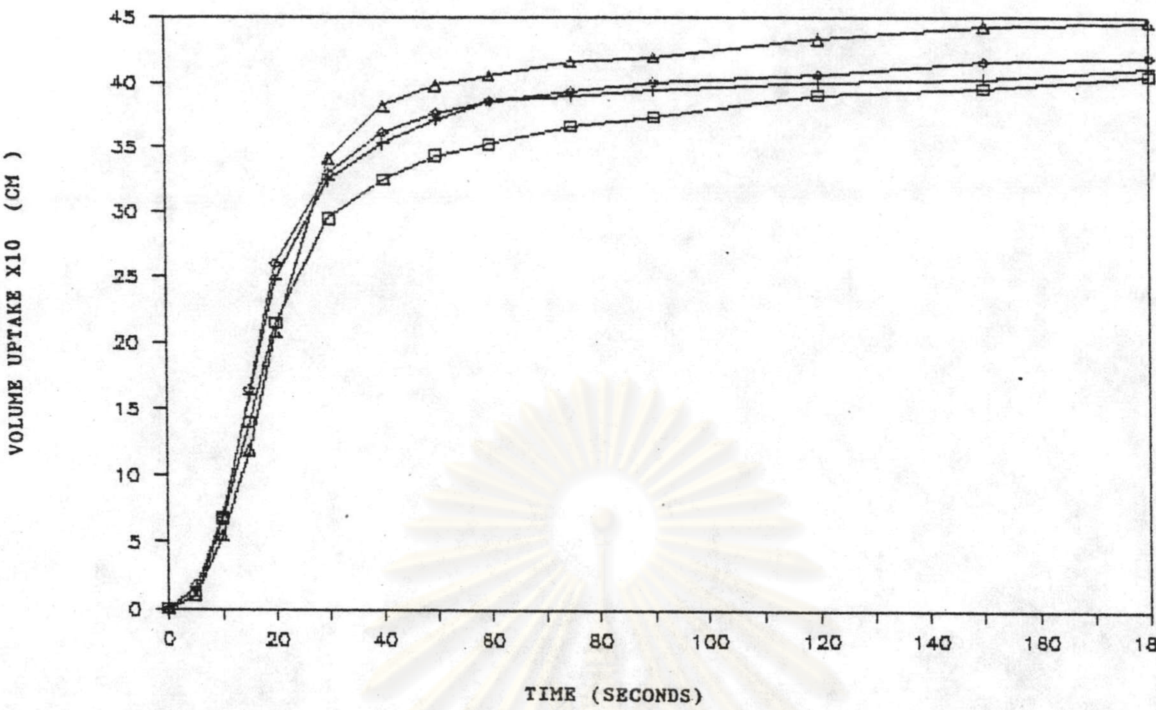

Figure 73 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 3% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

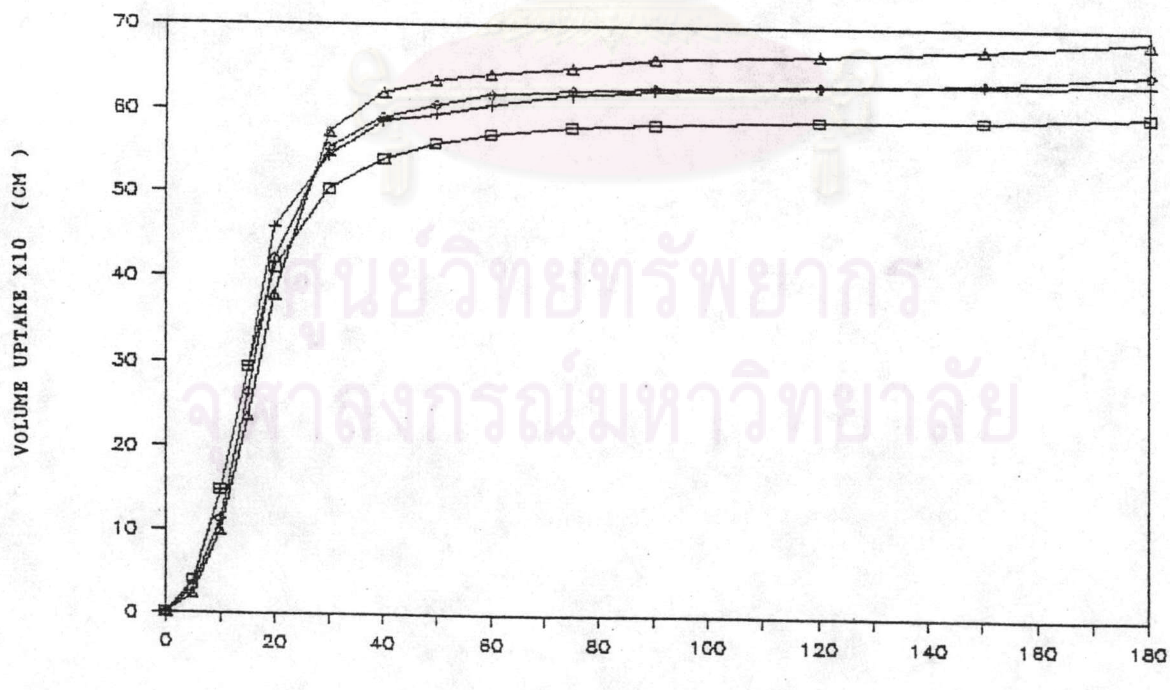

Figure 74 Water Uptake Profiles of Tablets Made from α-Lactose Monohydrate with 5% of L-HPC at Different Compressional Forces
(Key : □ 1200 lb, + 1800 lb, ◇ 2400 lb, △ 3000 lb)

Table 7 Disintegration Time of Dibasic Calcium Phosphate Dihydrate Tablets with Different Disintegrants at Various Compression Pressures

Disintegrant	Concentration (% w/w)	Disintegration Time (min) (S.D.) Compression Pressure (lb) 1200	1800	2400	3000
Blank	-	> 30	> 30	> 30	> 30
S_1	0.5	3.78(0.73)	11.62(2.38)	12.59(3.17)	13.69(1.26)
	1.0	1.30(0.08)	1.40(0.09)	1.61(0.15)	1.70(0.18)
	3.0	1.03(0.12)	1.09(0.06)	1.16(0.08)	1.20(0.07)
	5.0	2.65(0.12)	3.09(0.17)	3.14(0.10)	3.18(0.18)
S_2	0.5	1.23(0.18)	1.46(0.12)	1.52(0.17)	2.78(0.52)
	1.0	1.06(0.04)	1.21(0.04)	1.37(0.05)	1.61(0.05)
	3.0	1.01(0.03)	1.07(0.05)	1.30(0.05)	1.37(0.04)
	5.0	5.61(0.71)	5.15(0.39)	6.85(0.24)	8.69(1.86)
Ac-Di-Sol®	0.5	0.18(0.004)	0.24(0.004)	0.26(0.01)	0.32(0.03)
	1.0	0.11(0.01)	0.12(0.002)	0.14(0.003)	0.17(0.006)
	3.0	0.07(0.006)	0.08(0)	0.08(0.004)	0.1(0)
	5.0	0.08(0)	0.08(0)	0.09(0.01)	0.1(0)
Corn Starch	0.5	> 30	> 30	> 30	> 30
	1.0	> 30	> 30	> 30	> 30
	3.0	1.07(0.08)	1.45(0.13)	2.35(0.20)	2.60(0.24)
	5.0	0.52(0.10)	0.58(0.07)	0.64(0.03)	0.74(0.12)
ECG 505®	0.5	0.45(0.05)	0.62(0.08)	0.72(0.06)	0.93(0.12)
	1.0	0.22(0.08)	0.27(0.005)	0.27(0.005)	0.33(0.04)
	3.0	0.12(0.004)	0.14(0.004)	0.15(0.004)	0.18(0)
	5.0	0.13(0)	0.13(0)	0.15(0)	0.18(0)
Explotab®	0.5	1.04(0.07)	1.45(0.25)	1.96(0.15)	2.40(0.23)
	1.0	0.24(0.06)	0.32(0.006)	0.33(0.03)	0.44(0.08)
	3.0	0.15(0)	0.17(0.004)	0.15(0.006)	0.15(0.006)
	5.0	0.14(0.004)	0.15(0.02)	0.14(0.02)	0.14(0.01)
Kollidon CL®	0.5	0.65(0.05)	0.86(0.11)	1.72(0.21)	2.66(0.22)
	1.0	0.25(0.04)	0.31(0.04)	0.38(0.09)	0.45(0.03)
	3.0	0.12(0)	0.12(0.004)	0.13(0)	0.14(0.004)
	5.0	0.1(0)	0.1(0)	0.1(0)	0.11(0.004)
L-HPC	0.5	4.51(0.72)	12.45(0.64)	15.87(1.52)	> 30
	1.0	0.29(0.09)	0.73(0.11)	0.95(0.12)	1.22(0.09)
	3.0	0.16(0.01)	0.16(0)	0.18(0.004)	0.24(0.004)
	5.0	0.14(0.005)	0.16(0.01)	0.2(0)	0.23(0.005)

Table 8 Disintegration Time of α-Lactose Monohydrate Tablets with Different Disintegrants at Various Compression Pressures

Disintegrant	Concentration (% w/w)	Disintegration Time (min) (S.D.) Compression Pressure (lb)			
		1200	1800	2400	3000
Blank	-	1.50(0.07)	2.00(0.08)	3.14(0.19)	3.79(0.27)
S_1	0.5	1.37(0.06)	1.11(0.05)	1.09(0.03)	1.10(0.05)
	1.0	2.71(0.10)	3.04(0.12)	2.79(0.09)	2.84(0.14)
	3.0	7.82(0.16)	8.25(0.15)	6.51(0.18)	6.09(0.21)
	5.0	9.23(0.20)	9.85(0.18)	14.46(0.16)	15.37(0.17)
S_2	0.5	1.11(0.06)	1.15(0.09)	1.03(0.07)	0.87(0.06)
	1.0	1.32(0.08)	1.46(0.08)	1.54(0.09)	1.62(0.10)
	3.0	4.56(0.10)	3.94(0.12)	3.86(0.08)	3.59(0.09)
	5.0	13.79(0.11)	15.94(0.23)	15.90(0.24)	16.10(0.27)
Ac-Di-Sol(R)	0.5	0.67(0.03)	0.62(0.04)	0.59(0.03)	0.45(0.03)
	1.0	0.75(0.03)	0.69(0.03)	0.65(0.04)	0.64(0.03)
	3.0	1.23(0.16)	1.09(0.18)	0.97(0.10)	0.83(0.11)
	5.0	1.43(0.21)	1.25(0.15)	1.15(0.14)	1.18(0.12)
Corn Starch	0.5	0.71(0.02)	0.96(0.03)	1.08(0.05)	1.18(0.07)
	1.0	0.89(0.03)	0.99(0.04)	1.06(0.05)	1.06(0.05))
	3.0	1.0(0.03)	0.94(0.03)	0.99(0.04)	0.93(0.04)
	5.0	0.96(0.05)	0.96(0.05)	0.97(0.04)	0.97(0.04)
ECG 505(R)	0.5	0.59(0.04)	0.52(0.05)	0.54(0.04)	0.49(0.03)
	1.0	0.70(0.04)	0.65(0.03)	0.54(0.05)	0.49(0.06)
	3.0	0.62(0.05)	0.55(0.06)	0.61(0.07)	0.61(0.06)
	5.0	0.71(0.04)	0.73(0.05)	0.75(0.05)	0.76(0.06)
Explotab(R)	0.5	0.80(0.04)	0.72(0.05)	0.64(0.04)	0.56(0.05)
	1.0	0.72(0.05)	0.70(0.05)	0.66(0.06)	0.54(0.05)
	3.0	0.69(0.06)	0.67(0.05)	0.59(0.04)	0.69(0.03))
	5.0	0.77(0.04)	0.74(0.04)	0.64(0.05)	0.64(0.06)
Kollidon CL(R)	0.5	0.95(0.05)	0.74(0.04)	0.69(0.06)	0.60(0.05)
	1.0	0.93(0.05)	0.88(0.06)	0.78(0.06)	0.67(0.03)
	3.0	0.94(0.03)	0.89(0.04)	0.88(0.03)	0.78(0.03)
	5.0	0.94(0.04)	0.92(0.05)	0.78(0.06)	0.79(0.03)
L-HPC	0.5	0.61(0.04)	0.53(0.03)	0.50(0.04)	0.51(0.03)
	1.0	0.67(0.04)	0.68(0.05)	0.49(0.05)	0.49(0.04)
	3.0	0.65(0.03)	0.58(0.06)	0.61(0.05)	0.56((0.04)
	5.0	0.62(0.04)	0.64(0.04)	0.62(0.04)	0.58(0.05)

for dibasic calcium phosphate dihydrate system and for α-lactose monohydrate system, respectively.

6.1 Effect of Disintegrants on Disintegration Time of Dibasic Calcium Phosphate Dihydrate Tablet System

Disintegration time of the blank tablet wihout disintegrant was more than 30 minutes while all formulations containing various disintegrants were disintegrated with 6 seconds to 15 minutes except some disintegrants at low concentration gave disintegration time of tablets more than 30 minutes. This could be clearly seen that dibasic calcium phosphate dihydrate did not exhibit any disintegration property.

The disintegration time of tablets containing S_1 and S_2 decreased with increasing concentration of disintegrants until optimum concentration was reached at 3% level which showed the minimum disintegration time. Disintegration time of tablet was increased at the concentration of 5% .

Ac-Di-Sol$^{(R)}$ gave disintegration time of tablet less than 20 seconds at all concentrations and compressional forces. Corn starch when added at the concentrations of 0.5 and 1% was unable to make the tablets disintegrate within 30 minutes at all compressional forces. Higher concentration of corn starch resulted in shorter disintegration time.

Both concentration of ECG 505(R) and compressional force gave slightly influnce on the disintegration time, especially at the concentrations of 3 and 5% . At 0.5 and 1% concentrations of Explotab(R), slight increase in disintegration time were obtained as the compressional forces increased. However, no differences in disintegration time were noted when 3 and 5% levels of Explotab(R) incorporated in the tablets.

At 0.5 and 1% levels of Kollidon CL(R), the disintegration time of tablets were found within 170 seconds and 28 seconds, respectively. An increase of compressional force caused little effect on disintegration time of tablets containing Kollidon CL(R)at 0.5 and 1%. Disintegration time of tablets were unaffected by the increase in compressional force at concentrations from 3 to 5%. For tablets containing L-HPC as disintegrant at 0.5% level, the time of disintegration was clearly shown dependence on compression force. At the concentrations of 3 and 5%, the tablet disintegrations were rather short at all compressional forces.

6.2 Effect of Disintegrants on Disintegration Time of α-Lactose Monohydrate Tablet System

Disintegration time of the control formulation and formulations containing various disintegrants at different compressional forces were quite different from disintegrating properties of dibasic calcium phosphate dihydrate system.

For formulation without disintegrant, the increasing compressional force resulted in increasing disintegration time. Tablets using S_1 and S_2 as disintegrants exhibited longer disintegration time when concentration of disintegrants increased. Although Ac-Di-Sol(R) gave rapid disintegration time of tablets, the time of disintegration slightly increased when the concentration of disintegrant increased. The disintegration time of this disintegrant did not depend on the compressional force. For corn starch, both concentration and compressional force did not affect the disintegration time of tablets, all tablet formulations showed disintegration time not more than 75 seconds. Both the compressional force and concentration appeared to exert no effect on the disintegration time of tablets containing ECG 505(R), Explotab(R), Kollidon CL(R) and L-HPC.

The Evaluation of Hydrochlorothiazide Tablets

The tablets composed of hydrochlorothiazide and S_2 prepared by direct compression method using dibasic calcium phosphate dihydrate and α-lactose monohydrate as vehicles were evaluated for their physical properties as follows : weight variation, thickness, hardness, friability, disintegration time, content uniformity, percent labeled amount and dissolution. The results were presented in Tables 9,10 and Figures 75,76.

Table 9 Physical Properties of Hydrochlorothiazide Tablets with S_2 in Various Diluents

Physical Properties of Tablets	Types of HCTZ Tablets			
	$E-S_2-2^a$	$E-S_2-3^b$	$T-S_2-0^c$	$T-S_2-0.5^d$
Weight	349.52	350.41	349.68	351.67
S.D.	1.03	2.86	3.22	1.26
R.S.D.	0.29	0.82	0.92	0.36
Thickness	2.598	2.606	3.473	3.517
S.D.	0.006	0.010	0.018	0.005
Hardness	6.52	6.48	5.91	6.27
S.D.	0.33	0.23	0.29	0.33
Friability(%)	0.73	0.74	0.89	0.60
D.T.(sec)	54.51	73.67	931.0	43.0
Range	52-57	71-78	885-977	41-46

a = Emcompress(R) + 2% S_2 b = Emcompress(R) + 3% S_2

c = Tablettose(R) + 0% S_2 d = Tablettose(R) + 0.5% S_2

Table 10 Content Uniformity and Percent Labeled Amount of Hydrochlorothiazide Tablets with S_2 in Various Diluents

Sample Number	% Drug in Tablets			
	Types of HCTZ Tablets			
	$E-S_2-2^a$	$E-S_2-3^b$	$T-S_2-0^c$	$T-S_2-0.5^d$
1	98.12	97.58	98.84	103.69
2	97.58	101.54	101.18	101.90
3	100.64	101.54	102.08	102.98
4	103.52	101.00	100.10	101.54
5	97.94	100.10	99.56	100.46
6	97.76	100.64	99.02	102.98
7	98.30	101.00	99.02	99.74
8	96.32	100.28	98.84	102.98
9	97.58	100.46	101.72	100.46
10	98.66	100.28	99.02	102.08
mean	98.64	100.44	99.94	101.88
S.D.	2.03	1.13	1.26	1.32
R.S.D.	2.06	1.12	1.26	1.29
% L.A.[e]	99.25	100.15	99.50	100.66

a = Emcompress(R) + 2% S_2 b = Emcompress(R) + 3% S_2

c = Tablettose(R) + 0% S_2 d = Tablettose(R) + 0.5% S_2

e = Percent Labeled Amount

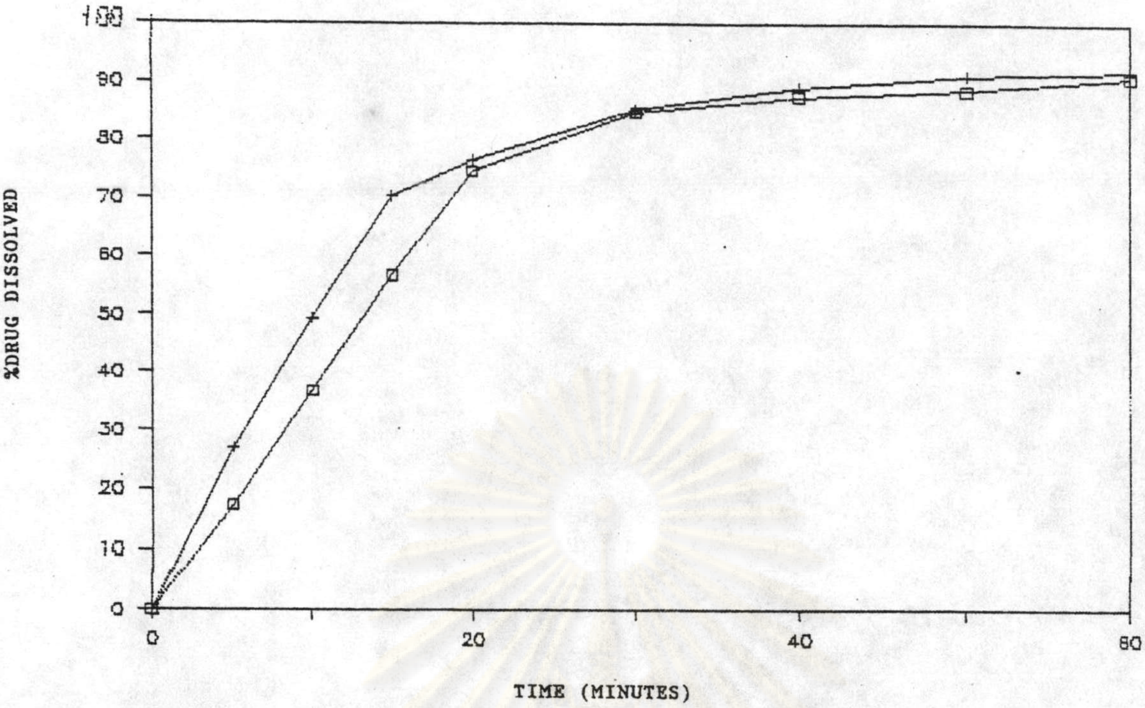

Figure 75 Dissolution Profiles of Hydrochlorothiazide from Hydrochlorothiazide Tablets Containing S_2 and Dibasic Calcium Phosphate Dihydrate as Disintegrant and Diluent, Respectively
(Key : □ 2%, + 3%)

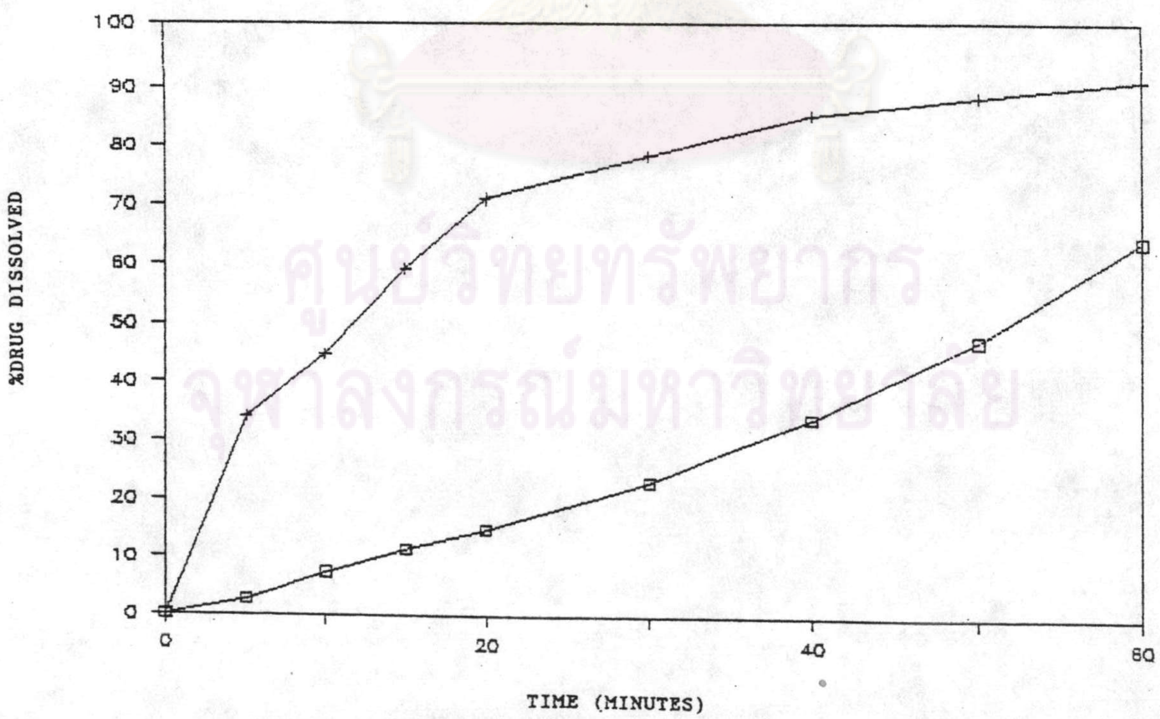

Figure 76 Dissolution Profiles of Hydrochlorothiazide from Hydrochlorothiazide Tablets Containing S_2 and α-Lactose Monohydrate as Disintegrant and Diluent, Respectively
(Key : □ 0%, + 0.5%)

1. Weight Variation, Thickness, Hardness and Friability

The average values and standard deviations of weight, thickness, hardness and friability for dibasic calcium phosphate dihydrate and α-lactose monohydrate systems were illustrated in Table 9 . In all conditions, weight variation and relative standard deviation (<1%) were complied with USP requirement(78). The thickness for each system was not significantly different and standard deviation was not more than 0.02. The hardness of tablets were in the range of 6±1 Kp. The friability of tablets were in the acceptable limit (not more than 1%).

2. Content Uniformity and Percent Labeled Amount of Tablets

The amount of hydrochlorothiazide was analyzed spectrophotometrically. The UV absorption spectrum of hydrochlorothiazide in ethanol was shown in Appendix 24. The hydrochlorothiazide standard solution at the concentration about 8.4 mcg/ml exhibited the maximum absorbance wavelength at 269 nm whereas the blank tablets containing S_2 did not have absorbance at this wavelength. The hydrochlorothiazide tablets containg S_2 as the same concentration showed the maximum absorbance at the same wavelength so that S_2 did not interfere the UV absorption of hydrochlorothiazide in ethanol.

The content uniformity and percent labeled amount of hydrochlorothiazide tablets using dibasic calcium phosphate dihydrate and α-lactose monohydrate as vehicles were given in Table 10. It was found that in all cases the content uniformity (relative standard deviation not more than 6%) and percent labeled amount met USP requirement (79).

3. Disintegration Time of Tablets

The disintegration time of hydrochlorothiazide tablets containing dibasic calcium phosphate dihydrate and α-lactose monohydrate were shown in Table 9 .

For dibasic calcium phosphate dihydrate system, the disintegration time of hydrochlorothiazide tablets containing S_2 at 2% level was shorter than of 3% level. In α-lactose monohydrate system, the disintegration time of hydrochlorothiazide tablets containing S_2 at 0.5% level was faster than of blank tablets.

4. Dissolution of Tablets

It was confirmed that S_2 did not interfere the UV absorption of hydrochlorothiazide in 0.1 N HCL as shown in Appendix 25 so that the amount of hydrochlorothiazide dissolved in 0.1 N HCL could be determined spectrophotometrically.

The dissolution rate profiles of hydrochlorothiazide tablets containing S_2 in dibasic calcium phosphate dihydrate and α-lactose monohydrate as vehicles are presented in Figures 75,76 , respectively (experimental data in Appendix 30).

It obviously indicated that the insoluble system of hydrochlorothiazide tablets using 3% concentration of S_2 exhibited higher dissolution rate than of 2% level. Dissolution rates of both tablet systems were complied with the USP requirement (74) (limit more than 65% of labeled amount dissolved within 60 minutes).

Dissolution rate profile of α-lactose monohydrate tablets with S_2 as disintegrant was greatly different from the control formulation. The dissolution rate of hydrochlorothiazide tablets with S_2 at 0.5% was well within acceptable limit of USP requirement, while the control formulation exhibited the release of drug lower than the standard limit.

Disintegrating Characteristics of Tablets with Different Disintegrants

The photographs of disintegrating characteristics of dibasic calcium phosphate dihydrate tablets with different disintegrants at concentration of 3% after contacting with water at various time intervals were shown in Figure 77. The tablets containing S_1 or S_2 exhibited disintegrating characteristics superior to tablet without disintegrant and tablet containing corn starch, but inferior to tablets containing Ac-Di-Sol$^{(R)}$ or Explotab$^{(R)}$.

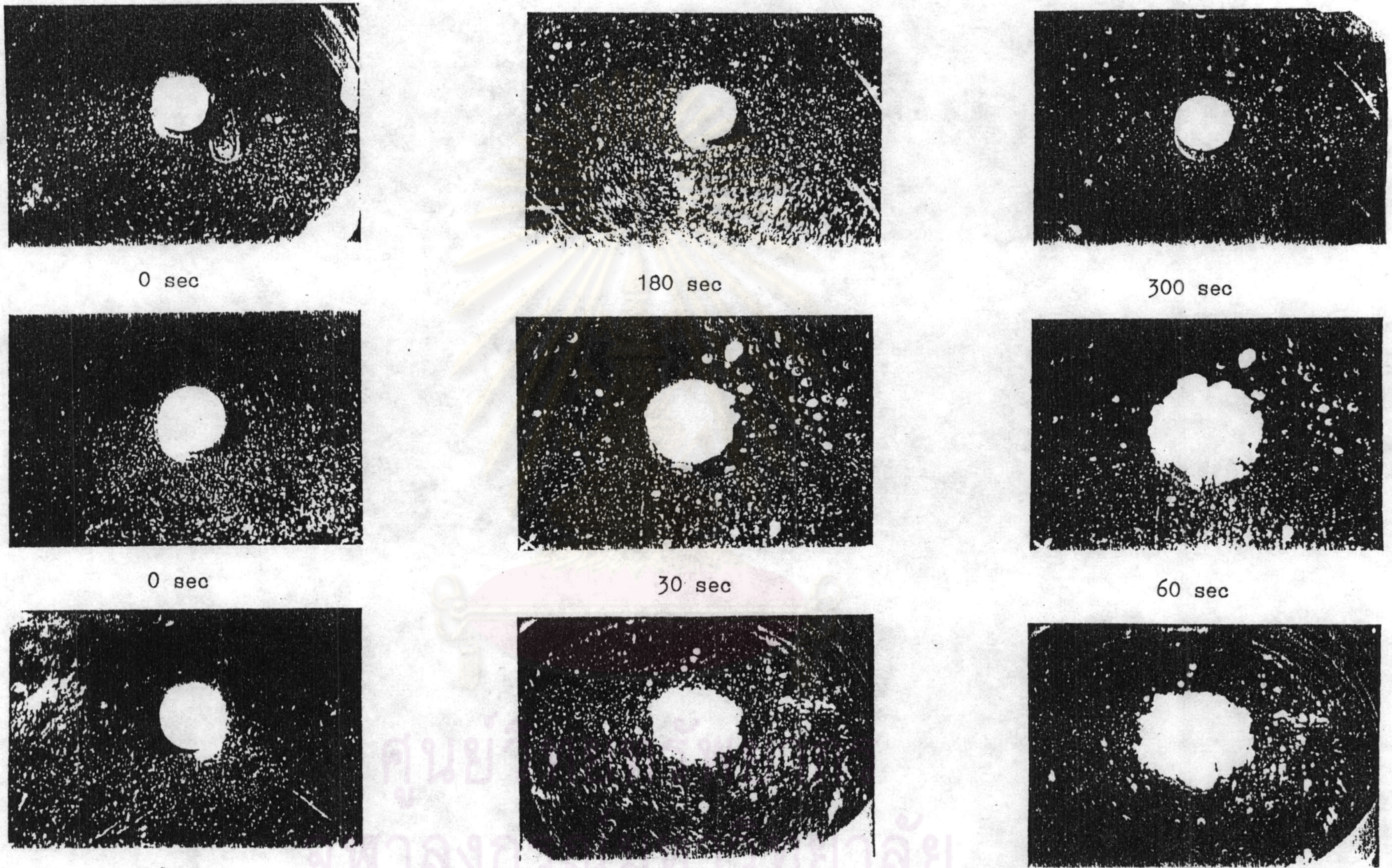

Figure 77 Photographs of Disintegrating Characteristics of Tablets Containing Different Disintegrant Materials

a Emcompress$^{(R)}$ Tablet without Disintegrant
b Emcompress$^{(R)}$ Tablet Containing 3% of S_1
c Emcompress$^{(R)}$ Tablet Containing 3% of S_2

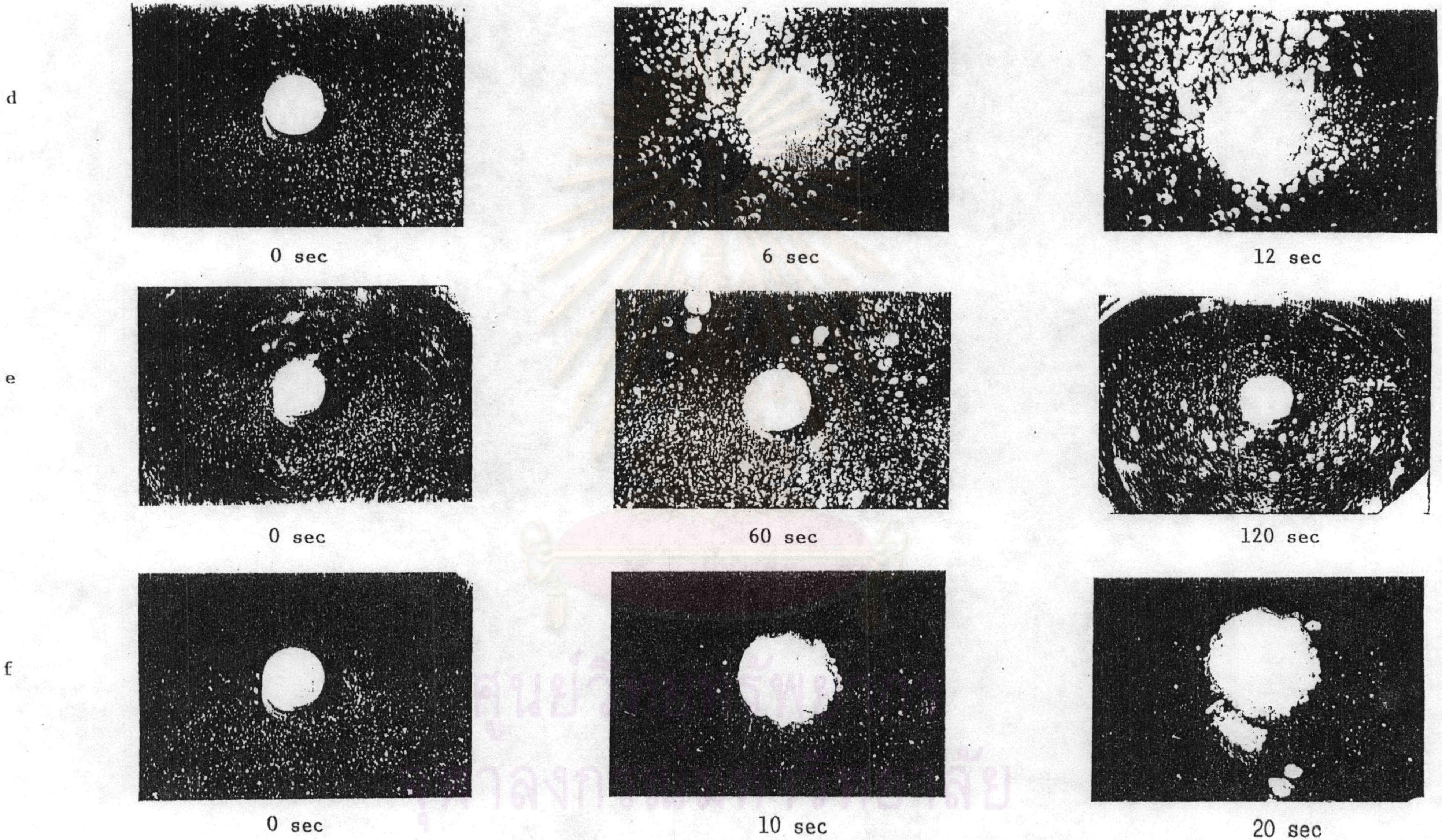

Figure 77 Photographs of Disintegrating Characteristics of Tablets Containing Different Disintegrant Materials (Continued)
d Emcompress(R) Tablet Containing 3% of Ac-Di-Sol(R)
e Emcompress(R) Tablet Containing 3% of Corn Starch
f Emcompress(R) Tablet Containing 3% of Explotab(R)

The blank tablet without disintegrant did not disintegrate whereas the tablets containing S_1 or S_2 exhibited similar to tablets containing Explotab $^{(R)}$ or Ac-Di-Sol $^{(R)}$. They expanded and exploded into primary particles but the rates of wetting of tablets containing S_1 or S_2 were slower than those containing Explotab $^{(R)}$ or Ac-Di-Sol$^{(R)}$. While the tablet containing corn starch only exhibited slight swelling but no disintegration took place during the time of observation.