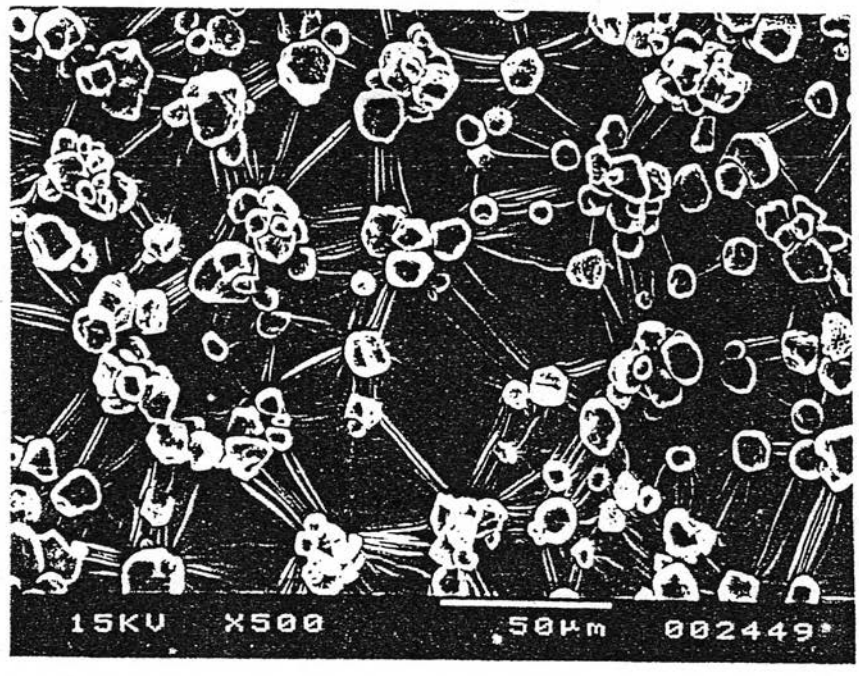
Chapter III

Results

Physical properties of pure disintegrant powders

a) Particle size and shape

The photomicrographic data of different disintegrants in different magnification were shown in Figure 18-25. The shape of individual particle could be clearly observed. It was apparent that the particles of chitin (J), chitin (U), chitosan (J), and chitosan (U) possessed an irregular shape. And they seemed to be flake-like. The shape of corn starch was polygonal whereas the shape of sodium starch glycolate was oval or spherical. The photomicrographs of sodium starch glycolate were differentfrom corn starch that cornstarch had a smooth surface whereas sodium starch glycolate had not. And the shapes of microcrystalline cellulose and croscarmellose sodium were fibrous-like. The photomicrographs were taken at various magnification. It was evident that these disintegrants were much different in particle size. From the data it could be noticed that chitin (J) powders contained the largest particle size among all disintegrants. The size decreased in the following order : chitosan (J), chitosan (U), chitin (U), croscarmellose sodium, microcrystalline cellulose, and sodium starch glycolate, respectively. And corn starch powders contained the smallest particle size.



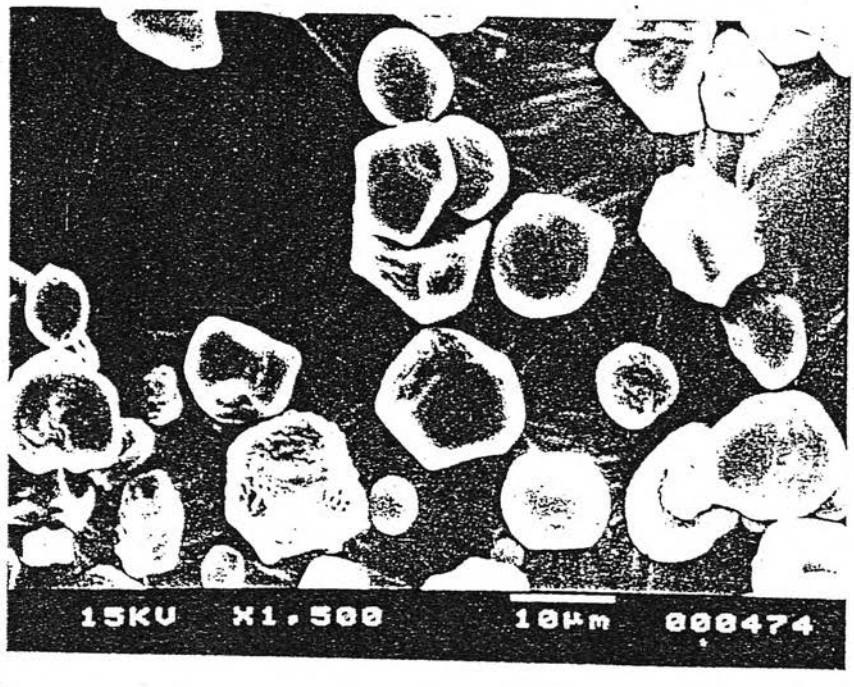
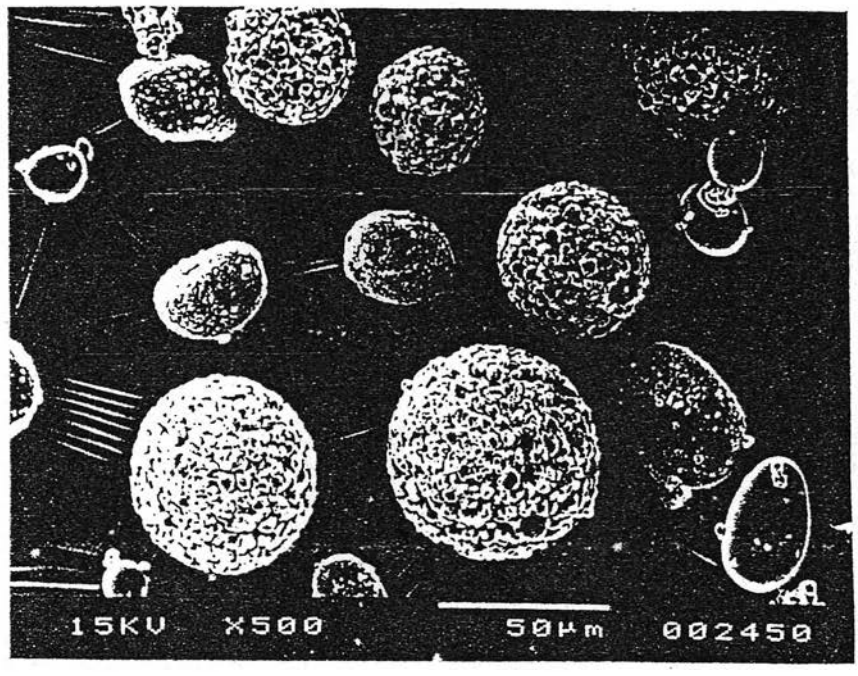


Figure 18 Electron photomicrographs of corn starch



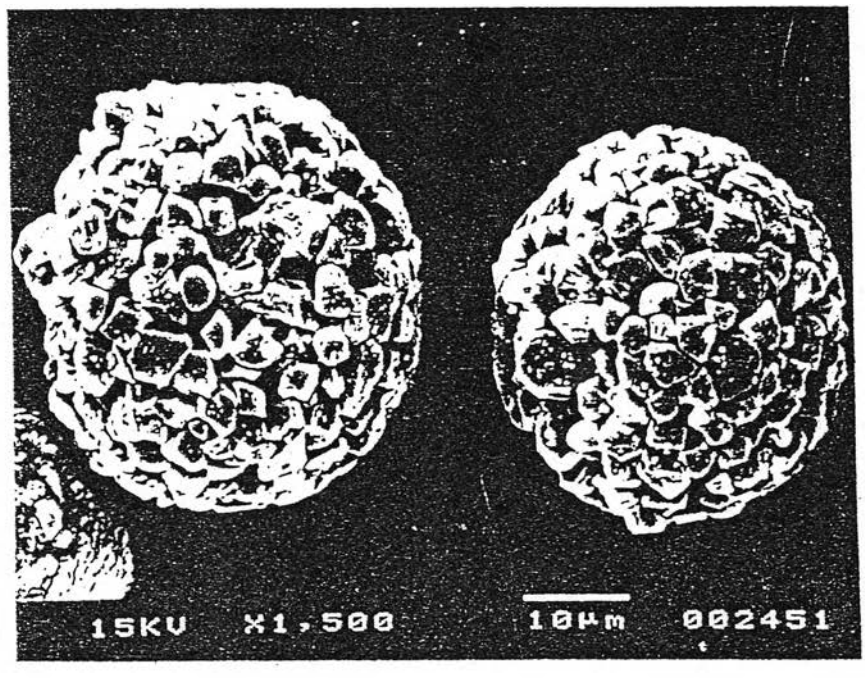


Figure 19 Electron photomicrographs of sodium starch glycolate

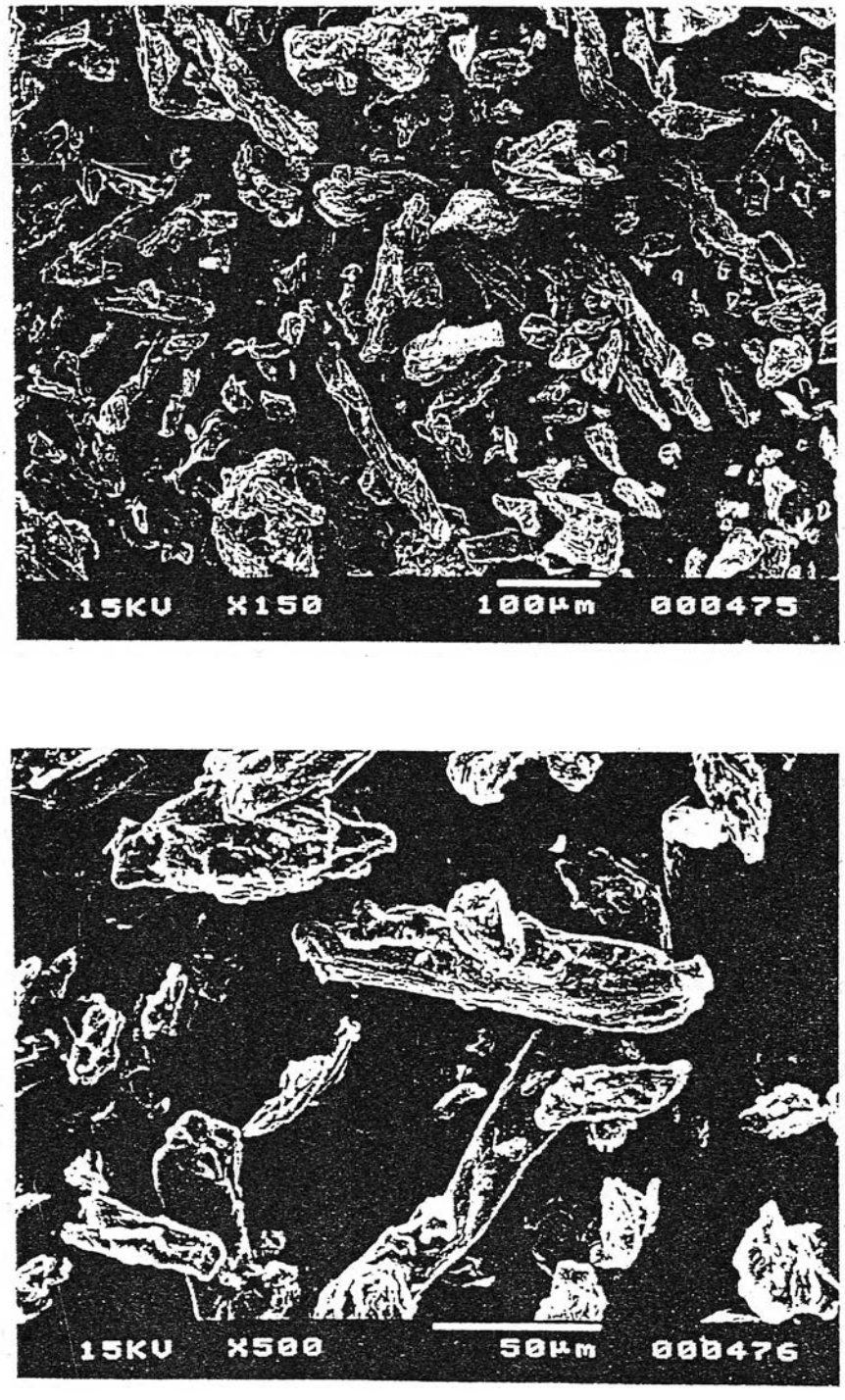
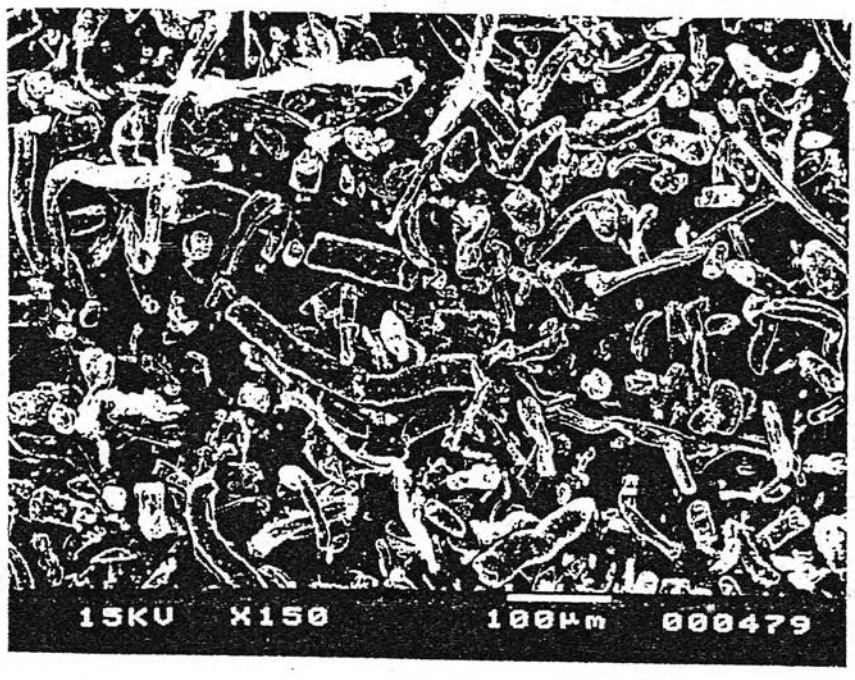


Figure 20 Electron photomicrographs of microcrystalline cellulose



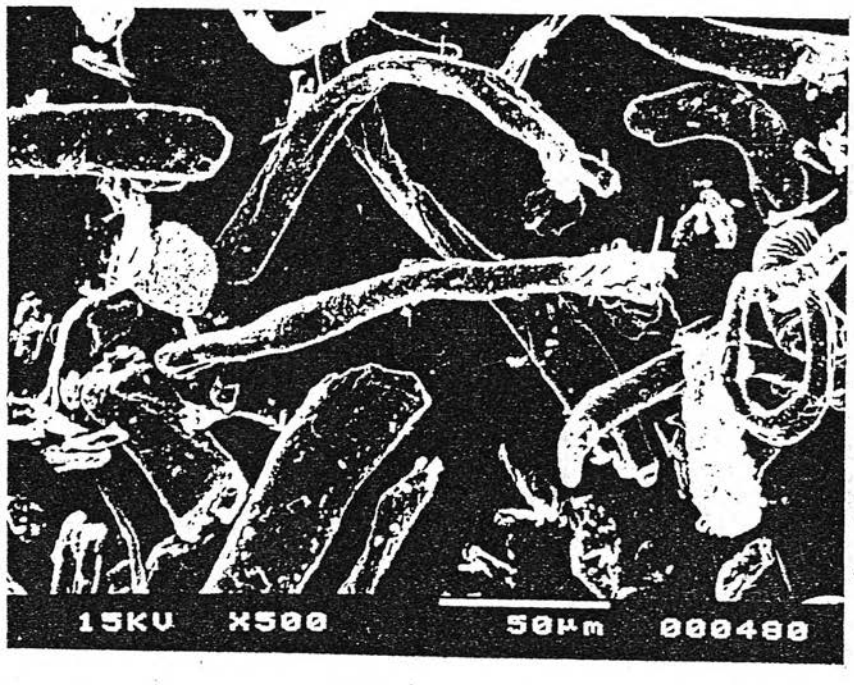
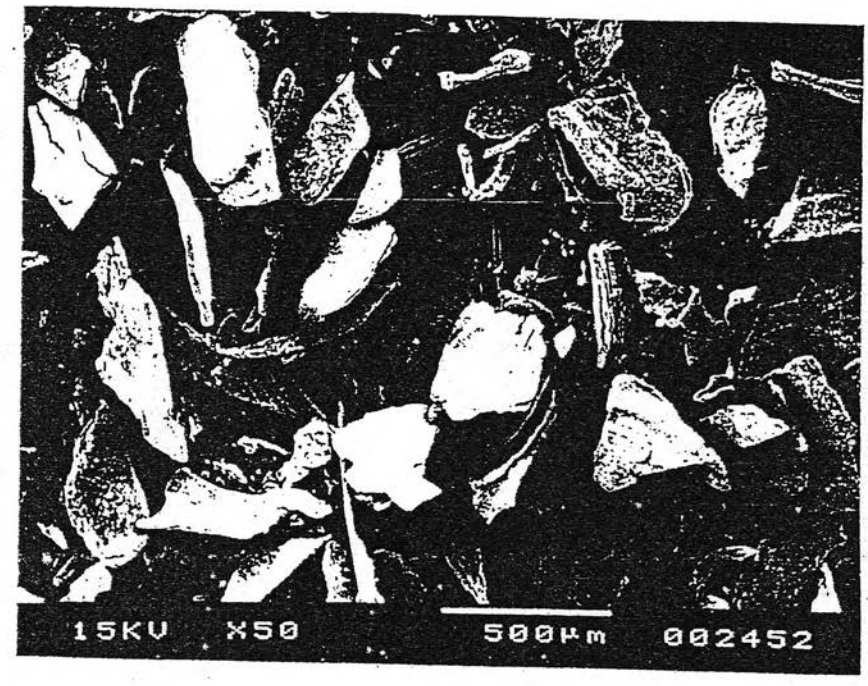


Figure 21 Electron photomicrographs of croscarmellose sodium



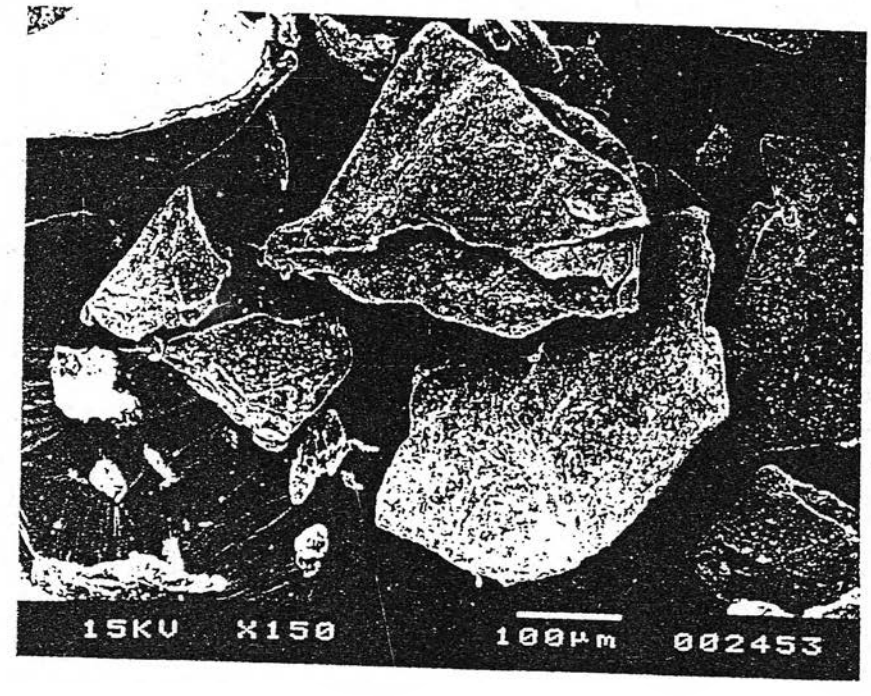
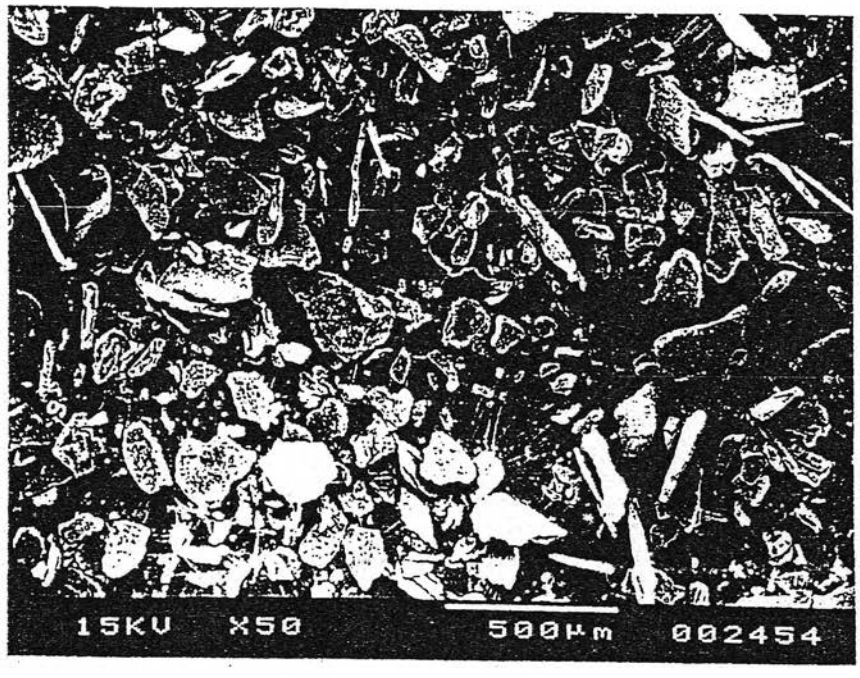


Figure 22 Electron photomicrographs of chitin (J)



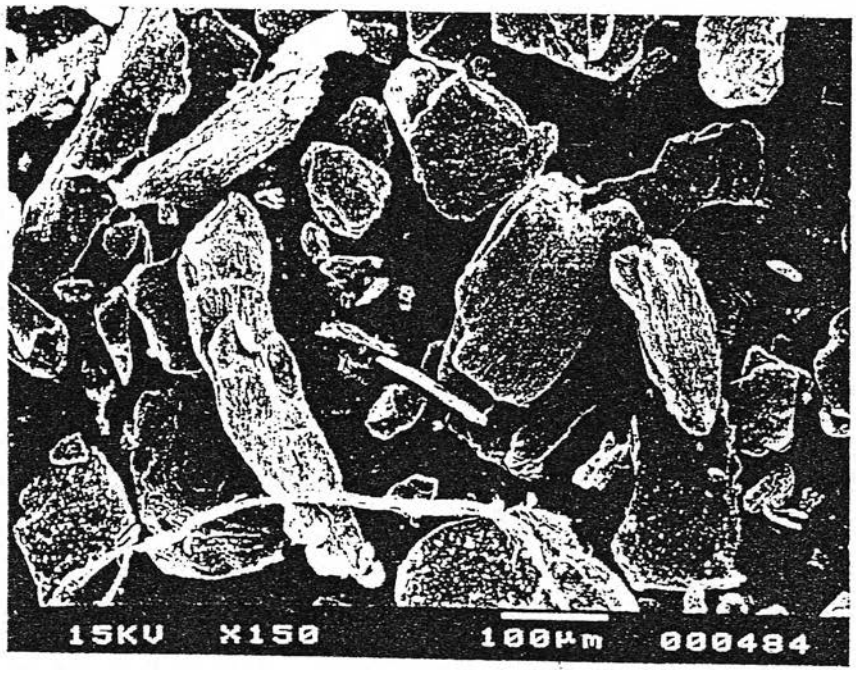


Figure 23 Electron photomicrographs of chitin (U)

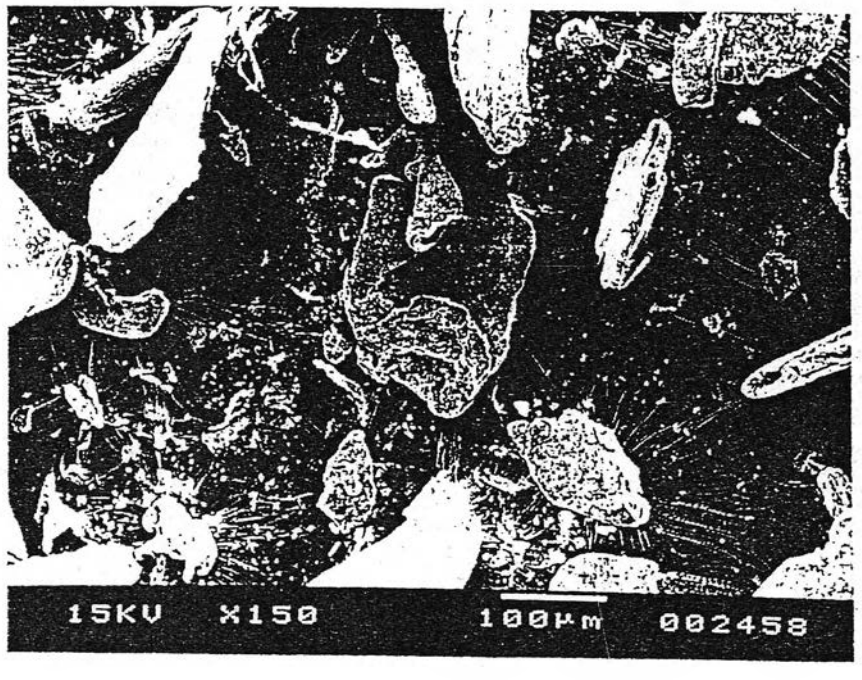
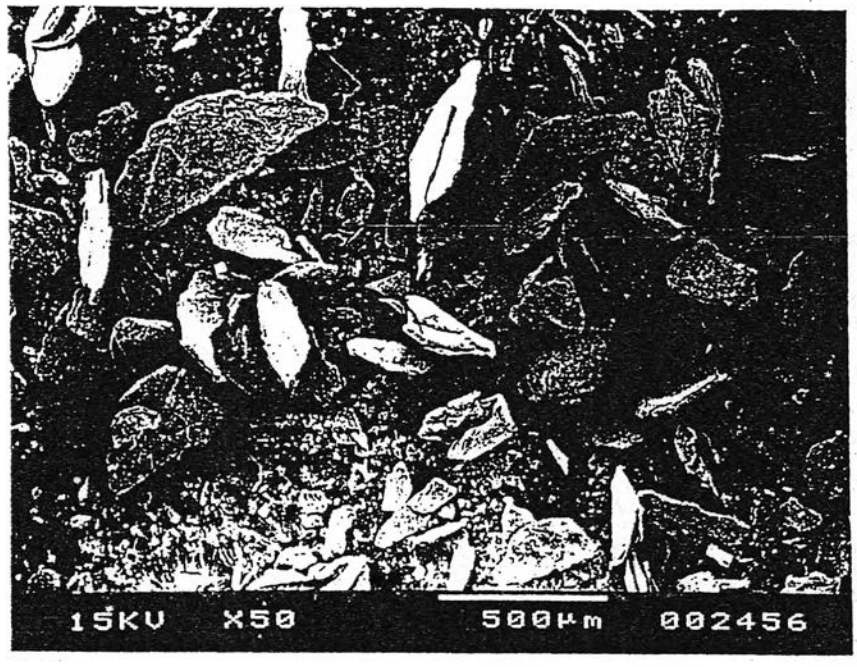


Figure 24 Electron photomicrographs of chitosan (J)



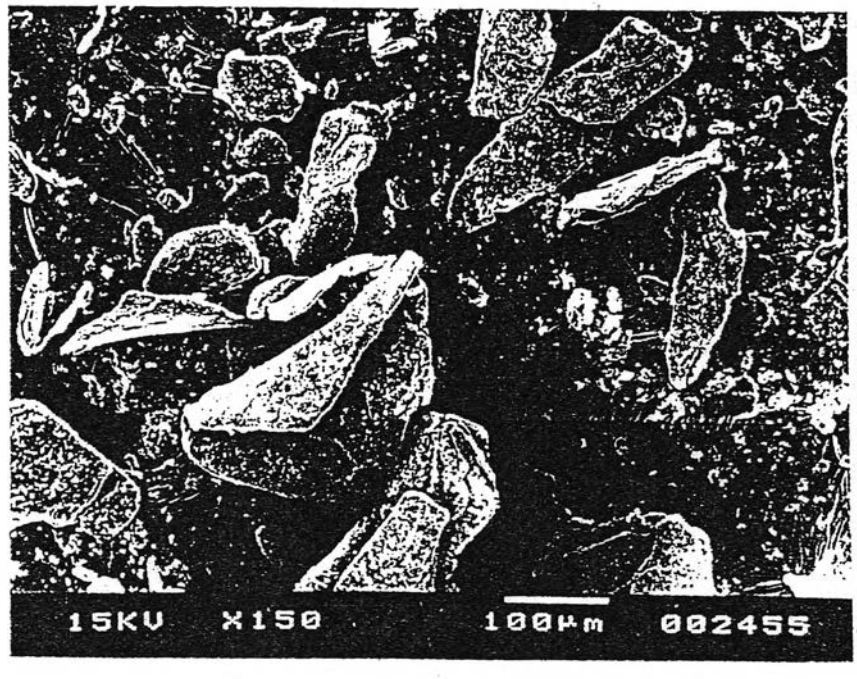


Figure 25 Electron photomicrographs of chitosan (U)

b) Particle size and size distribution

The particle size distribution of various disintegrant powders used in this study were analyzed by sieve analysis method. The sieve analysis data were shown in Table 6 and the histograms of particle size distribution were given in Figures 26-33. The results indicated that chitin and its derivative had larger particle size than starch and its derivative and cellulose and its derivative. It was found that among these disintegrants, more than 70% of corn starch, sodium starch glycolate, microcrystalline cellulose and croscarmellose sodium, the particle size was less than 90 micron. By this method, it seemed to be that these four disintegrants had the same particle size. But from the electron photomicrographic data showed that the particle size of corn starch was much smaller than the others. Since corn starch particles had electrostatic charges and they were aggregated while shaking on the mechanical sieve shaker, the particle size of corn starch determined by sieve analysis method was larger than by the photomicrographic method. In the case of chitin and chitosan, it was found that most particle sizes of chitin(J), chitosan (J), and chitosan (U) were larger than 250 micron and the size of chitin (U) was about 180-250 micron. And chitin (J) contained larger particles than the others. These results were similar to the results from the electron photomicrograph.

Table 6 Particle size distribution of pure disintegrants powder

Disintegrants	% Retained on size (micron)						
	250	180	150	106	90	45	< 45
Corn starch	0.00	0.62	7.62	10.54	2.92	77.26	1.04
Sodium starch glycolate	0.00	0.44	0.77	4.28	4.17	77.72	12.62
Microcrystalline cellulose	0.00	0.86	2.78	9.84	9.87	38.29	38.39
Croscarmellose sodium	0.53	3.89	1.16	4.11	9.89	63.47	16.95
Chitin (J)	56.91	23.76	7.34	6.91	1.95	3.13	0.00
Chitin (U)	16.46	25.95	16.88	19.02	8.12	13.50	0.00
Chitosan (J)	41.60	34.45	11.14	8.40	1.05	3.36	0.00
Chitosan (U)	32.90	26.66	16.16	13.28	5.35	5.65	0.00

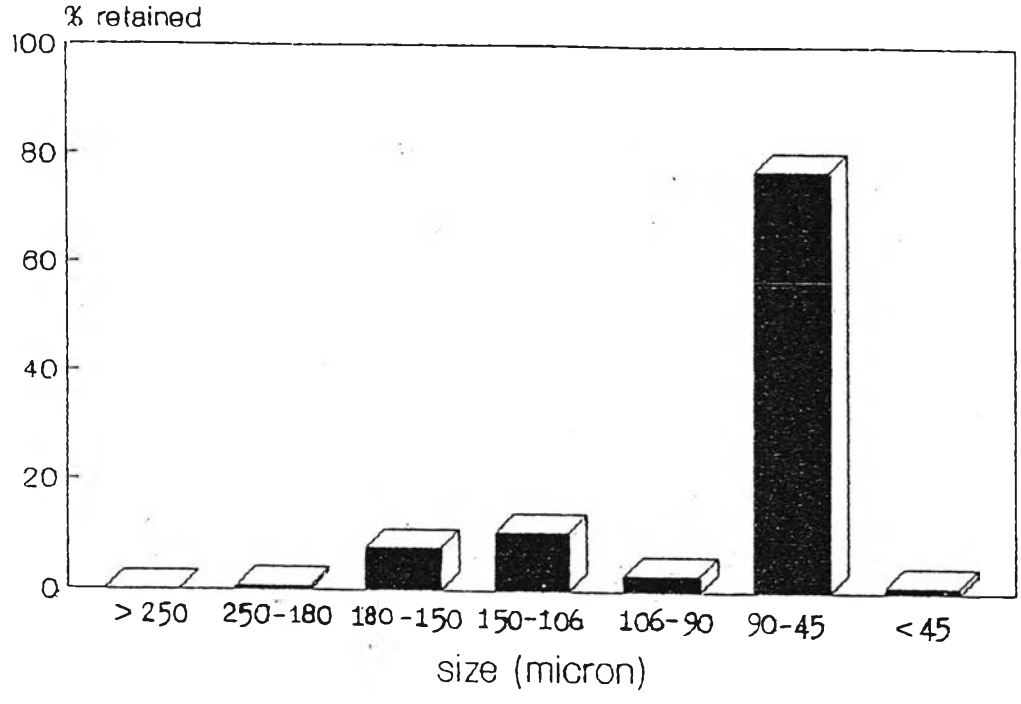


Figure 26 Histogram for the particle size distribution of corn starch

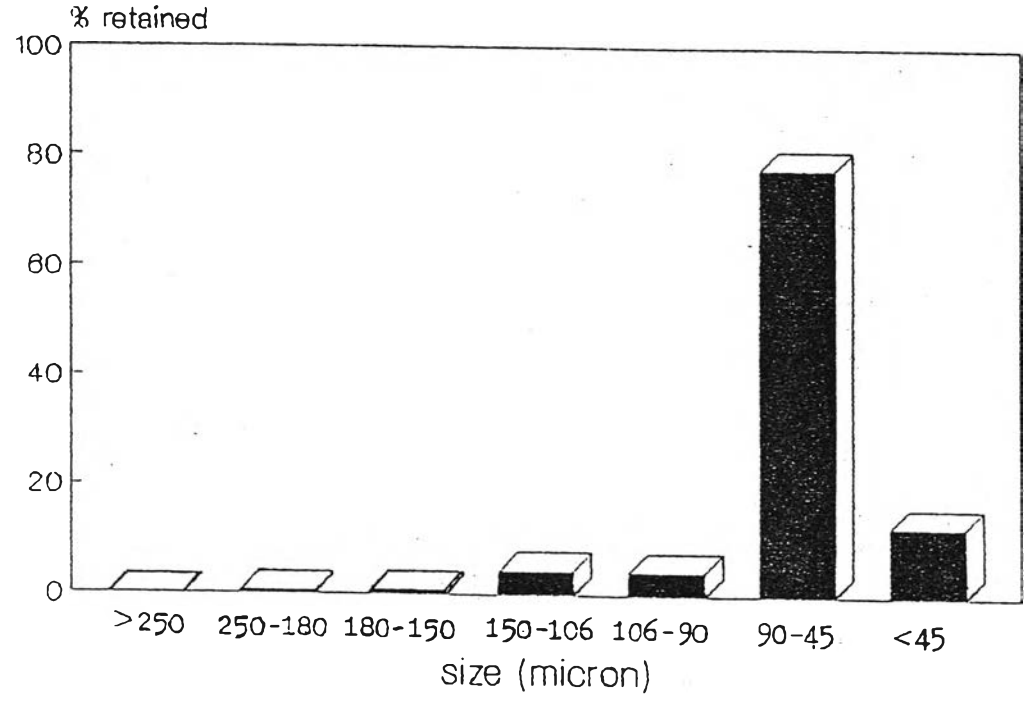


Figure 27 Histogram for the particle size distribution of sodium starch glycolate

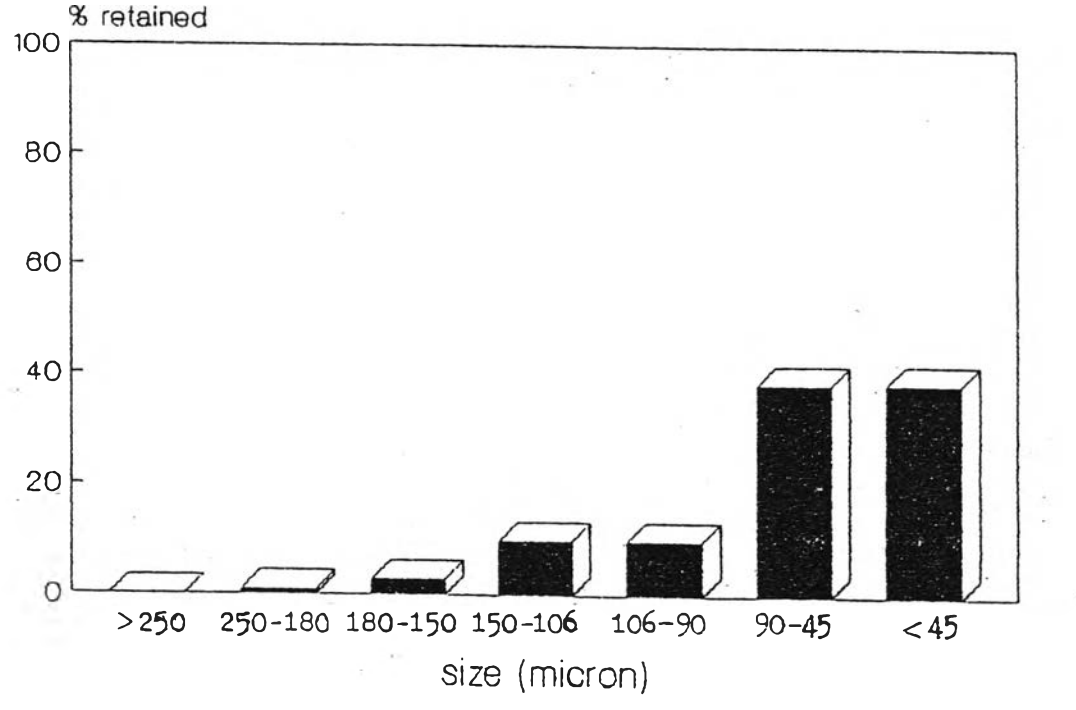


Figure 28 Histogram for the particle size distribution of microcrystalline cellulose

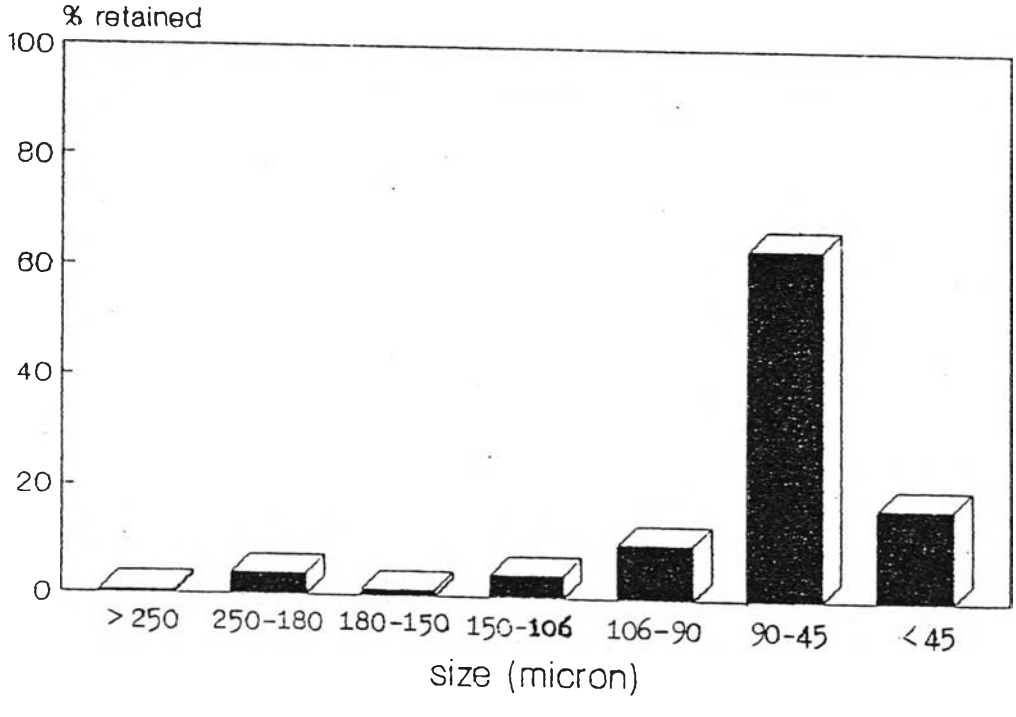


Figure 29 Histogram for the particle size distribution of croscarmellose sodium

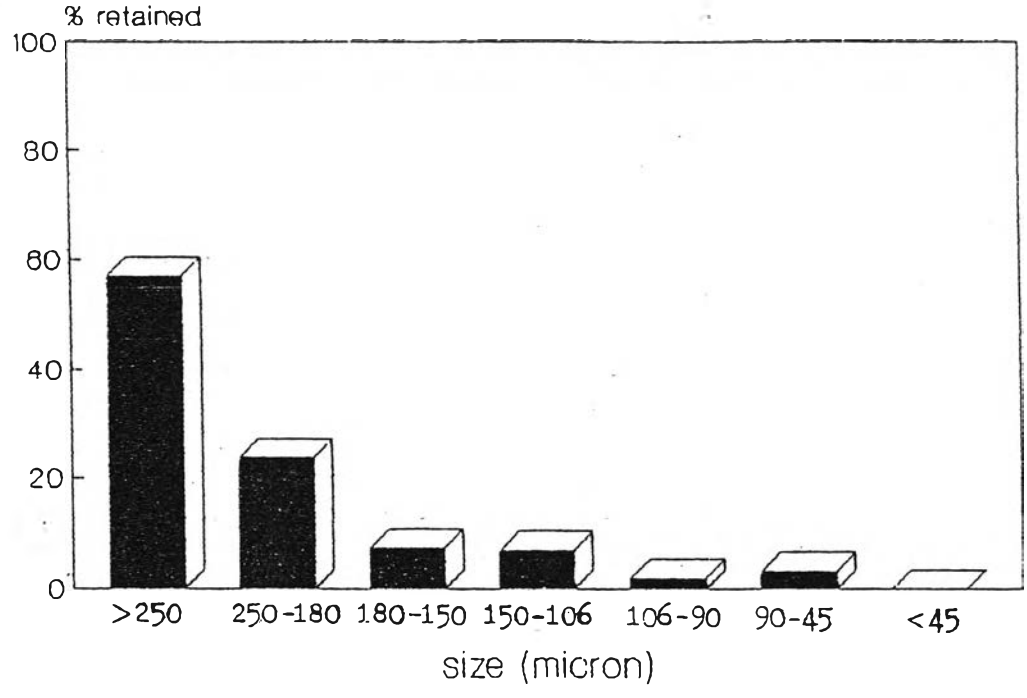


Figure 30 Histogram for the particle size distribution of chitin (J)

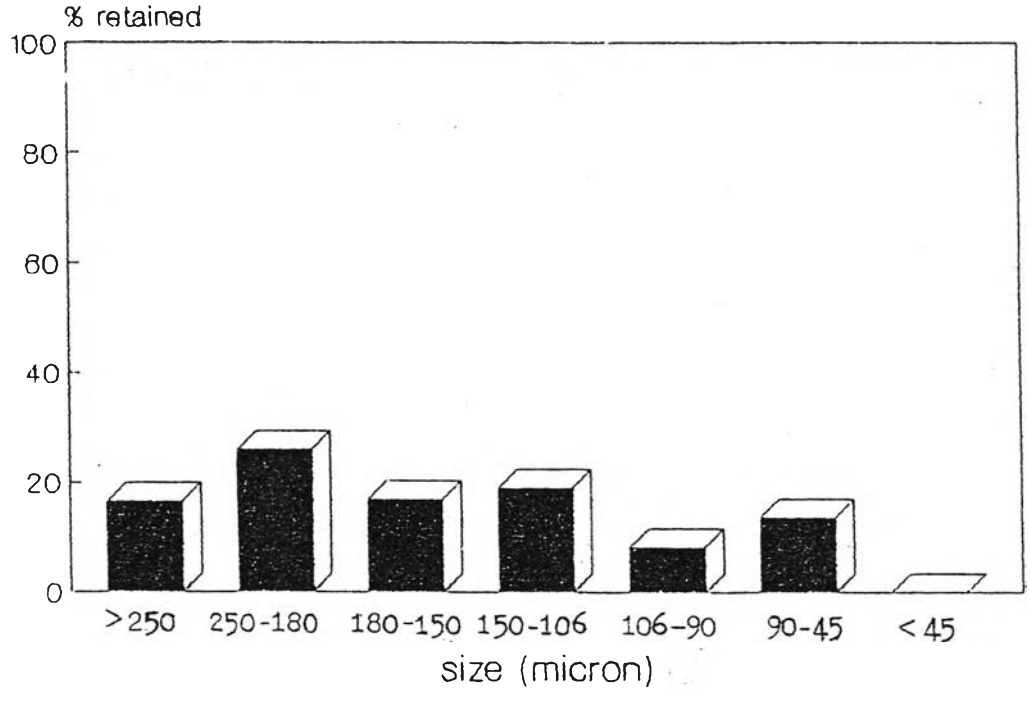


Figure 31 Histogram for the particle size distribution of chitin (U)

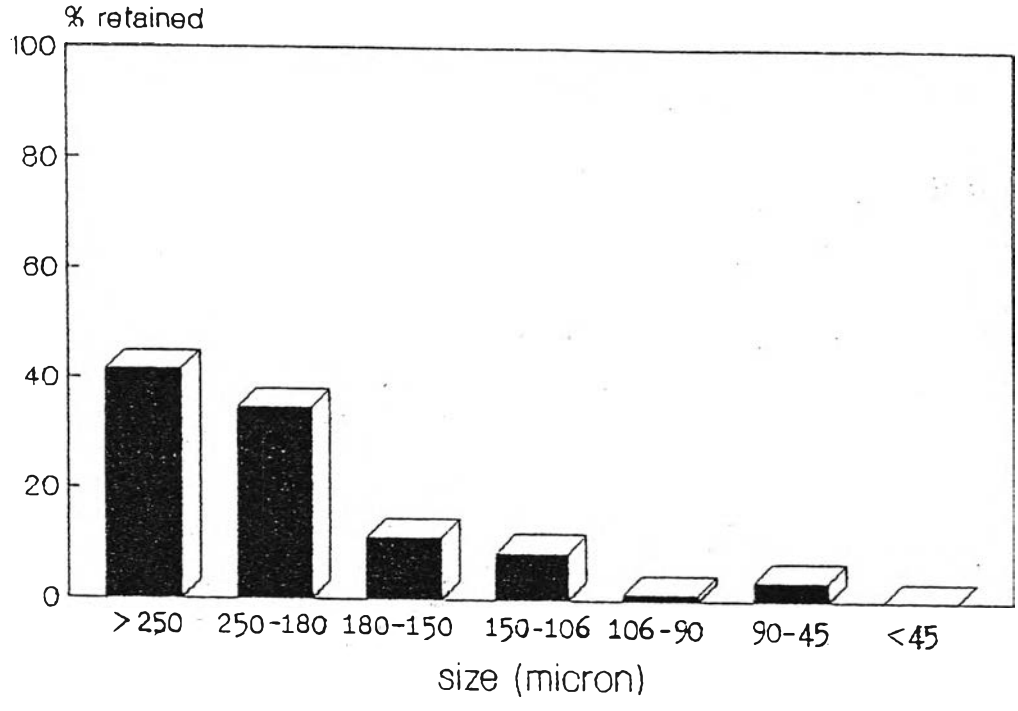


Figure 32 Histogram for the particle size distribution of chitosan (J)

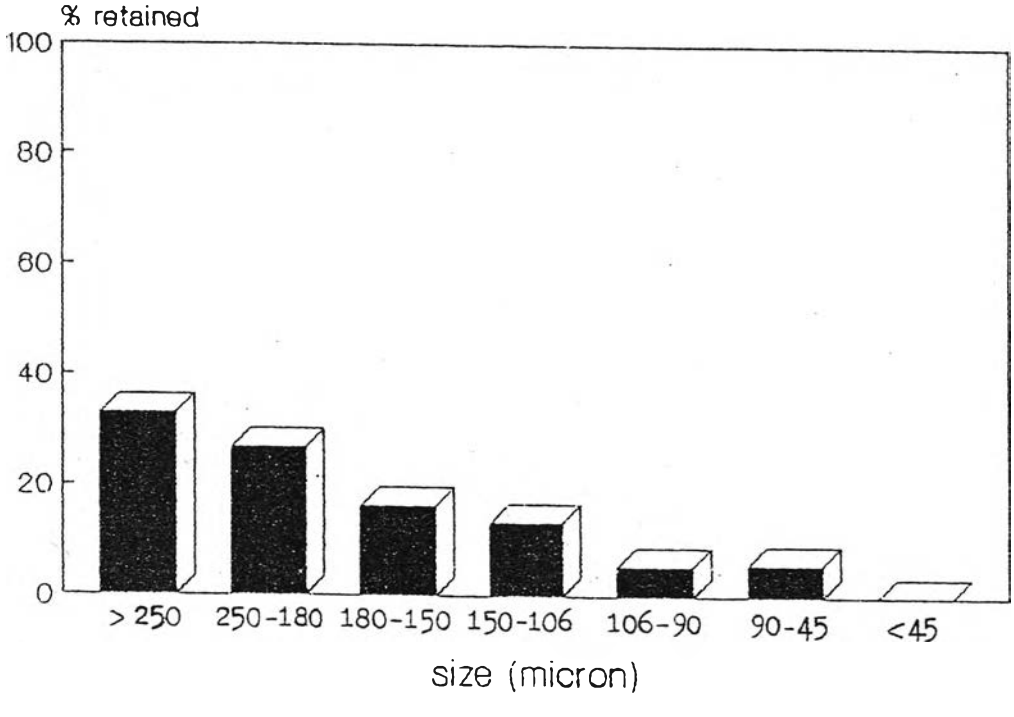


Figure 33 Histogram for the particle size distribution of chitosan (U)

In the case of particle size distribution, it could be seen that powders of corn starch, sodium starch glycolate, microcrystalline cellulose and croscarmellose sodium had a narrow range of size distribution while both powders of chitin and chitosan had a wide range of size distribution.

c) Moisture content

The results of moisture content of various disintegrant were presented as percent loss on drying and shown in Table 7. The moisture content in different disintegrant powders decreased in the following order: sodium starch glycolate > corn starch > chitin(J) > chitosan (U) > microcrystalline cellulose > chitin (U) > croscarmellose sodium > chitosan(J).

d) Swelling of particles

The swelling of disintegrant powders in this study was determined by sedimentation volume method. The swelling capacity was done in deionized water (DI water) and diluted hydrochloric acid (1 % v/v). The results were given in Table 8. All samples were swollen in deionized water, but the volume of the swollen samples varied dramatically. The samples settled to opaque sediment layer, and this layer could be clearly seen to separate to the swelling medium, shown in Figure 34. Swelling capacity of pure disintegrant powders in deionized water could be ranked as follow : sodium starch glycolate >

Table 7 Moisture content of pure disintegrant powder

Disintegrants	% Moisture# content	% CV
Corn starch	11.03	2.26
Sodium starch glycolate	12.13	2.63
Microcrystalline cellulose	5.23	2.86
Croscarmellose sodium	3.23	1.54
Chitin (J)	8.96	1.67
Chitin (U)	4.36	1.44
Chitosan (J)	2.33	2.14
Chitosan (U)	5.70	1.98

average of three determinations

croscarmellose sodium > chitosan(J) > chitosan(U) > chitin(J) = chitin (U) > microcrystalline cellulose > corn starch. The statistical analysis of swelling capacity among chitin (J), chitin (U), chitosan (U), and chitosan (J) showed that there was no significant difference among the three former disintegrants, but it was significantly different in the latter one ($p=0.05$). In diluted hydrochloric acid, it could be seen that the swelling capacity of sodium starch glycolate and croscarmellose sodium was decreased in acidic medium, while corn starch, microcrystalline cellulose and chitin (U) remained unchange. In contrast, chitin(J), chitosan(J) and chitosan(U) actually increased in swelling capacity, and a dramatic change occurred. These three disintegrants changed from an opaque sediment in graduated cylinder to a voluminous translucent mass, as shown in Figure 35, and this translucent mass was highly gelatinous. The swelling capacity of chitosan (J) and chitosan (U) were increased with the increasing volume of diluted hydrochloric acid.

Swelling of all samples, both in deionized water and diluted hydrochloric acid, occurred almost instantaneously, and did not change appreciably during the first 24 hours. The statistical analysis of swelling capacity of each disintegrant between in deionized water and in diluted hydrochloric acid was determined. It was apparent that there was no significant difference for corn starch, microcrystalline cellulose

Table 8 Swelling capacity of pure disintegrant powders

Disintegrants	DI water# (time)	0.1 N HCl# (time)
Corn starch	1.03	1.07
Sodium starch glycolate	9.00	2.56
Microcrystalline cellulose	1.24	1.12
Croscarmellose sodium	5.05	4.75
Chitin (J)	1.86	3.35
Chitin (U)	1.83	1.85
Chitosan (J)	2.08	4.57
Chitosan (U)	1.91	5.00

average of three determinations

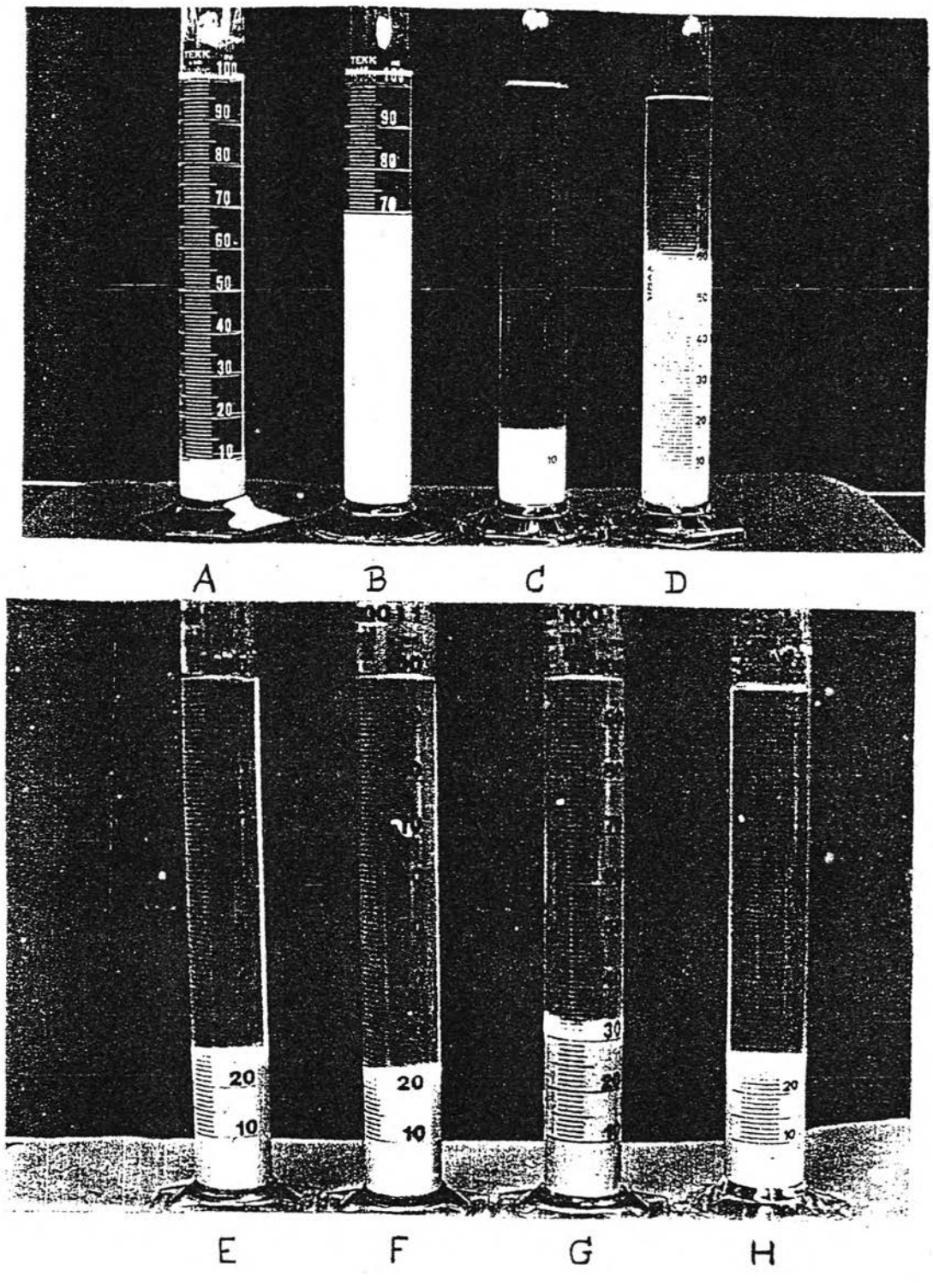


Figure 34 Swelling capacity of various disintegrants in deionized water

A. Corn starch
B. Sodium starch glycolate
C. Microcrystalline cellulose
D. Croscarmellose sodium
E. Chitin (J)
F. Chitin (U)
G. Chitosan (J)
H. Chitosan (U)

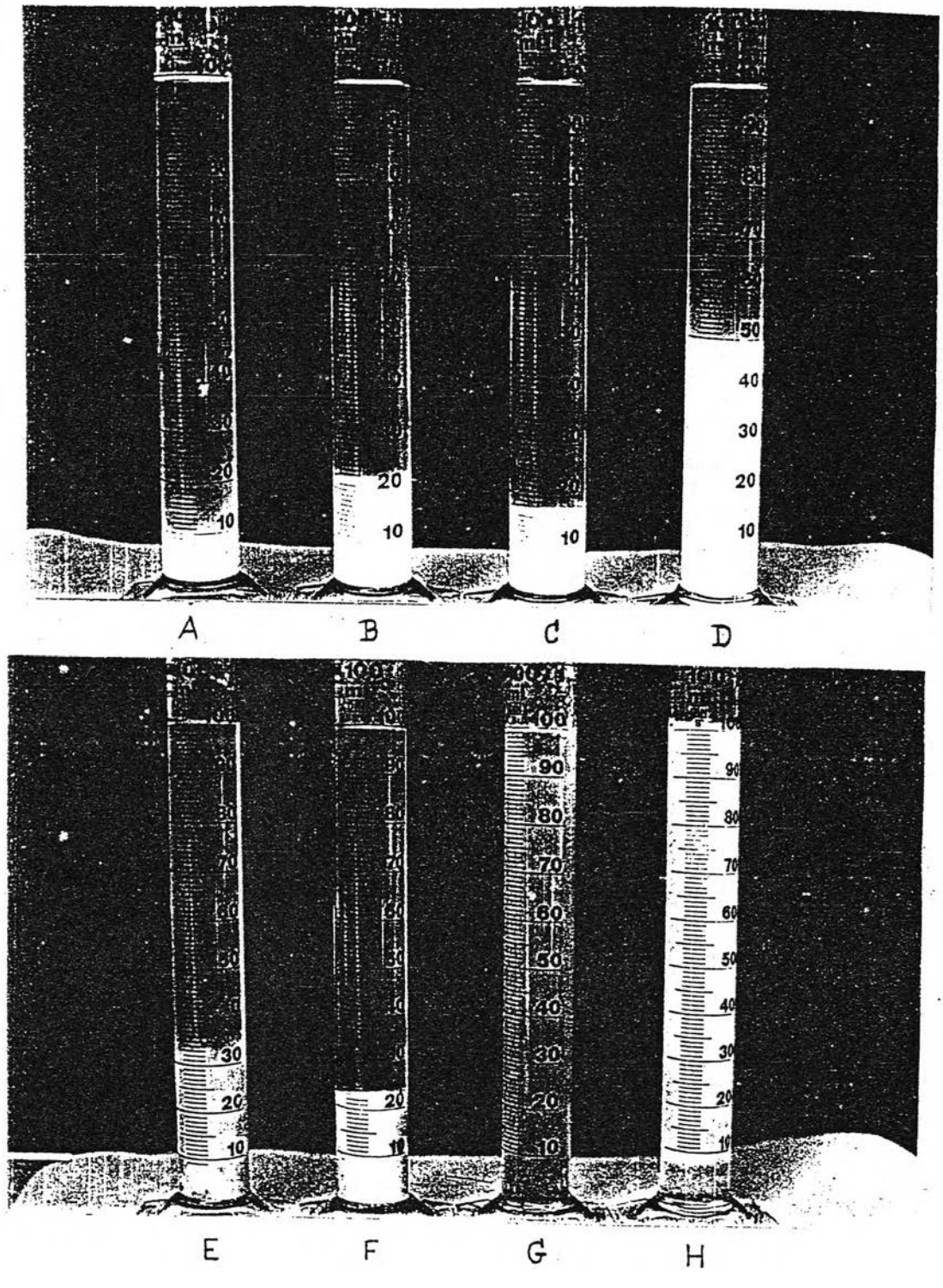


Figure 35 Swelling capacity of various disintegrants in diluted hydrochloric acid

A. Corn starch
B. Sodium starch glycolate
C. Microcrystalline cellulose
D. Croscarmellose sodium
E. Chitin (J)
F. Chitin (U)
G. Chitosan (J)
H. Chitosan (U)

and chitin (U), whereas there was significantly difference for sodium starch glycolate, croscarmellose sodium, chitin (J), chitosan (J), and chitosan (U) ($p=0.05$).

Physical properties of pure disintegrant tablets

a) Water uptake

The results of the water uptake and the rate of water uptake of various pure disintegrant tablets at compressional force of 1,500 pounds were shown in Table 9 and 10. And the rate and amount of water uptake plot were given in Figure 36-37. The comparison of the rate and amount of water uptake of disintegrants in this study showed that rate and amount of water uptake decreased in the following order : sodium starch glycolate, chitin(J), chitosan (J), chitosan (U), chitin (U), croscarmellose sodium, microcrystalline cellulose, and corn starch, respectively. It could be seen that among these disintegrants, sodium starch glycolate exhibited the highest rate and amount of water uptake, while corn starch exhibited the lowest. The rate of water uptake of disintegrants then decreased against time.

b) Moisture sorption

The percentage of moisture sorption of different pure disintegrant tablets at compressional force of 1,500 pounds after exposure to 75% relative humidity at room temperature were shown in Table 11. The

Table 9 Water uptake of 500 mg of pure disintegrant tablet compressed at 1500 pounds

Time (sec)	water uptake# (ml)							
	Corn starch	Sodium starch glycolate	Microcrystalline cellulose	Croscarmellose sodium	Chitin (J)	Chitin (U)	Chito san(J)	Chito san(U)
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
10	0.10	0.29	0.12	0.08	0.12	0.10	0.09	0.12
20	0.18	0.52	0.23	0.12	0.25	0.20	0.17	0.20
30	0.23	0.72	0.30	0.15	0.38	0.26	0.27	0.28
40	0.27	0.92	0.35	0.18	0.51	0.31	0.40	0.36
50	0.31	1.08	0.37	0.20	0.64	0.36	0.44	0.43
60	0.33	1.25	0.38	0.22	0.76	0.41	0.52	0.49
75	0.34	1.48	0.39	0.24	0.94	0.47	0.64	0.57
90	0.35	1.70	0.40	0.26	1.10	0.52	0.76	0.67
105	0.36	1.92	0.40	0.28	1.24	0.56	0.88	0.75
120	0.37	2.12	0.41	0.29	1.37	0.60	0.98	0.83
150	0.38	2.50	0.41	0.32	1.51	0.69	1.10	0.97
180	0.38	2.86	0.42	0.35	1.61	0.77	1.25	1.09
210	0.38	3.19	0.42	0.37	1.70	0.82	1.42	1.18
240	0.39	3.53	0.43	0.39	1.73	0.87	1.54	1.27
270	0.39	3.84	0.43	0.41	1.76	0.93	1.62	1.33
300	0.40	4.14	0.43	0.43	1.78	0.96	1.66	1.37
600	0.42	*	0.45	0.56	1.81	1.06	1.69	1.46
900	0.44	*	0.47	0.70	1.84	1.10	1.71	1.50
1200	0.47	*	0.48	0.82	1.86	1.14	1.72	1.53
1800	0.51	*	0.51	1.07	1.90	1.20	1.74	1.56

average of five determinations

* the results cannot be determined

Table 10 Rate of water uptake of 500 mg of pure disintegrant tablet compressed at 1500 pounds.

Time (sec)	rate of water uptake* (µl/sec)							
	Corn starch	Sodium starch glycolate	Microcrystalline cellulose	Croscarmellose sodium	Chitin (J)	Chitin (U)	Chito san(J)	Chito san(U)
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
10	10.00	29.00	12.00	8.00	12.00	10.00	8.00	12.00
20	9.00	26.00	11.50	6.00	12.50	10.00	8.50	10.00
30	7.67	24.00	10.00	5.00	12.67	8.67	9.00	9.33
40	6.75	23.00	8.75	4.50	12.75	7.75	10.00	9.00
50	6.20	21.60	7.40	4.00	12.80	7.20	8.80	8.60
60	5.50	20.83	6.33	3.67	12.67	6.83	8.67	8.17
75	4.53	19.73	5.20	3.20	12.53	6.27	8.53	7.60
90	3.89	18.89	4.44	2.89	12.22	5.78	8.44	7.44
105	3.43	18.29	3.81	2.67	11.81	5.33	8.38	7.14
120	3.08	17.67	3.42	2.42	11.42	5.00	8.17	6.92
150	2.53	16.67	2.73	2.13	10.07	4.60	7.33	6.47
180	2.11	15.89	2.33	1.94	8.94	4.28	6.94	6.06
210	1.81	15.19	2.00	1.76	8.10	3.91	6.76	5.62
240	1.63	14.71	1.79	1.63	7.21	3.63	6.42	5.29
270	1.44	14.22	1.59	1.52	6.52	3.44	6.00	4.93
300	1.33	13.80	1.43	1.43	5.93	3.20	5.53	4.57
600	0.70	*	0.75	0.93	3.02	1.77	2.82	2.43
900	0.49	*	0.52	0.78	2.04	1.22	1.90	1.67
1200	0.39	*	0.40	0.68	1.55	0.95	1.43	1.28
1800	0.28	*	0.34	0.59	1.06	0.67	0.97	0.87

* the results cannot be determined

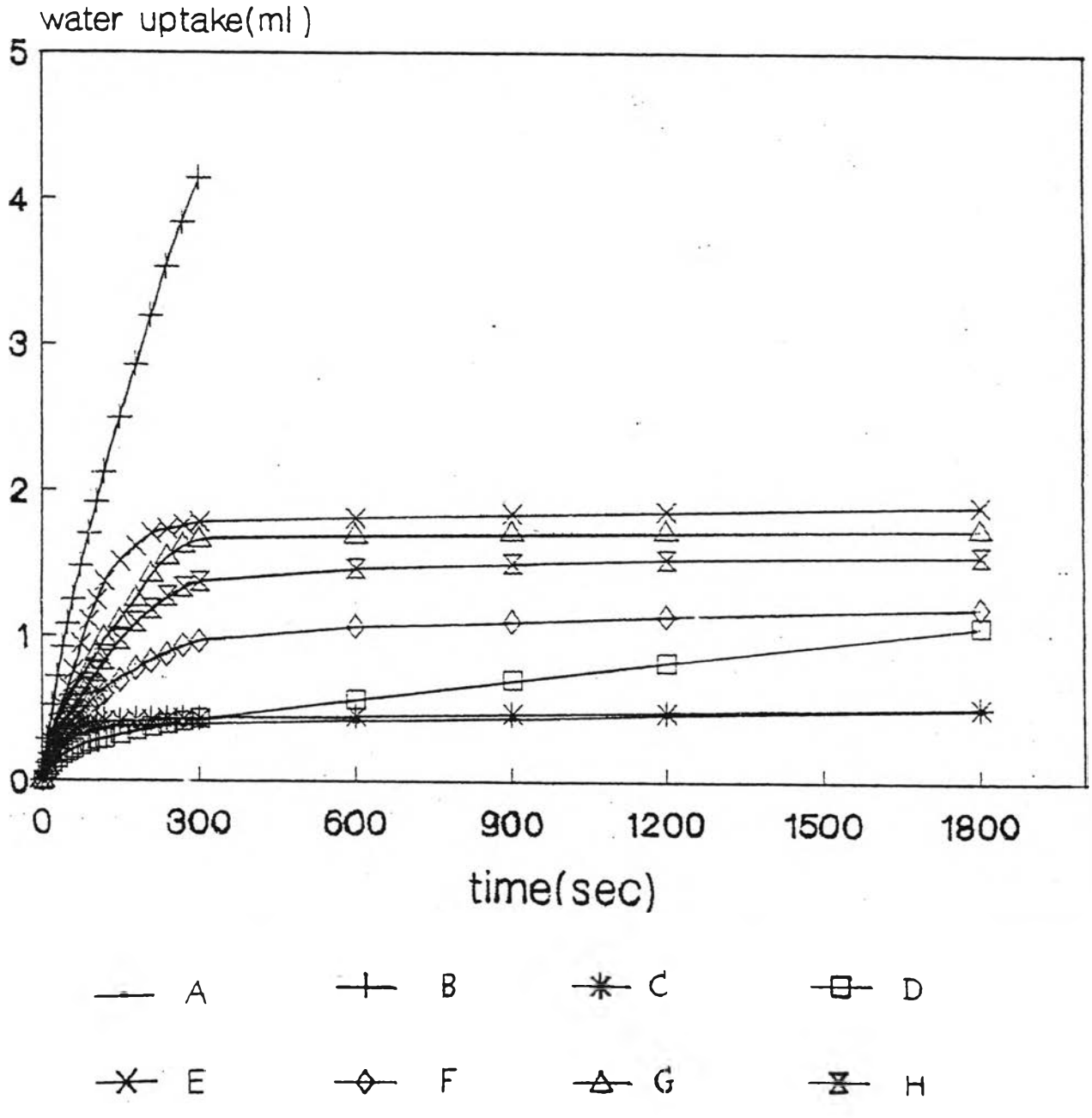


Figure 36 Water penetration profile of 500 mg of pure disintegrant tablet compressed at 1500 pounds

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

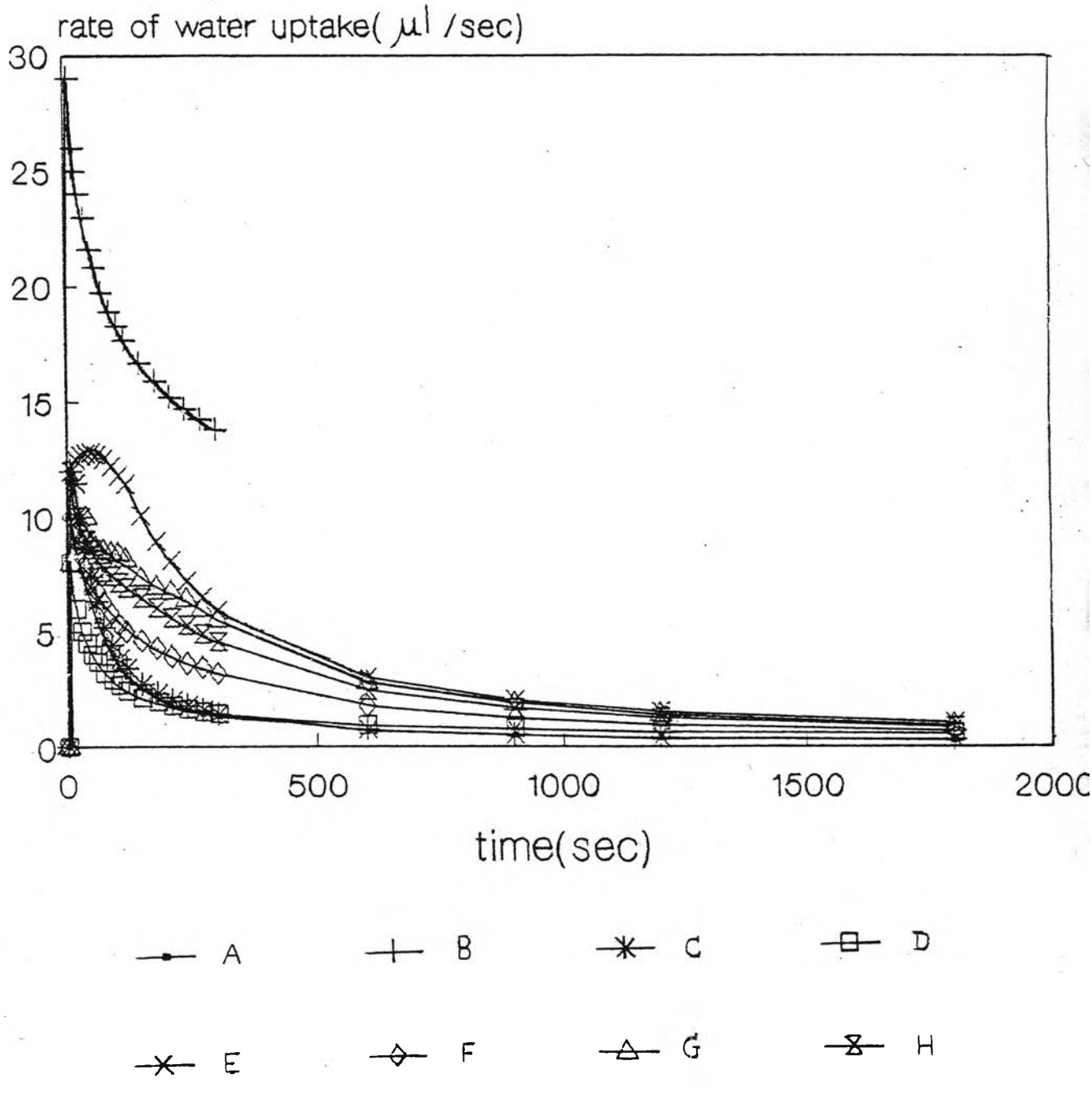


Figure 37 Rate of water penetration profile of 500 mg of pure disintegrant tablet compressed at 1500 pounds

A : corn starch B : sodium starch glycolate

C : microcrystalline cellulose D : croscarmellose sodium

E : chitin (J) F : chitin (U)

G : chitosan (J) H : chitosan (U)

plot against time was shown in Figure 38. The data indicated that after 48 hours, sodium starch glycolate exhibited the highest moisture sorption, followed by croscarmellose sodium, chitin(J), chitosan(J), chitosan(U), chitin(U), corn starch, and microcrystalline cellulose, respectively.

Evaluation of tablets

Paracetamol tablets prepared by wet granulation method using different disintegrants such as corn starch, sodium starch glycolate, microcrystalline cellulose, croscarmellose sodium, chitin (J), chitin (U), chitosan (J) and chitosan (U), and compressed at compressional forces of 600 and 900 pounds were determined for their physical properties before and after exposure to accelerated condition. These properties such weight variation, friability, hardness, disintegration time, dissolution, and percent labeled amount were evaluated and the data were summarized in Table 12-34.

A. Tablet evaluation before exposure to accelerated condition

1) Weight variation of tablet

The average weight, standard deviation, and coefficient of variation (%CV) of tablets from each formulation were given in Table 12-33. The coefficient of variation of each batch was depicted in Figure 39. It could be seen that weight variation of all batches of tablets complied with the requirements of the US standard

Table 11 Moisture sorption of pure disintegrant tablets compressed at 1,500 pounds after exposure to 75% relative humidity at room temperature at various time intervals

Disintegrants	% Moisture sorption at time intervals(hours)					
	0	2	4	8	24	48
Corn starch	0.00	1.56	2.66	4.62	6.99	8.00
Sodium starch glycolate	0.00	1.73	2.39	5.07	9.91	12.60
Microcrystalline cellulose	0.00	1.00	1.20	2.13	3.78	4.36
Croscarmellose sodium	0.00	1.51	3.40	4.97	7.05	10.55
Chitin (J)	0.00	1.49	1.86	3.51	7.01	9.18
Chitin (U)	0.00	1.27	1.44	3.42	5.21	6.35
Chitosan (J)	0.00	2.00	2.92	4.42	8.14	9.78
Chitosan (U)	0.00	1.60	2.15	3.45	6.58	8.01

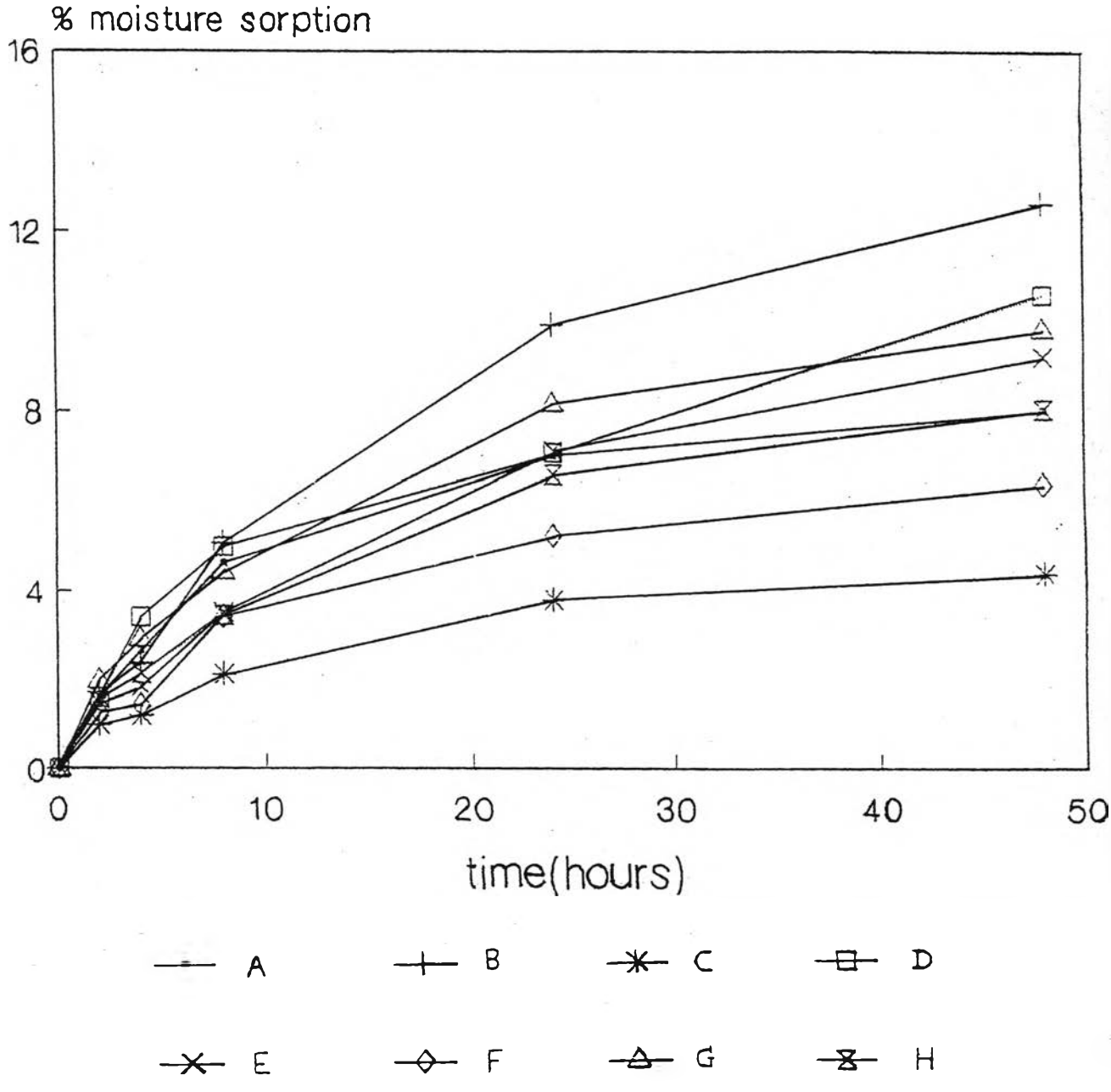


Figure 38 Moisture sorption profile of 500 mg of pure disintegrant tablets compressed at 1500 pounds after exposure to 75% relative humidity at room temperature at various time intervals

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

Table 12 Physical properties of paracetamol tablets containing 5% corn starch compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	551.81 ± 8.01	553.63 ± 8.03	553.83 ± 8.28	558.82 ± 8.26
% CV	1.45	1.45	1.48	1.47
range	526.14-581.52	525.94-581.31	528.02-583.60	528.03-583.61
friability				
%	0.62	0.48	0.48	0.31
hardness (kp)				
$\bar{X} \pm SD$	7.38 ± 0.08	9.23 ± 0.11	10.23 ± 0.10	13.32 ± 0.13
% CV	1.08	1.19	0.97	0.97
disintegration time (secs)				
$\bar{X} \pm SD$	159.50 ± 3.81	245.00 ± 2.78	340.83 ± 8.30	447.00 ± 12.55
% CV	2.38	1.95	2.43	2.80
% drug dissolved (mg)				
5 mins (% CV)	166.81 (1.83)	142.66 (1.82)	89.89 (2.10)	63.88 (2.11)
10 mins (% CV)	245.85 (1.52)	239.20 (1.72)	165.28 (1.82)	119.06 (1.85)
15 mins (% CV)	397.77 (1.64)	348.90 (1.60)	250.11 (1.90)	164.72 (1.51)
20 mins (% CV)	424.14 (1.37)	417.12 (1.59)	297.34 (1.62)	243.57 (1.56)
25 mins (% CV)	449.18 (0.98)	450.30 (1.28)	356.54 (1.29)	299.79 (1.22)
30 mins (% CV)	472.98 (1.06)	472.18 (1.16)	394.13 (1.09)	351.84 (1.14)

Table 13 Physical properties of paracetamol tablets containing 5% sodium starch glycolate compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
X ± SD	552.21 ± 6.41	556.16 ± 6.36	557.58 ± 6.82	560.61 ± 6.48
% CV	1.16	1.14	1.22	1.15
range	524.60-579.82	528.35-583.96	259.70-585.46	532.58-583.64
friability				
%	0.58	0.45	0.42	0.29
hardness (kp)				
X ± SD	8.28 ± 0.09	9.98 ± 0.11	10.92 ± 0.10	13.17 ± 0.13
% CV	1.23	1.10	0.91	0.98
disintegration time (secs)				
X ± SD	34.50 ± 0.46	36.83 ± 0.38	56.17 ± 0.86	60.83 ± 0.92
% CV	1.33	1.03	1.53	1.51
% drug dissolved (mg)				
5 mins (% CV)	305.54 (1.27)	300.34 (1.58)	297.74 (1.21)	288.87 (1.33)
10 mins (% CV)	406.44 (1.32)	393.97 (1.33)	392.99 (1.19)	390.73 (1.28)
15 mins (% CV)	451.27 (1.16)	439.66 (1.27)	443.41 (1.15)	441.43 (1.09)
20 mins (% CV)	461.50 (1.07)	464.76 (1.15)	461.95 (0.96)	461.61 (1.18)
25 mins (% CV)	469.69 (0.97)	469.63 (1.15)	471.50 (1.05)	468.90 (1.03)
30 mins (% CV)	482.63 (1.04)	481.50 (0.93)	481.62 (0.94)	479.35 (1.12)

Table 14 Physical properties of paracetamol tablets containing 5% microcrystalline cellulose compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	546.40 ± 5.23	554.03 ± 5.46	548.29 ± 5.39	555.95 ± 5.49
% CV	0.95	0.98	0.98	0.98
range	519.08-573.72	526.33-581.73	520.87-581.73	528.15-583.74
friability				
%	0.62	0.50	0.36	0.23
hardness (kp)				
$\bar{X} \pm SD$	7.83 ± 0.08	9.48 ± 0.10	11.65 ± 0.13	13.68 ± 0.13
% CV	1.02	1.05	1.11	0.95
disintegration time (secs)				
$\bar{X} \pm SD$	680.17 ± 11.42	> 30 mins	1264.67 ± 16.14	> 30 mins
% CV	1.67		1.27	
% drug dissolved (mg)				
5 mins (% CV)	18.58 (2.20)	14.87 (2.28)	14.88 (2.39)	12.25 (2.69)
10 mins (% CV)	37.56 (2.05)	29.33 (2.18)	31.44 (2.18)	25.84 (2.61)
15 mins (% CV)	65.03 (1.61)	52.34 (2.02)	59.04 (1.72)	45.08 (2.39)
20 mins (% CV)	91.60 (1.47)	84.54 (1.84)	86.25 (1.62)	74.44 (2.20)
25 mins (% CV)	126.36 (1.34)	117.84 (1.66)	119.48 (1.39)	106.48 (2.12)
30 mins (% CV)	150.50 (1.40)	144.55 (1.71)	144.48 (1.24)	136.55 (2.02)

Table 15 Physical properties of paracetamol tablets containing 10% microcrystalline cellulose compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	576.19 ± 5.23	575.10 ± 4.43	576.81 ± 5.26	576.13 ± 4.43
% CV	0.91	0.77	0.91	0.76
range	547.38-605.00	546.35-603.85	547.97-605.05	547.32-604.93
friability				
%	0.58	0.47	0.32	0.20
hardness (kp)				
$\bar{X} \pm SD$	8.05 ± 0.09	9.84 ± 0.09	11.81 ± 0.12	13.91 ± 0.15
% CV	1.11	0.91	1.01	1.07
disintegration time (secs)				
$\bar{X} \pm SD$	423.33 ± 8.16	1746.66 ± 24.63	784.33 ± 14.39	> 30 mins
% CV	1.92	1.41	1.83	
% drug dissolved (mg)				
5 mins (% CV)	26.84 (1.45)	20.36 (1.33)	22.92 (1.17)	18.83 (1.32)
10 mins (% CV)	42.89 (1.30)	34.39 (1.28)	34.84 (1.26)	29.58 (1.81)
15 mins (% CV)	74.25 (1.41)	57.71 (1.18)	63.19 (1.12)	52.73 (1.03)
20 mins (% CV)	116.99 (1.12)	94.70 (1.09)	109.92 (1.20)	85.87 (1.08)
25 mins (% CV)	147.10 (1.03)	123.27 (1.12)	133.75 (1.08)	111.85 (1.13)
30 mins (% CV)	169.13 (0.98)	150.80 (1.09)	152.96 (1.14)	134.31 (1.11)

Table 16 Physical properties of paracetamol tablets containing 2% croscarmellose sodium compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm$ SD	538.71 ± 6.90	537.41 ± 6.08	539.95 ± 7.05	538.18 ± 6.68
% CV	1.28	1.13	1.30	1.24
range	511.77-565.64	510.54-564.28	512.95-566.94	511.27-565.09
friability				
%	0.67	0.47	0.43	0.28
hardness (kp)				
$\bar{X} \pm$ SD	7.56 ± 0.07	9.30 ± 0.10	10.33 ± 0.11	13.71 ± 0.15
% CV	0.92	1.07	1.06	1.13
disintegration time (secs)				
$\bar{X} \pm$ SD	36.00 ± 0.54	39.50 ± 0.67	52.00 ± 0.84	71.67 ± 0.87
% CV	1.50	1.69	1.61	1.21
% drug dissolved (mg)				
5 mins (% CV)	306.56 (1.91)	299.89 (1.61)	190.42 (1.52)	173.41 (1.62)
10 mins (% CV)	383.72 (1.83)	384.51 (1.51)	285.70 (1.40)	284.98 (1.50)
15 mins (% CV)	450.93 (1.75)	448.21 (1.48)	371.53 (1.29)	371.01 (1.49)
20 mins (% CV)	462.74 (1.73)	455.95 (1.26)	432.98 (1.27)	427.32 (1.39)
25 mins (% CV)	470.33 (1.37)	467.09 (1.17)	457.45 (1.17)	452.94 (1.10)
30 mins (% CV)	479.80 (1.42)	478.15 (1.08)	472.36 (1.09)	473.69 (1.03)

Table 17 Physical properties of paracetamol tablets containing 5% croscarmellose sodium compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 ibs.
weight variation (mg)				
$\bar{X} \pm SD$	552.49 ± 6.65	552.53 ± 6.29	553.36 ± 6.78	556.28 ± 6.42
% CV	1.20	1.13	1.22	1.15
range	524.86-580.11	524.90-580.15	527.59-583.12	528.46-584.09
friability				
%	0.65	0.48	0.39	0.25
hardness (kp)				
$\bar{X} \pm SD$	7.53 ± 0.09	9.48 ± 0.10	10.39 ± 0.11	13.35 ± 0.15
% CV	1.19	1.06	1.05	1.12
disintegration time (secs)				
$\bar{X} \pm SD$	79.17 ± 1.34	114.33 ± 1.53	132.50 ± 2.19	175.50 ± 2.83
% CV	1.69	1.33	1.65	1.61
% drug dissolved (mg)				
5 mins (% CV)	294.46 (1.82)	287.56 (1.90)	173.78 (1.92)	167.26 (1.94)
10 mins (% CV)	383.03 (1.80)	378.65 (1.75)	281.99 (1.75)	282.18 (1.72)
15 mins (% CV)	440.51 (1.59)	426.50 (1.49)	358.86 (1.76)	346.76 (1.73)
20 mins (% CV)	452.79 (1.47)	451.02 (1.56)	434.33 (1.39)	432.11 (1.57)
25 mins (% CV)	467.65 (1.08)	462.67 (1.28)	454.85 (1.30)	447.26 (1.48)
30 mins (% CV)	475.28 (0.95)	478.12 (1.09)	475.67 (1.16)	475.10 (1.06)

Table 18 Physical properties of paracetamol tablets containing 1.5% chitin (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	549.58 ± 5.95	556.63 ± 5.27	551.31 ± 5.97	558.93 ± 5.44
% CV	1.08	0.94	1.08	0.97
range	522.10-576.06	528.79-584.46	523.74-578.87	530.98-586.87
friability				
%	0.56	0.40	0.43	0.24
hardness (kp)				
$\bar{X} \pm SD$	7.93 ± 0.09	9.65 ± 0.10	11.29 ± 0.16	13.70 ± 0.14
% CV	1.13	1.03	1.07	1.02
disintegration time (secs)				
$\bar{X} \pm SD$	445.00 ± 8.41	506.17 ± 9.14	860.67 ± 12.71	1325.00 ± 20.76
% CV	1.88	1.80	1.47	1.56
% drug dissolved (mg)				
5 mins (% CV)	37.43 (1.83)	34.93 (1.63)	33.66 (1.94)	29.85 (1.86)
10 mins (% CV)	74.55 (1.70)	68.78 (1.57)	68.30 (1.71)	61.70 (1.75)
15 mins (% CV)	128.06 (1.77)	108.81 (1.20)	105.08 (1.80)	102.02 (1.48)
20 mins (% CV)	167.78 (1.75)	161.88 (1.17)	153.89 (1.21)	144.99 (1.36)
25 mins (% CV)	219.73 (1.40)	202.54 (1.20)	193.51 (1.34)	181.33 (1.32)
30 mins (% CV)	247.50 (1.12)	238.28 (1.15)	239.64 (1.07)	218.14 (1.17)

Table 19 Physical properties of paracetamol tablets containing 3% chitin (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm$ SD	547.75 ± 5.87	555.88 ± 5.74	548.64 ± 5.92	557.29 ± 5.59
% CV	1.07	1.03	1.08	1.00
range	520.36-575.13	528.08-583.67	521.20-576.07	529.42-585.15
friability				
%	0.58	0.46	0.44	0.26
hardness (kp)				
$\bar{X} \pm$ SD	7.90 ± 0.08	9.48 ± 0.10	11.16 ± 0.11	13.55 ± 0.12
% CV	1.01	1.05	0.98	0.88
disintegration time (secs)				
$\bar{X} \pm$ SD	121.17 ± 2.66	241.00 ± 4.70	319.00 ± 5.95	575.00 ± 12.07
% CV	2.19	1.95	1.86	2.10
% drug dissolved (mg)				
5 mins (% CV)	74.68 (1.21)	64.22 (1.62)	61.24 (1.43)	55.31 (1.65)
10 mins (% CV)	123.87 (1.33)	118.70 (1.65)	119.33 (1.31)	106.03 (1.33)
15 mins (% CV)	177.13 (1.18)	167.72 (1.32)	162.80 (1.23)	156.06 (1.26)
20 mins (% CV)	282.70 (1.05)	279.92 (1.09)	260.88 (1.34)	233.37 (1.23)
25 mins (% CV)	313.03 (1.02)	302.83 (1.18)	298.46 (1.17)	278.96 (1.17)
30 mins (% CV)	356.09 (1.12)	346.26 (1.13)	337.40 (1.07)	319.48 (1.01)

Table 20 Physical properties of paracetamol tablets containing 5% chitin (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	551.11 ± 5.85	560.50 ± 6.13	552.93 ± 5.83	563.24 ± 6.08
% CV	1.06	1.09	1.05	1.08
range	523.55-578.66	532.47-588.52	525.28-580.57	535.07-591.40
friability				
%	0.59	0.48	0.46	0.26
hardness (kp)				
$\bar{X} \pm SD$	7.80 ± 0.07	9.39 ± 0.10	11.18 ± 0.12	13.48 ± 0.14
% CV	0.89	1.06	1.07	1.03
disintegration time (secs)				
$\bar{X} \pm SD$	97.17 ± 1.11	119.67 ± 1.92	152.83 ± 2.49	203.33 ± 2.38
% CV	1.14	1.60	1.63	1.17
% drug dissolved (mg)				
5 mins (% CV)	155.36 (1.83)	132.88 (1.90)	139.22 (1.82)	115.79 (1.90)
10 mins (% CV)	226.81 (1.64)	212.86 (1.85)	226.89 (1.41)	189.80 (1.95)
15 mins (% CV)	368.53 (1.46)	329.61 (1.92)	301.23 (1.59)	294.04 (1.79)
20 mins (% CV)	405.26 (1.25)	398.88 (1.87)	359.30 (1.41)	380.51 (1.71)
25 mins (% CV)	449.52 (1.27)	425.73 (1.78)	414.97 (1.20)	419.81 (1.60)
30 mins (% CV)	477.28 (1.24)	472.04 (1.65)	459.04 (1.38)	453.61 (1.68)

Table 21 Physical properties of paracetamol tablets containing 7% chitin (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	561.07 ± 6.03	565.01 ± 5.95	562.57 ± 6.19	566.80 ± 6.12
% CV	1.07	1.05	1.10	1.08
range	533.01-589.12	536.76-593.26	534.44-590.69	538.46-595.14
friability				
%	0.61	0.50	0.49	0.29
hardness (kp)				
$\bar{X} \pm SD$	7.73 ± 0.09	9.28 ± 0.10	11.17 ± 0.13	13.46 ± 0.12
% CV	1.16	1.07	1.16	0.89
disintegration time (secs)				
$\bar{X} \pm SD$	46.50 ± 0.73	60.54 ± 0.77	70.83 ± 0.98	134.33 ± 1.65
% CV	1.57	1.27	1.38	1.22
% drug dissolved (mg)				
5 mins (% CV)	212.77 (1.46)	192.87 (1.86)	194.13 (1.68)	160.91 (2.23)
10 mins (% CV)	336.46 (1.08)	302.54 (1.71)	261.37 (1.47)	242.40 (1.91)
15 mins (% CV)	414.61 (1.34)	398.98 (1.80)	338.02 (1.27)	321.32 (1.51)
20 mins (% CV)	448.36 (1.12)	425.95 (1.44)	415.43 (1.32)	389.69 (1.47)
25 mins (% CV)	463.00 (1.08)	450.60 (1.33)	442.73 (1.17)	440.05 (1.39)
30 mins (% CV)	481.11 (1.04)	478.16 (1.28)	478.37 (1.19)	475.12 (1.12)

Table 22 Physical properties of paracetamol tablets containing 1.5% chitin (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	546.74 ± 6.24	545.46 ± 5.26	548.23 ± 6.28	546.87 ± 5.43
% CV	1.14	0.96	1.15	0.99
range	519.40-574.07	518.18-572.73	520.82-575.64	519.52-574.21
friability				
%	0.58	0.41	0.39	0.26
hardness (kp)				
$\bar{X} \pm SD$	7.90 ± 0.09	9.58 ± 0.10	11.04 ± 0.13	13.62 ± 0.15
% CV	1.13	1.04	1.17	1.10
disintegration time (secs)				
$\bar{X} \pm SD$	577.67 ± 9.82	669.67 ± 12.70	934.17 ± 19.56	1359.17 ± 23.64
% CV	1.70	1.89	2.09	1.74
% drug dissolved (mg)				
5 mins (% CV)	18.15 (1.72)	15.98 (1.92)	13.97 (1.84)	13.81 (1.82)
10 mins (% CV)	43.51 (1.81)	40.64 (1.80)	36.82 (1.85)	31.23 (1.59)
15 mins (% CV)	79.26 (1.59)	74.76 (1.81)	56.37 (1.55)	52.97 (1.49)
20 mins (% CV)	121.44 (1.60)	111.25 (1.59)	84.24 (1.42)	87.41 (1.46)
25 mins (% CV)	149.51 (1.35)	145.84 (1.36)	118.69 (1.50)	116.70 (1.28)
30 mins (% CV)	172.85 (1.26)	163.80 (1.30)	145.55 (1.35)	135.86 (1.19)

Table 23 Physical properties of paracetamol tablets containing 3% chitin (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm$ SD	543.04 ± 6.02	542.19 ± 5.55	543.96 ± 6.14	543.37 ± 5.64
% CV	1.11	1.02	1.13	1.04
range	515.89-570.19	515.08-569.30	516.76-571.16	516.20-570.54
friability				
%	0.60	0.48	0.40	0.26
hardness (kp)				
$\bar{X} \pm$ SD	7.87 ± 0.08	9.49 ± 0.10	11.37 ± 0.11	13.58 ± 0.14
% CV	1.01	1.05	0.96	1.04
disintegration time (secs)				
$\bar{X} \pm$ SD	165.83 ± 2.81	386.33 ± 4.22	507.83 ± 6.54	872.50 ± 10.27
% CV	1.69	1.09	1.28	1.17
% drug dissolved (mg)				
5 mins (% CV)	48.56 (1.72)	37.67 (1.83)	32.40 (1.91)	29.98 (1.72)
10 mins (% CV)	92.93 (1.73)	85.87 (1.82)	80.43 (1.82)	79.53 (1.76)
15 mins (% CV)	153.36 (1.60)	143.82 (1.90)	124.76 (1.52)	128.01 (1.71)
20 mins (% CV)	214.93 (1.39)	208.59 (1.58)	188.99 (1.45)	190.72 (1.59)
25 mins (% CV)	289.46 (1.24)	271.95 (1.24)	259.27 (1.32)	253.45 (1.37)
30 mins (% CV)	329.80 (1.11)	314.82 (1.19)	317.59 (1.21)	308.15 (1.55)

Table 24 Physical properties of paracetamol tablets containing 5% chitin (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	552.17 ± 5.85	552.89 ± 5.29	553.44 ± 5.98	554.82 ± 5.38
% CV	1.06	0.95	1.08	0.97
range	524.56-579.77	525.24-580.53	525.76-581.11	527.08-582.56
friability				
%	0.64	0.47	0.43	0.27
hardness (kp)				
$\bar{X} \pm SD$	7.80 ± 0.07	9.39 ± 0.10	11.33 ± 0.10	13.42 ± 0.13
% CV	0.89	1.06	0.88	0.96
disintegration time (secs)				
$\bar{X} \pm SD$	115.50 ± 1.63	176.50 ± 2.93	175.00 ± 2.07	319.17 ± 3.96
% CV	1.41	1.66	1.18	1.24
% drug dissolved (mg)				
5 mins (% CV)	142.92 (1.76)	125.55 (1.82)	118.32 (1.73)	113.36 (1.91)
10 mins (% CV)	222.53 (1.58)	202.55 (1.56)	201.06 (1.52)	172.96 (1.89)
15 mins (% CV)	331.58 (1.46)	316.81 (1.58)	309.51 (1.57)	289.08 (1.52)
20 mins (% CV)	413.35 (1.37)	391.68 (1.34)	357.52 (1.34)	342.81 (1.52)
25 mins (% CV)	441.22 (1.38)	427.25 (1.16)	415.57 (1.21)	400.30 (1.49)
30 mins (% CV)	475.79 (1.22)	465.91 (1.19)	458.25 (1.15)	448.85 (1.33)

Table 25 Physical properties of paracetamol tablets containing 7% chitin (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	560.25 ± 6.21	560.09 ± 6.21	560.91 ± 6.33	561.26 ± 6.28
% CV	1.11	1.10	1.13	1.11
range	532.23-588.26	532.08-588.09	532.86-588.95	533.19-589.32
friability				
%	0.62	0.39	0.45	0.28
hardness (kp)				
$\bar{X} \pm SD$	7.78 ± 0.08	9.41 ± 0.10	11.20 ± 0.12	13.42 ± 0.15
% CV	1.02	1.06	1.07	1.11
disintegration time (secs)				
$\bar{X} \pm SD$	41.17 ± 0.82	67.67 ± 1.25	72.33 ± 1.33	136.67 ± 2.08
% CV	1.99	1.84	1.83	1.52
% drug dissolved (mg)				
5 mins (% CV)	188.49 (1.62)	151.75 (1.72)	151.80 (1.65)	128.61 (1.93)
10 mins (% CV)	293.23 (1.60)	274.46 (1.64)	266.24 (1.70)	227.06 (1.63)
15 mins (% CV)	375.58 (1.48)	350.48 (1.58)	354.34 (1.61)	333.82 (1.59)
20 mins (% CV)	428.89 (1.30)	425.16 (1.28)	429.08 (1.44)	395.11 (1.40)
25 mins (% CV)	460.02 (1.00)	460.60 (1.09)	461.56 (1.30)	451.29 (1.40)
30 mins (% CV)	479.43 (0.98)	480.10 (1.00)	477.89 (1.33)	475.44 (1.11)

Table 26 Physical properties of paracetamol tablets containing 1.5% chitosan (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	536.72 ± 5.02	537.13 ± 4.48	537.87 ± 4.99	537.46 ± 4.46
% CV	0.93	0.78	0.92	0.83
range	509.88-563.55	510.27-563.98	510.97-564.76	510.58-564.33
friability				
%	0.59	0.41	0.39	0.25
hardness (kp)				
$\bar{X} \pm SD$	7.83 ± 0.08	9.51 ± 0.10	11.17 ± 0.11	13.40 ± 0.15
% CV	1.02	1.05	0.98	1.11
disintegration time (secs)				
$\bar{X} \pm SD$	298.33 ± 3.83	498.33 ± 5.58	506.67 ± 7.14	1065.33 ± 12.02
% CV	1.28	1.11	1.41	1.12
% drug dissolved (mg)				
5 mins (% CV)	40.70 (1.65)	35.64 (1.82)	38.03 (1.05)	31.84 (1.72)
10 mins (% CV)	72.69 (1.67)	63.59 (1.70)	59.21 (1.26)	51.86 (1.81)
15 mins (% CV)	118.56 (1.46)	116.85 (1.59)	110.43 (1.05)	96.25 (1.20)
20 mins (% CV)	152.28 (1.27)	143.53 (1.38)	140.31 (1.13)	118.50 (1.26)
25 mins (% CV)	179.89 (1.31)	165.27 (1.41)	167.74 (1.11)	158.57 (1.07)
30 mins (% CV)	226.68 (1.17)	206.69 (1.32)	213.99 (1.03)	200.65 (1.11)

Table 27 Physical properties of paracetamol tablets containing 3% chitosan (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	547.97 ± 3.51	546.02 ± 3.33	549.20 ± 3.32	546.26 ± 3.17
% CV	0.64	0.61	0.60	0.58
range	520.57-575.36	518.72-573.32	521.74-576.66	518.94-573.57
friability				
%	0.61	0.44	0.40	0.24
hardness (kp)				
$\bar{X} \pm SD$	7.77 ± 0.07	9.38 ± 0.10	11.02 ± 0.11	13.43 ± 0.15
% CV	0.90	1.06	0.99	1.11
disintegration time (secs)				
$\bar{X} \pm SD$	140.00 ± 2.47	198.00 ± 3.16	290.00 ± 4.36	405.83 ± 6.70
% CV	1.76	1.59	1.50	1.65
% drug dissolved (mg)				
5 mins (% CV)	70.27 (1.61)	65.75 (1.83)	55.30 (1.93)	51.74 (1.56)
10 mins (% CV)	132.70 (1.57)	115.12 (1.43)	117.11 (1.82)	103.63 (1.54)
15 mins (% CV)	184.73 (1.63)	167.50 (1.20)	169.50 (1.51)	153.99 (1.58)
20 mins (% CV)	248.25 (1.71)	242.48 (1.24)	242.76 (1.62)	222.85 (1.35)
25 mins (% CV)	306.64 (1.35)	300.61 (1.31)	299.87 (1.29)	291.09 (1.12)
30 mins (% CV)	368.94 (1.16)	358.36 (1.11)	347.90 (1.12)	334.31 (1.03)

Table 28 Physical properties of paracetamol tablets containing 5% chitosan (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	545.21 ± 3.32	544.37 ± 3.39	546.81 ± 3.33	544.81 ± 3.51
% CV	0.61	0.62	0.61	0.64
range	517.95-572.47	517.15-571.59	519.47-574.15	517.51-572.05
friability				
%	0.61	0.47	0.41	0.24
hardness (kp)				
$\bar{X} \pm SD$	7.71 ± 0.08	9.26 ± 0.09	11.02 ± 0.11	13.28 ± 0.12
% CV	1.03	0.97	0.99	0.90
disintegration time (secs)				
$\bar{X} \pm SD$	76.33 ± 1.07	81.00 ± 1.03	104.33 ± 1.54	123.00 ± 1.66
% CV	1.40	1.27	1.47	1.35
% drug dissolved (mg)				
5 mins (% CV)	166.45 (1.96)	154.12 (1.97)	141.12 (1.83)	135.80 (1.71)
10 mins (% CV)	254.88 (1.85)	234.54 (1.64)	231.26 (1.60)	219.16 (1.64)
15 mins (% CV)	369.59 (1.36)	344.94 (1.57)	343.25 (1.33)	334.97 (1.63)
20 mins (% CV)	408.65 (1.53)	403.10 (1.44)	396.83 (1.47)	387.26 (4.47)
25 mins (% CV)	446.12 (1.37)	434.92 (1.30)	433.56 (1.21)	424.96 (1.20)
30 mins (% CV)	474.56 (1.10)	473.98 (1.23)	471.96 (1.15)	468.09 (1.29)

Table 29 Physical properties of paracetamol tablets containing 7% chitosan (J) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	555.69 ± 2.55	556.30 ± 3.71	556.90 ± 2.55	559.24 ± 3.73
% CV	0.46	0.67	0.46	0.66
range	527.90-583.47	528.48-584.11	529.05-584.74	531.27-587.20
friability				
%	0.62	0.49	0.44	0.29
hardness (kp)				
$\bar{X} \pm SD$	7.68 ± 0.08	9.30 ± 0.09	10.89 ± 0.11	13.14 ± 0.14
% CV	1.04	0.96	1.01	1.06
disintegration time (secs)				
$\bar{X} \pm SD$	36.17 ± 0.59	39.50 ± 0.61	53.33 ± 0.72	79.17 ± 1.24
% CV	1.63	1.54	1.35	1.56
% drug dissolved (mg)				
5 mins (% CV)	236.90 (1.50)	214.67 (1.72)	219.14 (1.89)	200.44 (1.93)
10 mins (% CV)	382.12 (1.39)	375.11 (1.43)	345.26 (1.39)	350.57 (1.60)
15 mins (% CV)	441.42 (1.26)	426.72 (1.24)	431.92 (1.23)	417.10 (1.36)
20 mins (% CV)	467.82 (1.09)	459.95 (1.13)	446.78 (1.25)	447.00 (1.28)
25 mins (% CV)	473.53 (1.33)	474.42 (1.23)	470.58 (1.34)	467.86 (1.47)
30 mins (% CV)	480.68 (1.23)	481.03 (1.02)	480.79 (1.20)	478.46 (1.18)

Table 30 Physical properties of paracetamol tablets containing 1.5% chitosan (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	535.45 ± 6.19	545.59 ± 5.56	535.69 ± 6.17	545.95 ± 5.57
% CV	1.15	1.02	1.15	1.02
range	508.67-562.22	518.31-572.87	508.90-562.47	518.65-573.24
friability				
%	0.56	0.42	0.40	0.23
hardness (kp)				
$\bar{X} \pm SD$	7.86 ± 0.08	8.45 ± 0.10	11.09 ± 0.11	13.43 ± 0.15
% CV	1.01	1.05	0.99	1.11
disintegration time (secs)				
$\bar{X} \pm SD$	507.50 ± 10.04	644.83 ± 12.82	997.50 ± 20.89	1342.85 ± 25.65
% CV	1.97	1.98	2.09	1.91
% drug dissolved (mg)				
5 mins (% CV)	26.82 (1.82)	21.74 (1.96)	24.78 (1.77)	18.46 (1.95)
10 mins (% CV)	68.94 (1.62)	62.81 (1.85)	62.56 (1.69)	56.57 (1.82)
15 mins (% CV)	107.43 (1.32)	103.63 (1.51)	92.79 (1.48)	85.16 (1.65)
20 mins (% CV)	144.56 (1.46)	132.80 (1.67)	127.06 (1.51)	122.76 (1.68)
25 mins (% CV)	181.56 (1.36)	172.54 (1.44)	171.86 (1.35)	163.11 (1.59)
30 mins (% CV)	242.34 (1.12)	226.00 (1.16)	226.67 (1.17)	203.41 (1.45)

Table 31 Physical properties of paracetamol tablets containing 3% chitosan (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	538.21 ± 6.04	540.58 ± 5.61	540.10 ± 6.04	541.69 ± 5.50
% CV	1.12	1.03	1.11	1.01
range	511.30-565.12	513.55-567.61	513.09-567.10	514.60-568.77
friability				
%	0.61	0.44	0.42	0.26
hardness (kp)				
$\bar{X} \pm SD$	7.67 ± 0.07	9.34 ± 0.10	10.93 ± 0.10	13.39 ± 0.15
% CV	0.91	1.07	0.91	1.12
disintegration time (secs)				
$\bar{X} \pm SD$	162.00 ± 3.12	314.83 ± 6.09	375.83 ± 6.82	925.33 ± 17.90
% CV	1.92	1.93	1.81	1.93
% drug dissolved (mg)				
5 mins (% CV)	60.02 (1.71)	55.00 (1.96)	51.11 (2.25)	34.87 (1.86)
10 mins (% CV)	118.46 (1.79)	92.68 (1.64)	94.64 (1.93)	71.12 (1.88)
15 mins (% CV)	176.65 (1.63)	149.63 (1.37)	148.89 (1.63)	118.00 (1.45)
20 mins (% CV)	238.70 (1.52)	200.06 (1.44)	202.45 (1.56)	165.30 (1.40)
25 mins (% CV)	292.92 (1.42)	266.49 (1.16)	262.81 (1.64)	233.91 (1.33)
30 mins (% CV)	347.00 (1.44)	324.84 (1.05)	322.25 (1.56)	310.20 (1.02)

Table 32 Physical properties of paracetamol tablets containing 5% chitosan (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	553.68 ± 6.04	550.40 ± 6.26	555.02 ± 6.13	550.77 ± 6.24
% CV	1.09	1.14	1.10	1.13
range	525.99-581.36	522.88-577.92	527.27-582.77	523.23-578.31
friability				
%	0.63	0.45	0.45	0.25
hardness (kp)				
$\bar{X} \pm SD$	7.65 ± 0.08	9.34 ± 0.11	10.97 ± 0.12	13.31 ± 0.15
% CV	1.04	1.17	1.09	1.12
disintegration time (secs)				
$\bar{X} \pm SD$	86.33 ± 1.62	133.00 ± 2.47	200.83 ± 3.67	313.83 ± 5.84
% CV	1.87	1.85	1.82	1.86
% drug dissolved (mg)				
5 mins (% CV)	185.81 (1.68)	172.60 (1.97)	112.53 (1.88)	107.39 (1.82)
10 mins (% CV)	234.70 (1.46)	231.17 (1.90)	188.77 (1.53)	160.84 (1.71)
15 mins (% CV)	325.72 (1.27)	321.02 (1.67)	290.78 (1.38)	243.82 (1.76)
20 mins (% CV)	407.18 (1.19)	406.84 (1.50)	368.01 (1.28)	348.86 (1.50)
25 mins (% CV)	443.64 (1.07)	447.48 (1.43)	421.94 (1.25)	409.96 (1.30)
30 mins (% CV)	475.24 (1.16)	476.78 (1.24)	460.52 (1.07)	459.52 (1.27)

Table 33 Physical properties of paracetamol tablets containing 7% chitosan (U) compressed at 600 and 900 pounds, before and after exposure to accelerated condition

	Before exposure		After exposure	
	600 lbs.	900 lbs.	600 lbs.	900 lbs.
weight variation (mg)				
$\bar{X} \pm SD$	566.26 ± 7.11	566.73 ± 6.58	567.62 ± 7.10	568.93 ± 6.78
% CV	1.26	1.16	1.25	1.19
range	537.94-594.57	538.39-595.06	539.24-596.00	540.48-597.37
friability				
%	0.62	0.41	0.40	0.23
hardness (kp)				
$\bar{X} \pm SD$	6.86 ± 0.10	9.05 ± 0.10	11.29 ± 0.13	14.17 ± 0.17
% CV	1.45	1.10	1.15	1.19
disintegration time (secs)				
$\bar{X} \pm SD$	53.63 ± 1.26	72.17 ± 1.56	77.33 ± 1.52	134.50 ± 1.99
% CV	2.35	2.16	1.96	1.48
% drug dissolved (mg)				
5 mins (% CV)	227.15 (1.49)	212.67 (1.51)	189.34 (1.81)	160.03 (1.82)
10 mins (% CV)	365.41 (1.12)	338.36 (1.31)	313.29 (1.57)	294.64 (1.66)
15 mins (% CV)	401.82 (1.26)	403.53 (1.29)	393.31 (1.39)	394.62 (1.33)
20 mins (% CV)	461.71 (1.25)	461.47 (1.22)	449.25 (1.22)	451.47 (1.41)
25 mins (% CV)	471.78 (1.12)	475.10 (1.19)	470.18 (1.16)	466.16 (1.28)
30 mins (% CV)	480.55 (1.05)	483.30 (1.12)	479.67 (1.05)	478.76 (1.03)

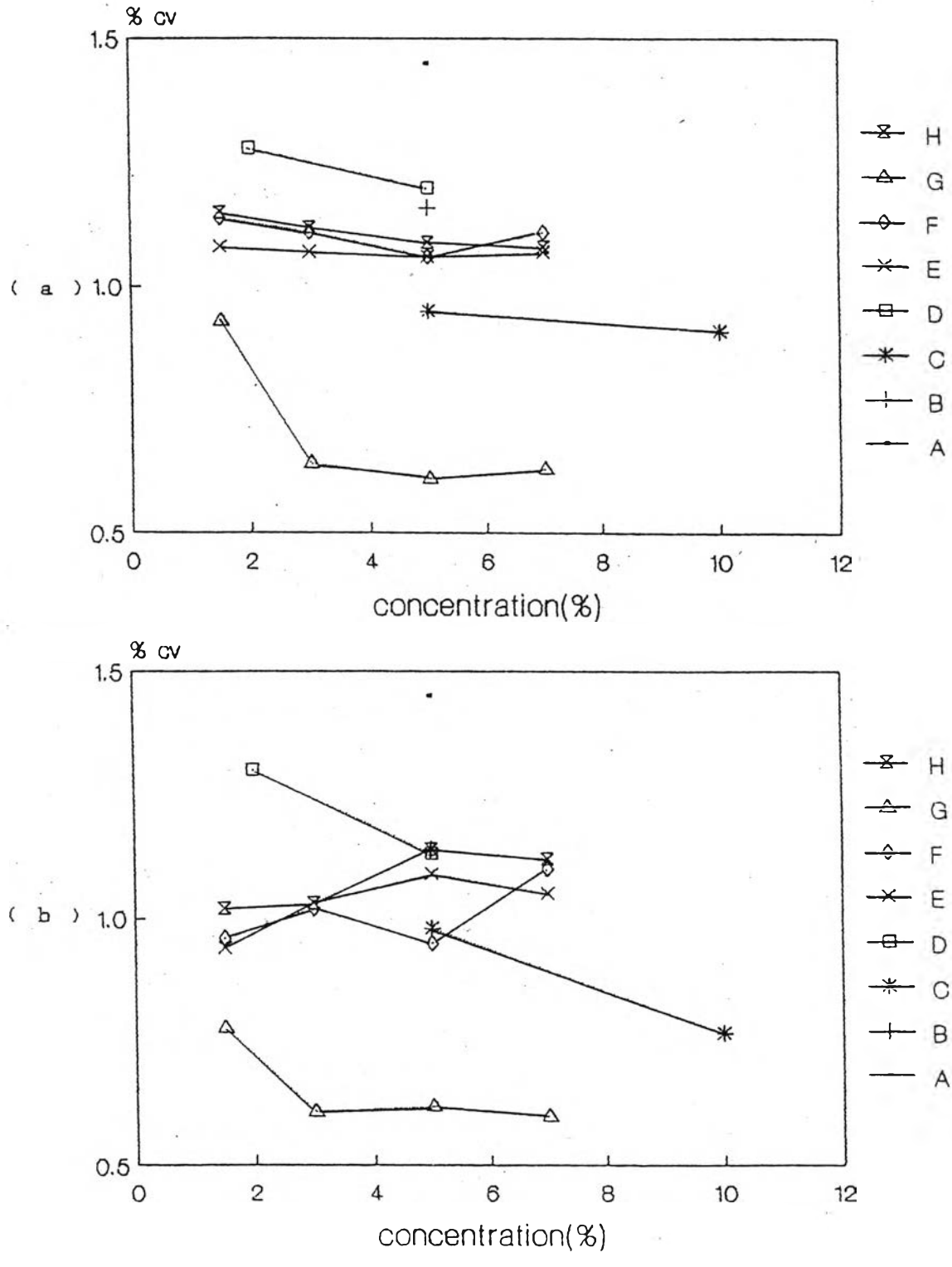


Figure 39 Percent standard weight variation of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds before exposure to accelerated condition

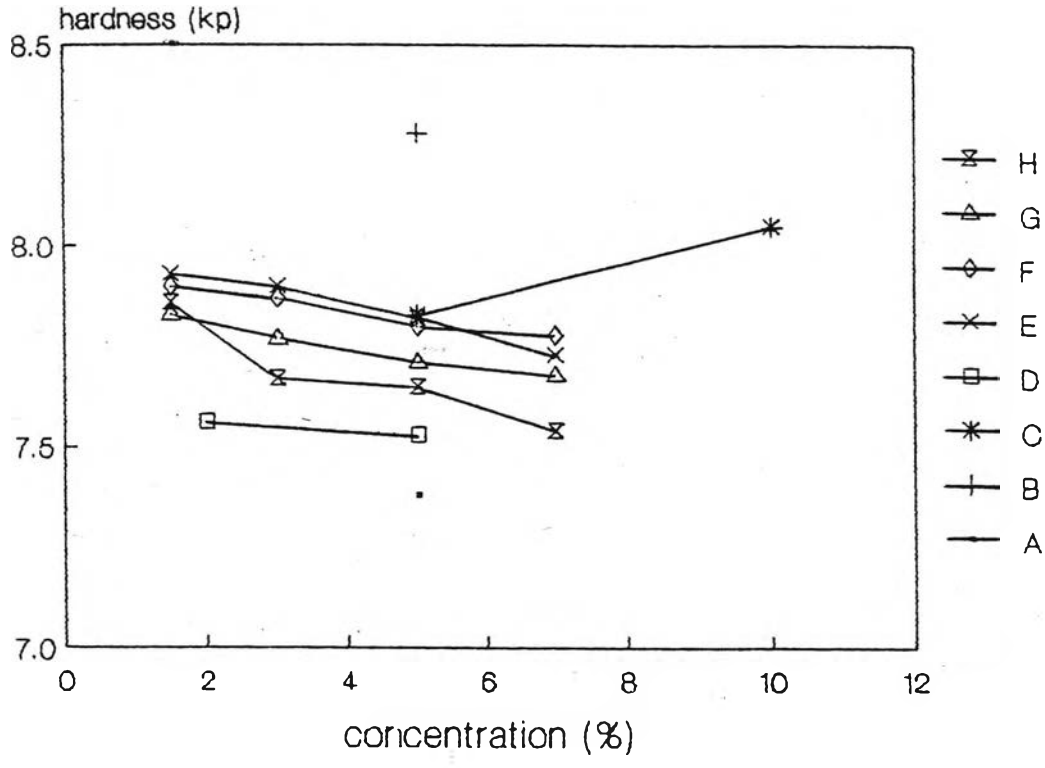
A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

that for uncoated tablets of more than 324 mg the standard required that not more than two tablets out of 20 would differ from the average weight by more than ± 5%, and none of the 20 would differ by more than ± 10% from the average weight(87), regardlessofthetype and concentration of the disintegrant. For any formulation, the coefficient of variation of tablet was less than 2 percent

2) Tablet hardness

The hardness of a random sample of ten tablets was determined for each formulation containing a certain concentration of disintegrant. The mean value, standard deviation and coefficient of variation were presented in Table 12-33. The mean value of tablet hardness was depicted in Figure 40. Tablet hardness was not dependent on disintegration type. For the concentration of disintegrant, it found that the concentration of some disintegrants affected the tablet hardness whereas some disintegrants did not. Moreover, as the amount of disintegrant increased, the results varied. Such tablets containing microcrystalline cellulose showed a slightly increase in tablet hardness by the increase of the disintegrant concentration. In croscarmellose sodium tablets showed essentially no change in tablet hardness as the concentration of disintegrant increased. And in chitin and chitosan tablets, the hardness was slightly decreased with increasing disintegrant

(a)



(b)

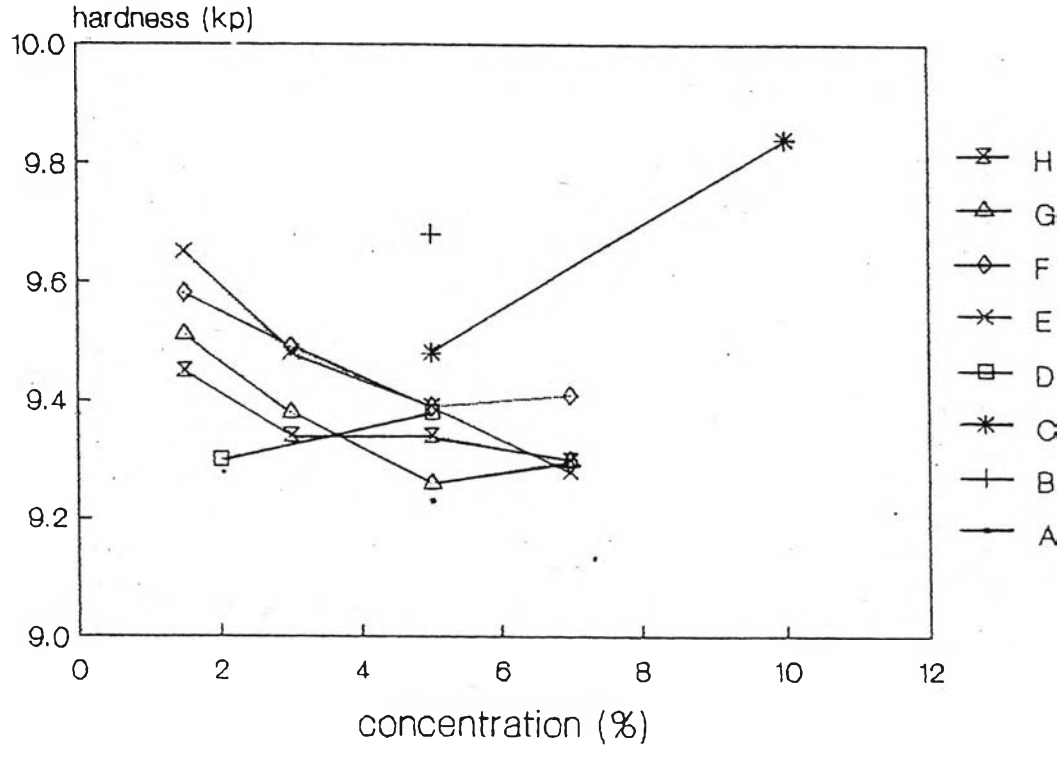


Figure 40 Hardness of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds before exposure to accelerated condition

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

concentration. Nevertheless, there were very slight differences in the variability of tablet hardness between formulations. And for all formulations, the increase of tablet hardness was found with the increasing of compressional force.

3) Tablet friability

The effect of disintegrant type and concentration on the friability cf tablets were shown in Table 12-33 and Figure 41. The results showed that the friability of tablets was less than one percent for all formulations. These values were well within the acceptable limit (less than 0.8%)(88). It was noticed that, for all formulations, the friability decreased as compressional force increased.

4) Disintegration time of tablet

The results of disintegration time of tablets made with different disintegrant types and concentrations at various compressional forces were illustrated in Table 12-33 and Figure 42. The tablets containing 5% sodium starch glycolate and 2% croscarmellose sodium gave much faster disintegration times than other formulations. These tablets disintegrated within one minute. The disintegration time increased very slightly as compressional force increased. It was suggested that an increase in compressional force was not affected to the disintegration time of these tablets. However, at the 5% level of croscarmellose sodium, the disintegration time

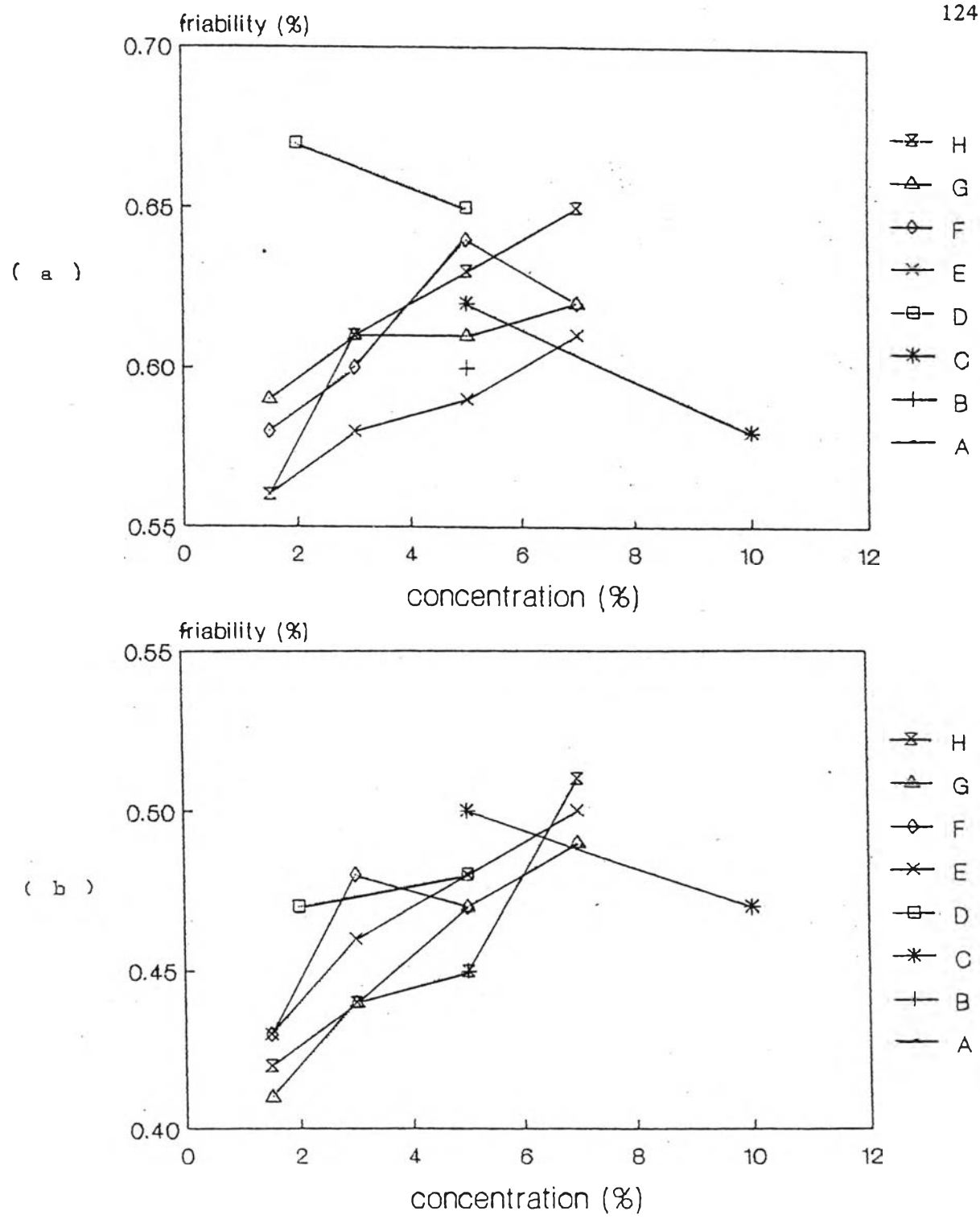


Figure 41 Percent friability of paracetamol tablets containing different disintegrants compressed at forces at 600 (a) and 900 (b) pounds before exposure to accelerated condition

A : corn starch B : sodium starch glycolate

C : microcrystalline cellulose D : croscarmellose sodium

E : chitin (J) F : chitin (U)

G : chitosan (J) H : chitosan (U)

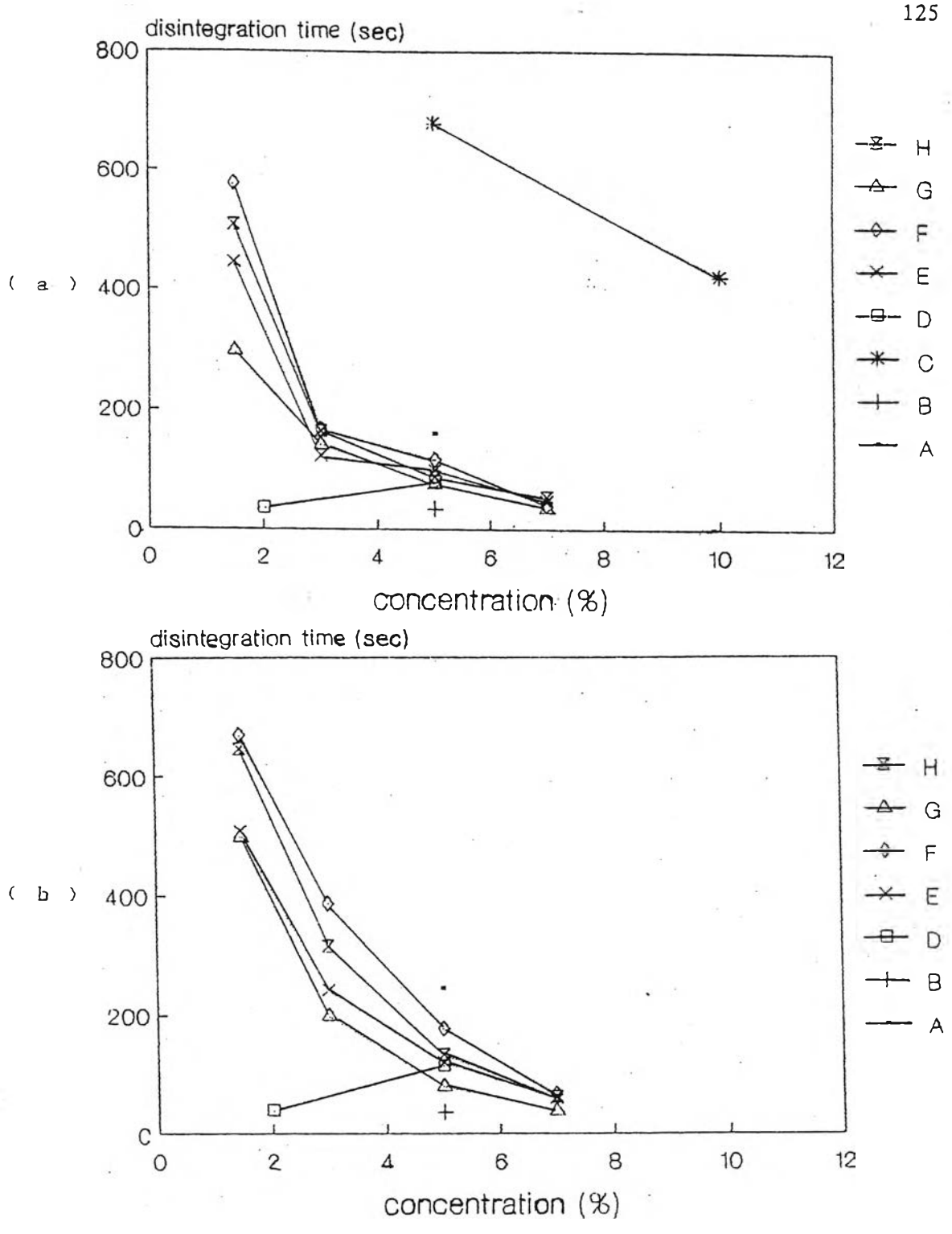


Figure 42 Disintegration time of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds before exposure to accelerated condition

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

was longer than those containing 2% level. These tablets disintegrated after one minute. And the disintegration time of this formulation was more affected by the increment in compressional force than the formulation containing about 2% level. The disintegration time of tablets containing 5% microcrystalline cellulose was the slowest. The disintegration time of these tablets compressed at the force of 600 pounds was longer than other formulations. When increasing the compressional force to 900 pounds, these tablets did not disintegrate within 30 minutes. In addition, the disintegration time decreased with increasing the concentration of disintegrant. Tablets containing 10% microcrystalline cellulose was rapidly disintegrated than those containing 5% level at the same compressional force. The ability of tablet disintegration of microcrystalline cellulose tablets had been found to be worse than those tablets made with 5% corn starch. Tablets containing 5% corn starch could disintegrate in about 3 minutes with the compressional force of 600 pounds and about 4 minutes when compressed at force of 900 pounds. For corn starch, as well as other disintegrants, the disintegration time was increased as increasing the compressional force. The disintegration time of corn starch tablets was longer than those of chitin (J), chitin (U), chitosan (J) and chitosan (U) at the same concentration and compressional force. At concentration level of 1.5%, the disintegration times of both tablets of chitin and chitosan tablets from

both sources were longer than 5% corn starch tablets at the two compressional forces. When the concentration was increased to 3%, the disintegration time of chitin (J) and chitosan (J) tablets was better than that of 5% corn starch tablets at the same compressional force but the disintegration time of chitin (U) and chitosan (U) tablets was worse than that of corn starch tablets. It was apparent that tablets containing chitin (J), chitin (U), chitosan (J) and chitosan (U) at the concentration about 5% and 7% showed a better disintegration time than 5% corn starch tablets at the same compressional force. Comparison between these four disintegrants was noticed that tablets containing chitosan (J) exhibited faster disintegration time followed by chitin (J), chitosan (U) and chitin (U), respectively. At low concentration (1.5%), these four disintegrants were slowly disintegrated. When the concentration increased about 3%, the disintegration time was dramatically decreased. At concentration level about 7%, tablets containing these disintegrants exhibited about one minute in disintegration time. From the results, it was suggested that the disintegration time increased as compressional force increased and disintegrant concentration decreased.

5) Dissolution of tablet

The dissolution data for paracetamol tablets compressed at two force levels at the time intervals of

five minutes were shown in Table 12-33. The dissolution profiles of tablets containing different disintegrants and concentrations were illustrated in Figure 43-45. It was noted that tablets containing corn starch, sodium starch glycolate and croscarmellose sodium at every concentrations and compressional forces used in this study complied with the requirments of the US standard, that was not less than 80% (Q) of the labeled amount of drug was dissolved in 30 minutes (89). In contrast, both formulations of microcrystalline cellulose tablets compressed at both forces of 600 and 900 pounds were not passed the limit of the US standard. For tablets made with chitin or chitosan, it was noticed that tablets using 1.5% and 3% of these two disintegrants from both sources were also not passed the limit of the US standard, but tablets containing these disintegrants at higher levels of 5% and 7% complied with the requirements of the US standard. Comparison of percent drug dissolved of tablets containing chitin and chitosan from both sources at the same concentration and compressional force, it could be found that percent drug dissolved decreased in the following order :chitosan(J) > chitosan(U) > chitin(J) >chitin (U). There was no difference in percent drug dissolved in tablets containing 5% and 7% chitin and chitosan from both sources compressed at forces of 600 and 900 pounds at 30 minute. But this difference could seen in the first initial time. Comparison of the percent drug dissolved profile suggested that the

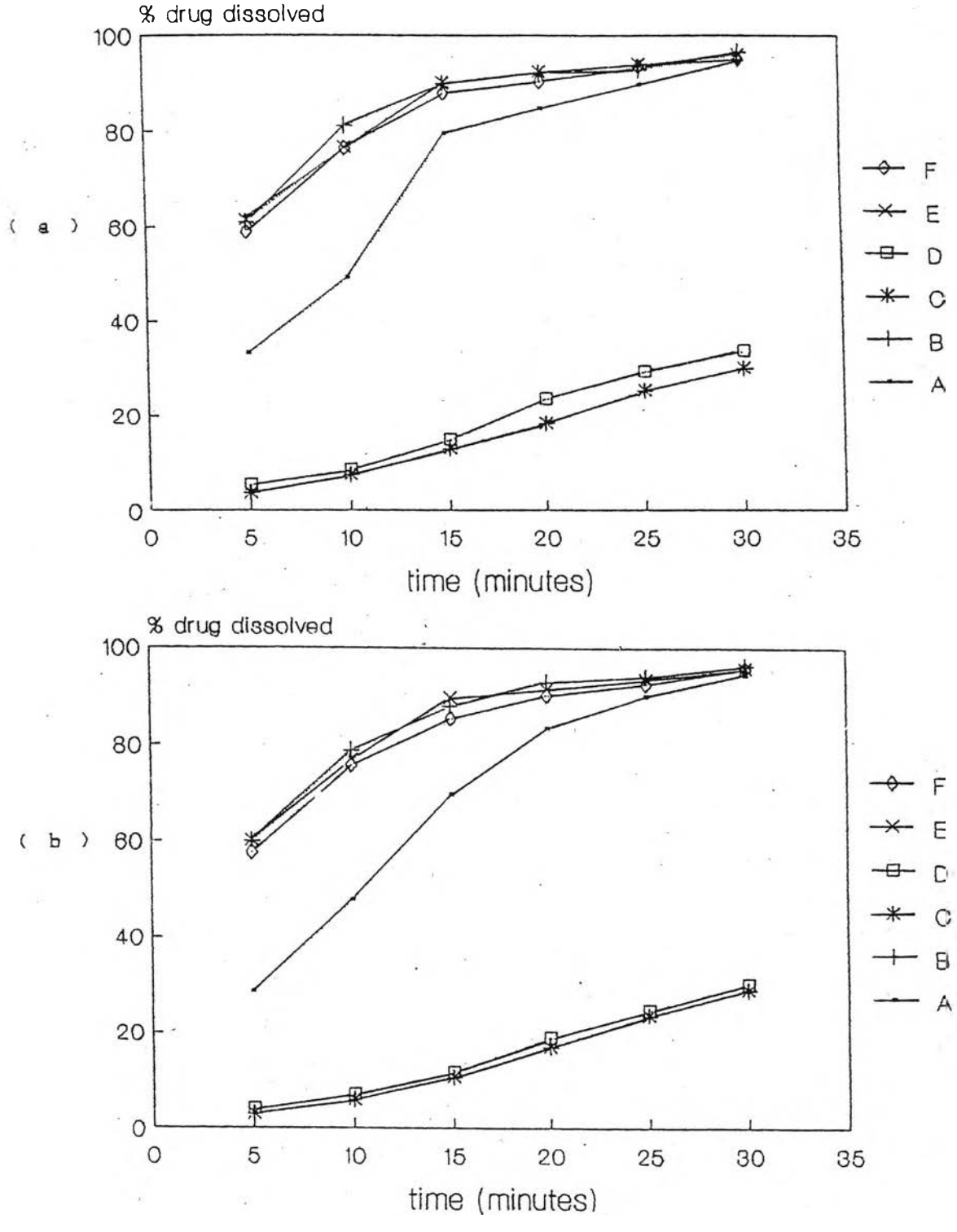


Figure 43 Percent drug dissolved of paracetamol tablets containing 5% corn starch (A), 5% sodium starch glycolate (B), 5% and 10% microcrystalline cellulose (C-D) and 2% and 5% croscarmellose sodium (E-F) compressed at forces of 600 (a) and 900 (b) pounds before exposure to accelerated condition

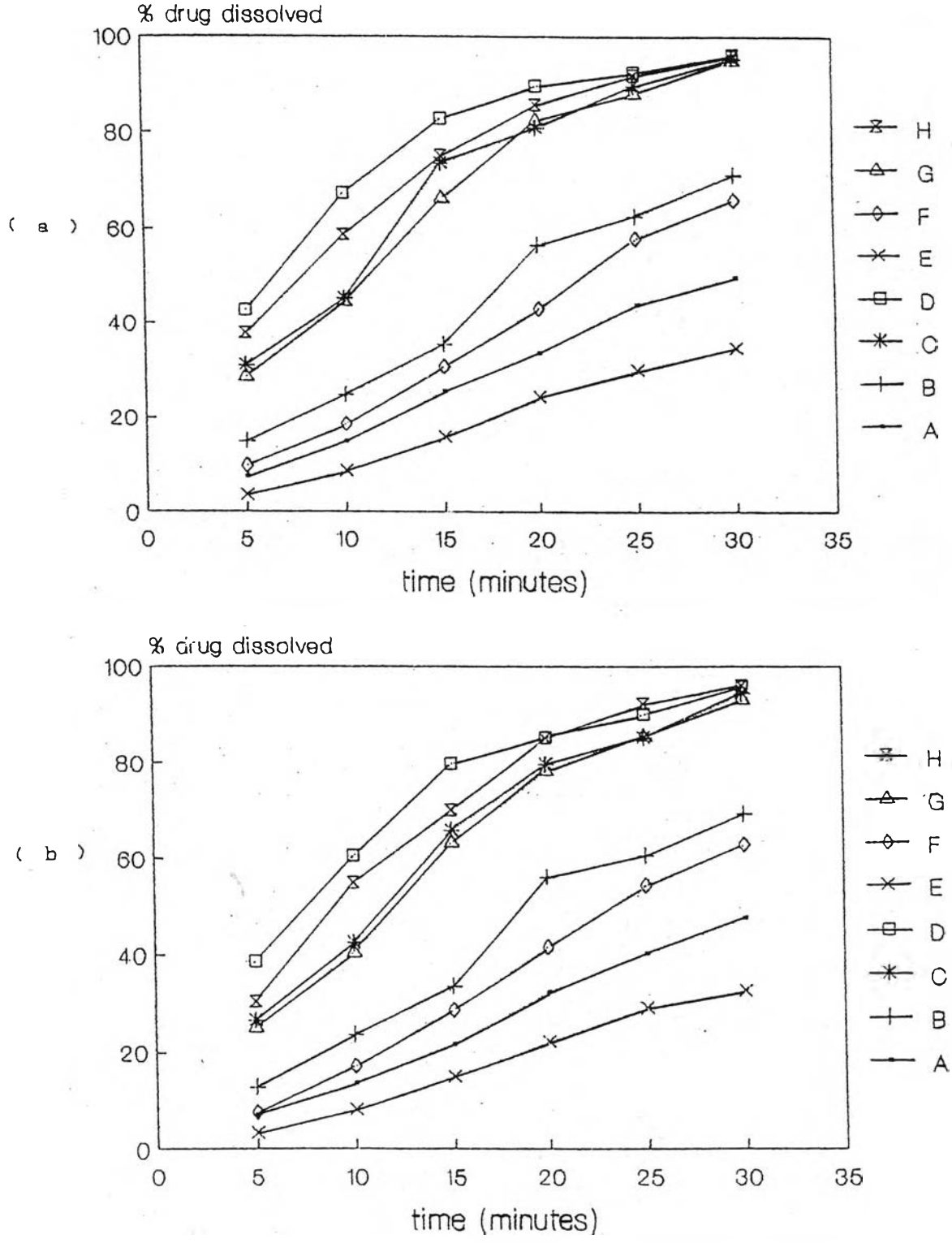


Figure 44 Percent drug dissolved of paracetamol tablets containing 1.5%, 3%, 5% and 7% chitin (J) (A-D) and 1.5%, 3%, 5% and 7% chitin (U) (E-H) compressed at forces of 600 (a) and 900 (b) pound before exposure to accelerated condition

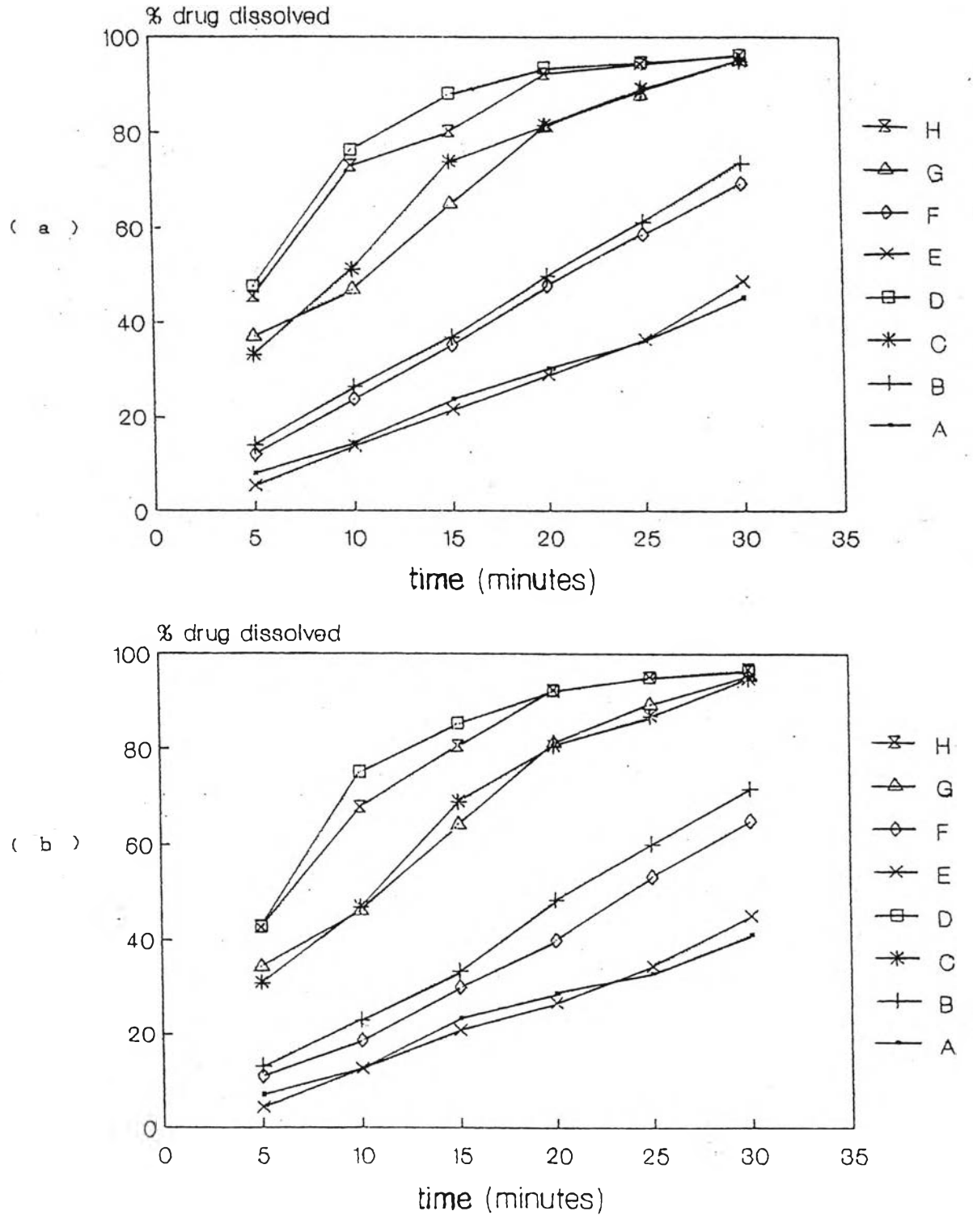


Figure 45 Percent drug dissolved of paracetamol tablets containing 1.5%, 3%, 5% and 7% chitosan (J) (A-D) and 1.5%, 3% 5% and 7% chitosan (U) (E-H) compressed at forces of 600 (a) and 900 (b) pounds before exposure to accelerated condition

percent drug dissolved from formulations containing 7% chitosan of both sources was similar to those of 5% sodium starch glycolate and 2% and 5% croscarmellose sodium except at the initially 5 minutes that the drug was less dissolved and slightly more than those of 7% chitin followed by 5% chitosan and chitin, respectively. Percent drug dissolved decreased with increasing the compressional force and decreased the concentration. In formulations of sodium starch glycolate and croscarmellose sodium, the difference in dissolution among different concentration of disintegrant and different compressional force could not be observed.

6) Percent labeled amount of tablet

The data of percent labeled amount of tablets containing different disintegrant were shown in Table 34. The high-pressure liquid chromatogram was shown in Figure 46. For all the prepared batches of tablets were well within the requirements of the US standard, the acetaminophen tablets contained not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_8 H_9 NO_2$ (89).

B. Tablet evaluation after exposure to accelerated condition

1) Weight variation of tablet

After storage in 75% relative humidity at 45 C, the changes in tablet weight variation compared to the initial values were presented in Table 12-33, and the

Table 34 Percent labeled amount of drug in tablet containing different disintegrants, before and after exposure to accerelated condition (75% RH 45°C)

Formulations	Percent labeled amount (mg)	
	Before exposure	After exposure
5% Corn starch	486.12	491.00
5% Sodium starch glycolate	495.01	493.18
5% Microcrystalline cellulose	490.43	489.50
10% Microcrystalline cellulose	494.01	501.14
2% Croscarmellose sodium	504.06	504.40
5% Croscarmellose sodium	484.18	491.37
1.5% Chitin (J)	491.52	483.71
3% Chitin (J)	498.67	493.49
5% Chitin (J)	491.00	486.14
7% Chitin (J)	491.32	490.33
1.5% Chitin (U)	503.23	496.29
3% Chitin (U)	497.95	503.93
5% Chitin (U)	490.26	490.45
7% Chitin (U)	495.39	500.97
1.5% Chitosan (J)	498.24	496.03
3% Chitosan (J)	496.52	499.57
5% Chitosan (J)	480.39	484.44
7% Chitosan (J)	494.46	486.23
1.5% Chitosan (U)	478.49	481.61
3% Chitosan (U)	493.69	492.58
5% Chitosan (U)	498.12	498.64
7% Chitosan (U)	491.47	484.84

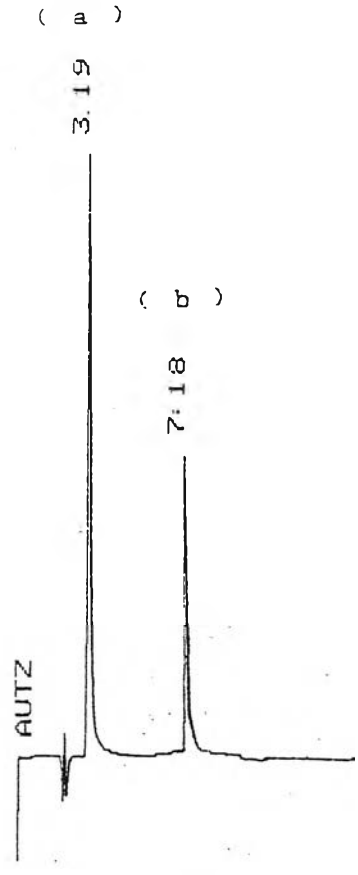


Figure 46 Liquid chromatogram of paracetamol (a) and internal standard (b) used 40% methanol, 60% distilled water and 0.1% phosphoric acid as mobile phase

coefficient of variation was shown in Figure 47. Weight of tablets increased after exposure to high humidity and temperature, but all the prepared batches of tablets were well within the limit of the US standard. In addition, all standard weight variation and coefficient of variation were slightly altered.

2) Tablet hardness

The results of tablet hardness after aging study were given in Table 12-33 and Figure 48. Tablets were exposed to high humidity and temperature after five days. the increase in hardness value was surprisingly observed in all formulations. The increasing in tablet hardness of microcrystalline cellulose formulation was particularly higher than other formulations.

3) Tablet friability

The effects of aging on tablet friability shown in Table 12-33 and Figure 49. It was noticed that the results of tablet friability confirmed those of hardness. The friability of tablets correspondingly decreased after exposure to high humidity and temperature over five days. From data, the tablet friability was less than 0.5 percent for all formulations. These values were well within the acceptable limitted (less than 0.8%).

4) Disintegration time of tablet

The results of disintegration time of tablets

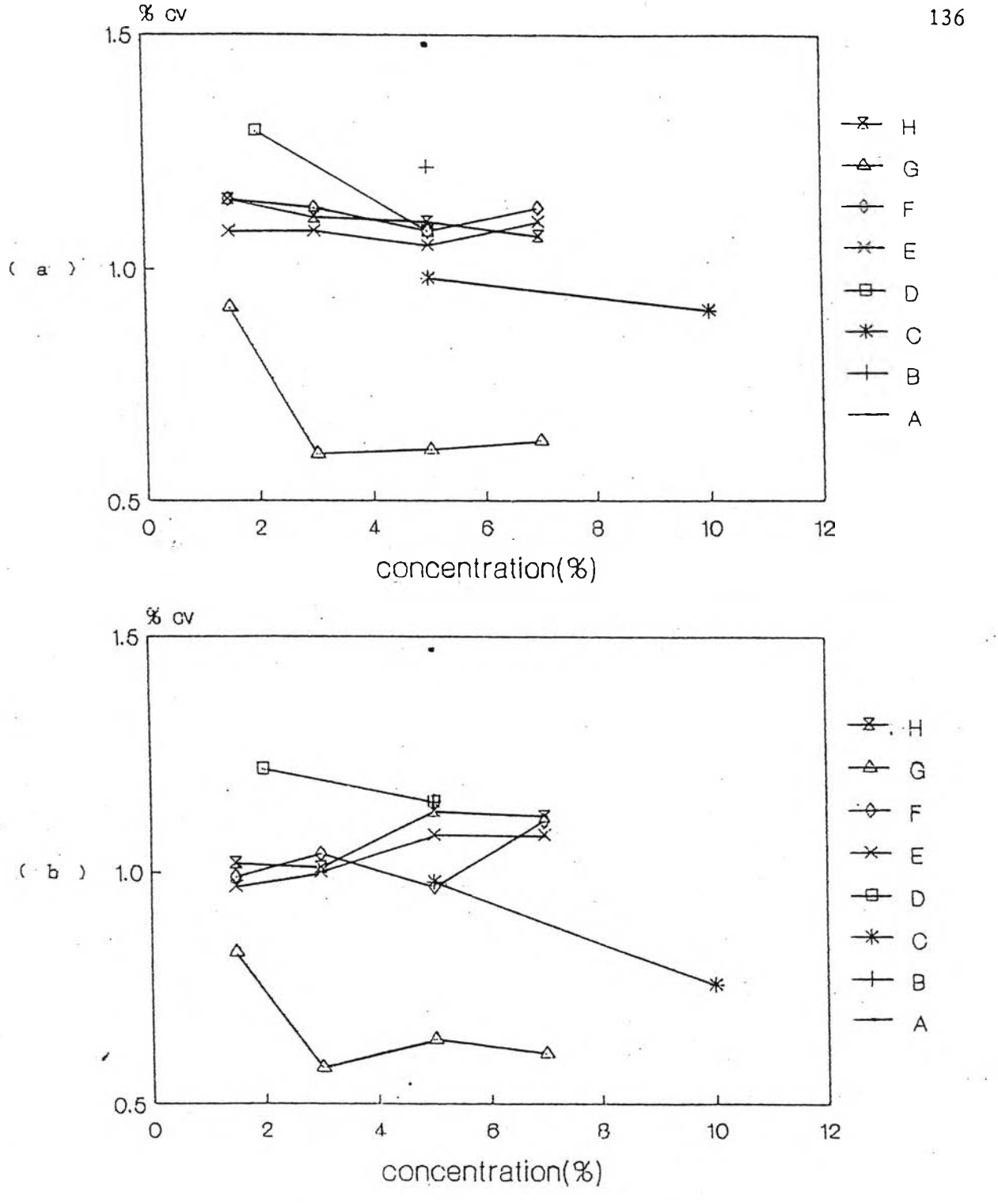


Figure 47 Percent standard weight variation of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

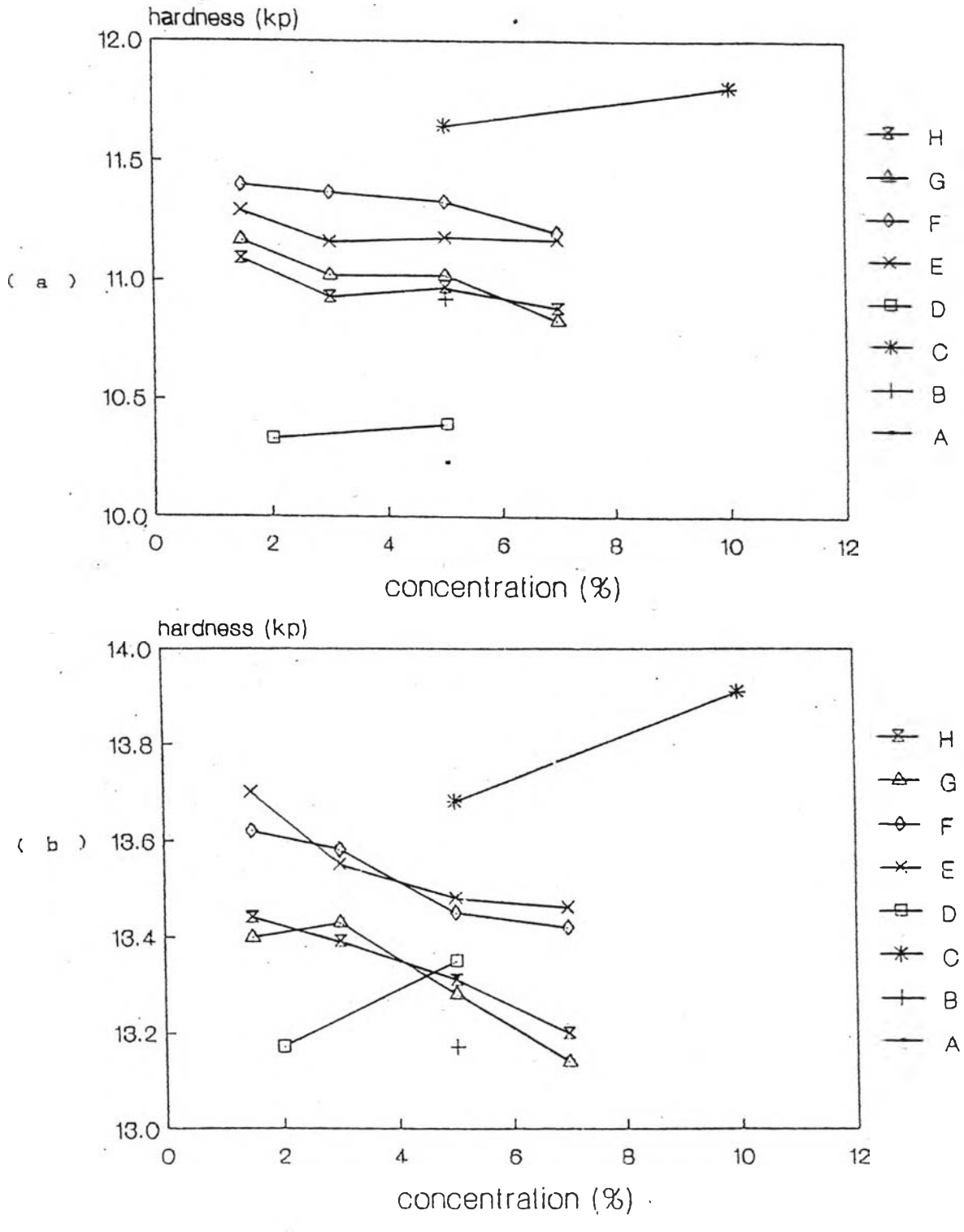


Figure 48 Hardness of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

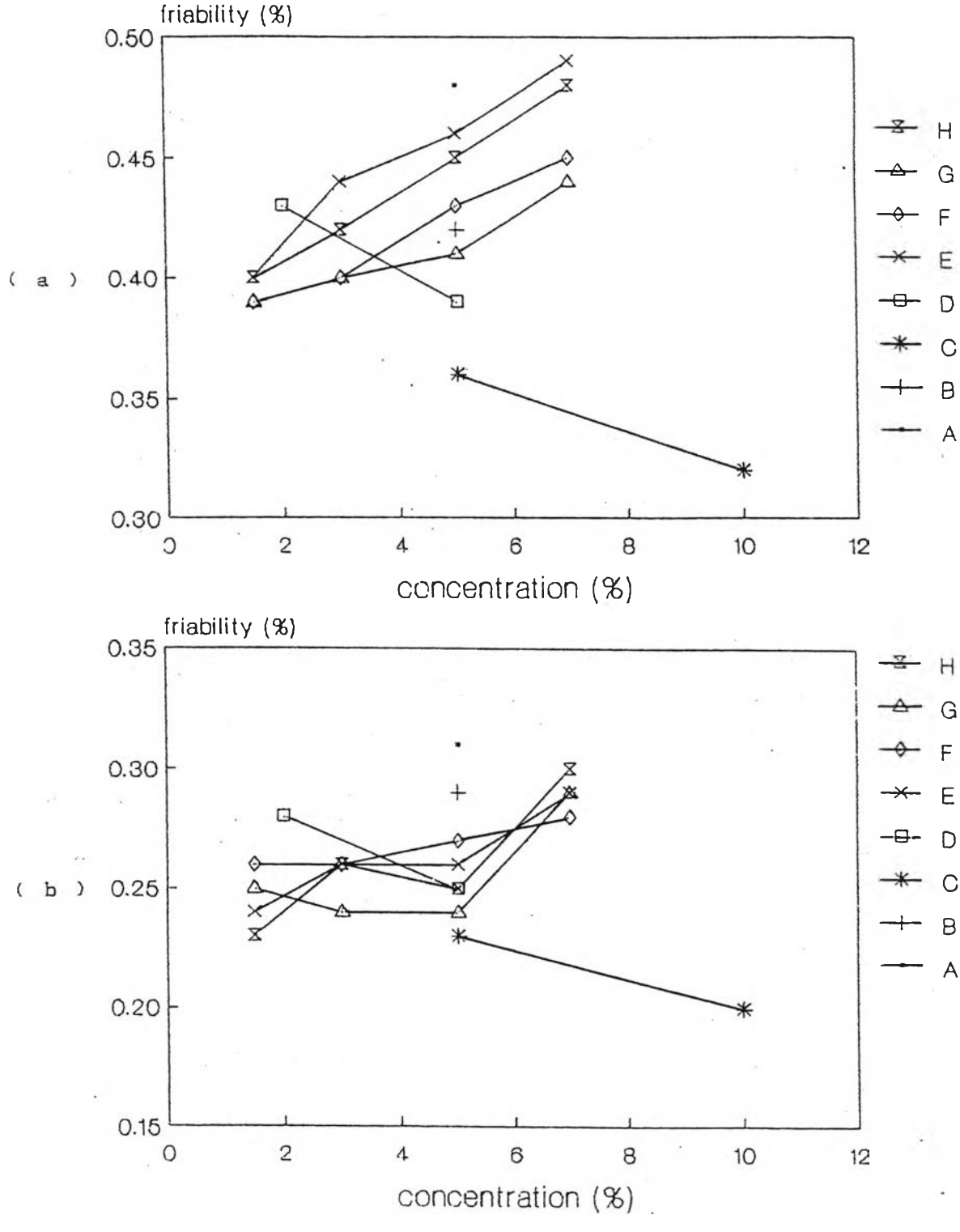


Figure 49 Percent friability of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

A : corn starch B : sodium starch glycolate

C : microcrystalline cellulose D : croscarmellose sodium

E : chitin (J) F : chitin (U)

G : chitosan (J) H : chitosan (U)

after exposure to 75% relative humidity at 45°C over five days were shown in Table 12-33 and Figure 50. The data suggested that tablet disintegration times mostly increased after storage under accelerated condition. In formulations prepared with sodium starch glycolate and croscarmellose sodium, aging slightly affected the disintegration time. On the other hand, exposure to high humidity and temperature was highly affected disintegration time in microcrystalline cellulose tablets. In the case of chitin and chitosan tablets, the disintegration time was affected by aging. When tablets exposed high humidity and temperature, the disintegration time was increased. The results showed that aging had a greater effect in the disintegration time in tablets containing these disintegrants in low concentrations (1.5% and 3%) than those containing high concentrations (5% and 7%).

5) Dissolution of tablet

The dissolution data of all formulations after storage in 75% relative humidity at 45°C were shown in Table 12-33, and the dissolution profiles that plotted between percent drug dissolved (%) VS time (mins) were depicted in Figure 51-53. The drug dissolution of tablets containg 5% sodium starch glycolate had a little change in the first five minutes, after this time percent drug dissolved had a similar value as before exposure to accelerated condition. However, the comparison of

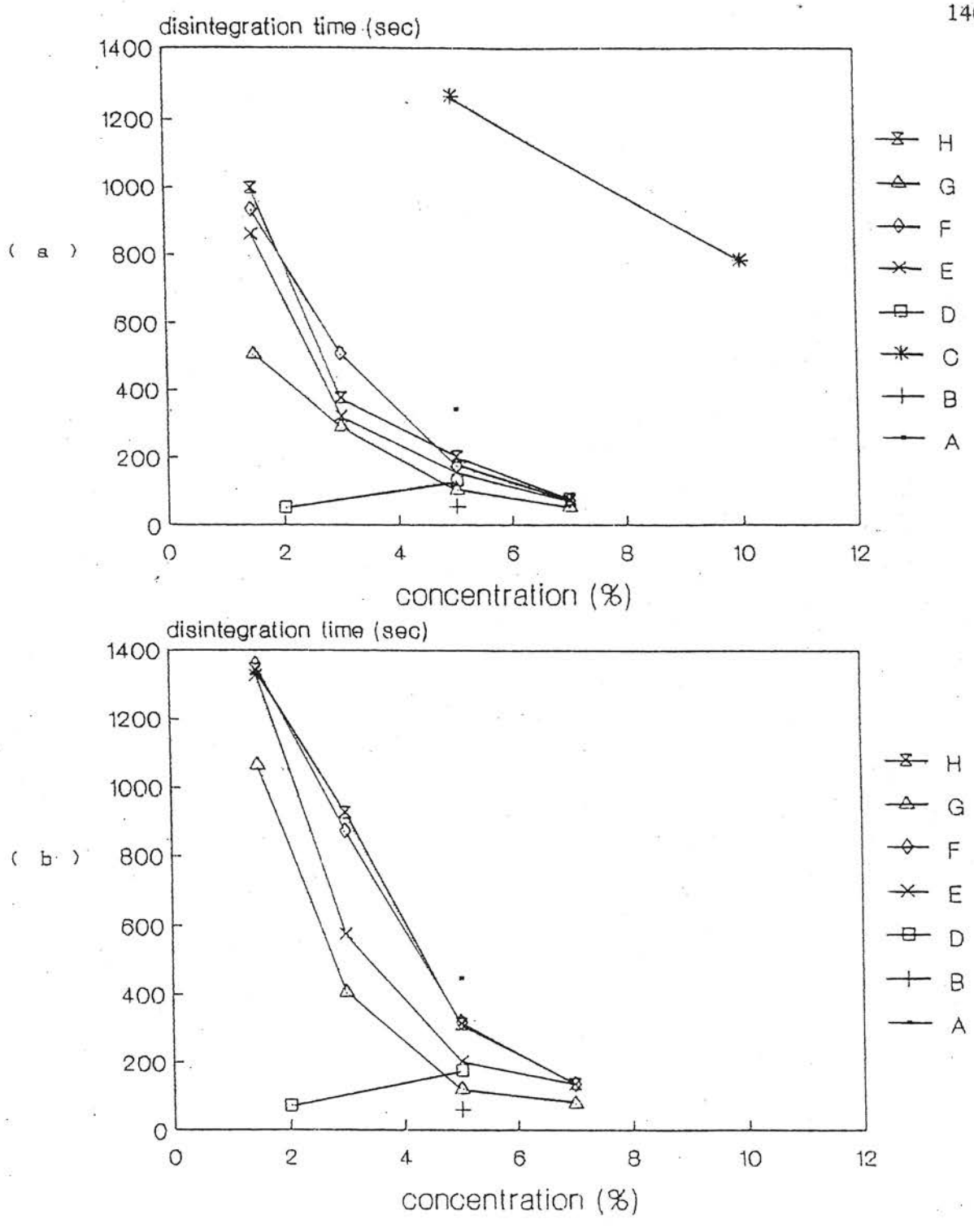


Figure 50 Disintegration time of paracetamol tablets containing different disintegrants compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

A : corn starch
B : sodium starch glycolate
C : microcrystalline cellulose
D : croscarmellose sodium
E : chitin (J)
F : chitin (U)
G : chitosan (J)
H : chitosan (U)

percent drug dissolved before and after exposure to accelerated condition could not be clearly differentiated in this formulation. For other formulations the dissolution of drug decreased after storage in accelerated condition. For formulations that composed of 2% and 5% croscarmellose sodium, the drug dissolution slightly decreased after exposure to high humidity and temperature. On the other hand, a tremendous decrease in drug dissolution was noticed in tablets containing corn starch after exposure to 75% relative humidity at 45°C. In the case of chitin and chitosan tablets from two sources, they were affected by aging. As well as the disintegration time, aging larger affected on drug dissolution of tablets containing chitosan (U) than chitin (J), chitin (U) and chitosan (J) respectively. This effect was occurred in tablets containing low concentration more than high concentration of disintegrant. From the results, it could be seen that tablets containing 5% and 10% microcrystalline cellulose, 5% corn starch, 1.5% and 3% chitin and chitosan from both sources were not passed the specifications of the US standard, while the formulations of 5% sodium starch glycolate, 2% and 5% croscarmellose sodium, 5% and 7% chitin and chitosan from both sources were well within the requirements of the US standard.

6) Percent labeled amount

Percent labeled amount of tablets after exposure

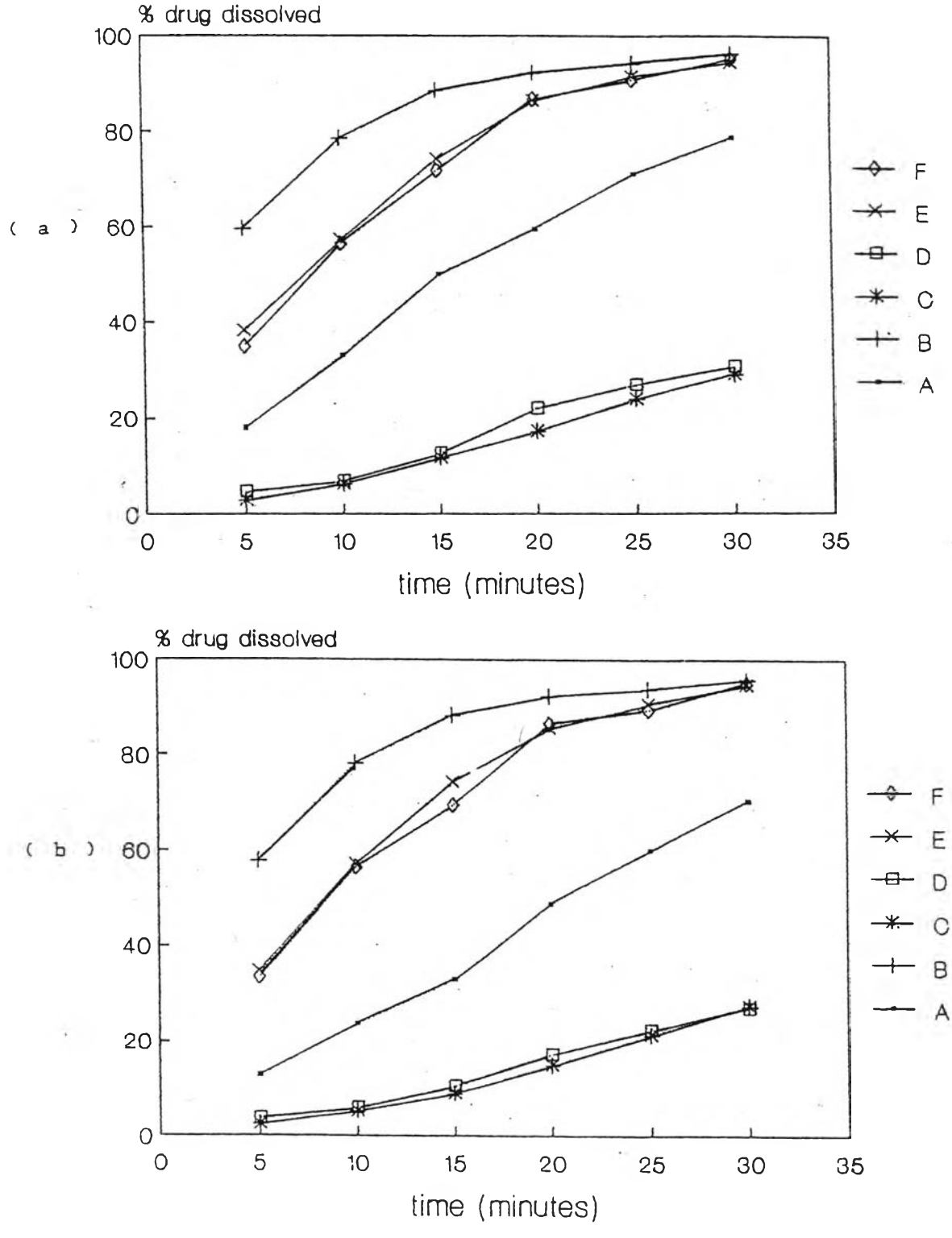


Figure 51 Percent drug dissolved of paracetamol tablets containing 5% corn starch (A), 5% sodium starch glycolate (B), 5% and 10% microcrystalline cellulose (C-D) and 2% and 5% croscarmellose sodium (E-F) compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

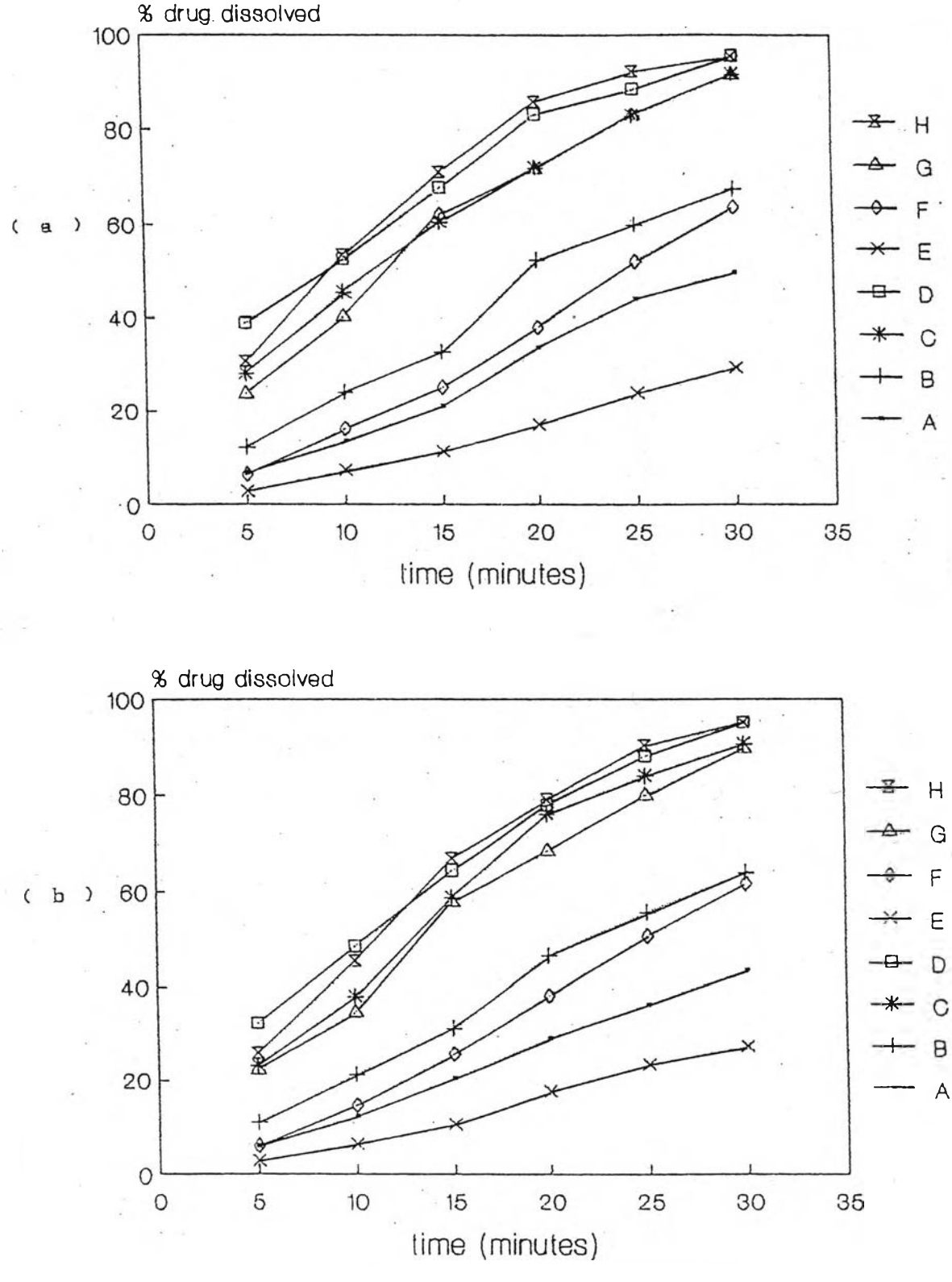


Figure 52 Percent drug dissolved of paracetamol tablets containing 1.5%, 3%, 5% and 7% chitin (J) (A-D) and 1.5%, 3%, 5% and 7% chitin (U) (E-H) compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

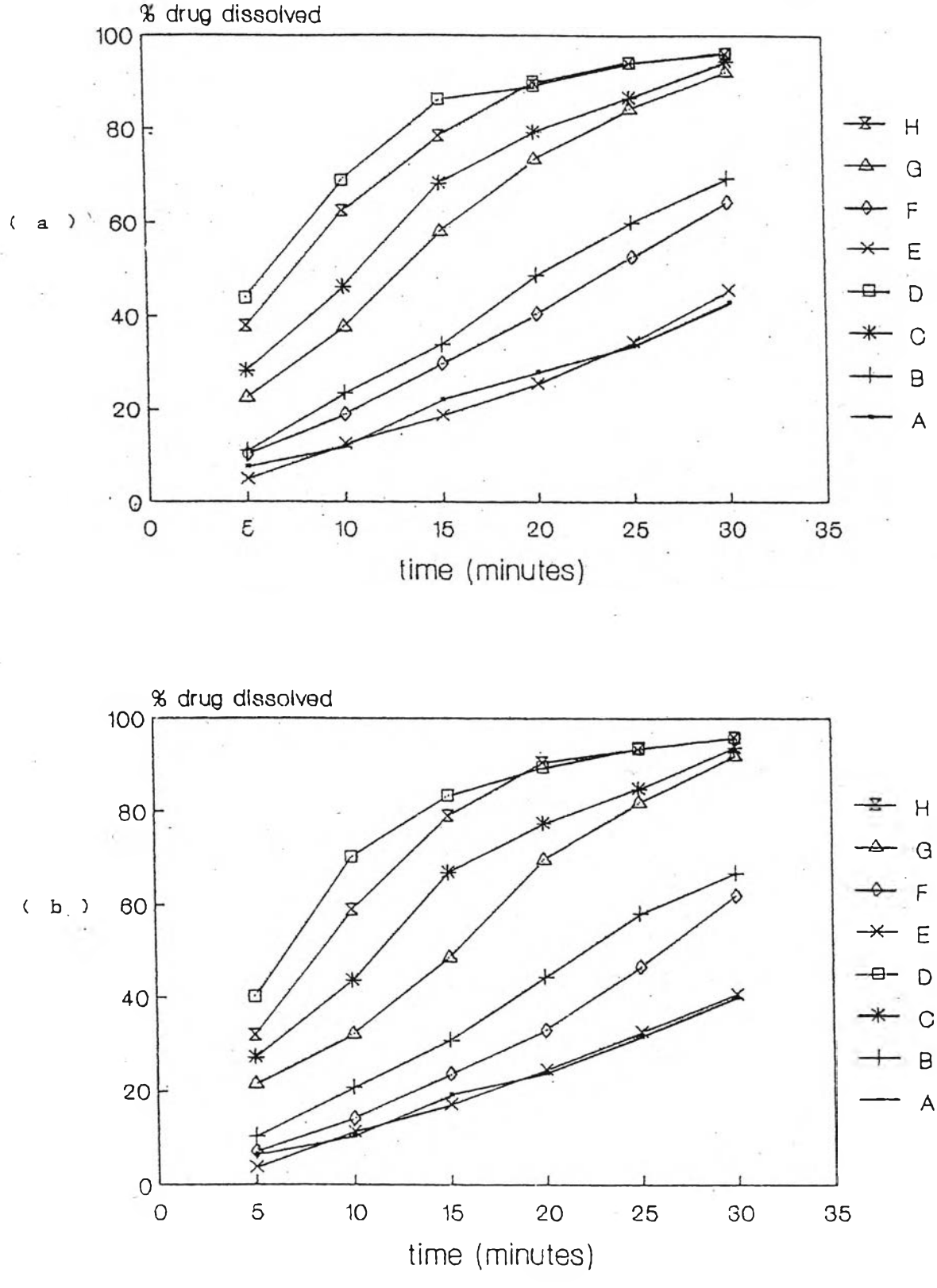


Figure 53 Percent drug dissolved of paracetamol tablets containing 1.5%, 3%, 5% and 7% chitosan (J) (A-D) and 1.5%, 3%, 5% and 7% chitosan (U) (E-H) compressed at forces of 600 (a) and 900 (b) pounds after exposure to accelerated condition

to high humidity and temperature were shown in Table 34. It was not clearly seen that percent labeled amount of drug in tablets changed after exposure to accelerated condition.