Chapter III

Results

1. Evaluation of Physicochemical Characteristics

1.1 Determination of degree of deacetylation of chitosan products

1.1.1 Colloidal titration

Degree of deacetylation of chitosan products was determined and calculated using the method described in Appendix A. Deacetylation of chitin by method A, B, and C produced chitosans in different degree of deacetylation as shown in Table 5.

Table 5 Degree of deacetylation of chitosan products from various methods and reaction times.

Method	Chitosan	Reaction time (hr)	% deacetylation
A	CTS3A	3	68.11
A	CTS3.5A	3.5	72.21
A	CTS7A	7	75.87
A	CTS73A	7 + 3	79.83
B	CTS2.5N	2.5	67.86
B	CTS3N	3	71.11
B	CTS7N	7	75.69
C	CTS60N	60	58.51 (74.13*)

* This value was obtained when chitosan solution and Hydrochloric acid had been refluxed for 10 minutes before chitosan hydrochloride precipitate was obtained.

Code of chitosan products was composed of 3 parts: CTS , number and letter A or N. CTS was abbreviated from chitosan. Number followed came from the reaction time using. Letter A and N represented the conditions using in deacetylation process: air and nitrogen atmosphere, respectively.

Under air atmosphere, it was found that an increasing time beyond 7 hours could not increase degree of deacetylation. It was essential to wash and dry chitosan at the seventh hours so as to remove the impurity. Then, the reaction would run again for another 3 hours. Chitosan produced by this method have approximately 80% degree of deacetylation.

1.1.2 Infrared spectrometry

Infrared spectrometry was employed in this study to aid the determination of the residual CONH groups in chitin and chitosan products. The IR spectra are depicted in Figure 4 and 5. Each spectrum shows a peak at about 1650 cm $^{-1}$ for C=O stretching and NH bending. Although the absorption at 1650 cm^{-1} was from stretching and bending, the majority was from C=O stretching vibration. Note that, it could not be differntiated the absorption peak of NH from NH$_2$ because they absorbed energy in the region adjacent to CH stretching and OH stretching.

It was seen that the following spectra were appear to be similar: CTS3A and CTS2.5N, CTS3.5A and CTS3N and CTS60N, and CTS7A and CTS7N. From this observation, The absorption peak at about 1650 cm $^{-1}$ in each chitin and chitosans associated with the degree of deacetylation measured by colloidal titration. The lower the 1650 cm $^{-1}$ peak (The lower the amount of carbonyl groups), the higher the degree of deacetylation. Unlike chitosans, chitin showed C=O stretching vibration in the region 1550 -1700 cm $^{-1}$ separated into two peaks. This difference resulted from two types of amide groups, which had different hydrogen bonding. (Backwell, Minke, and Gardner, 1978)
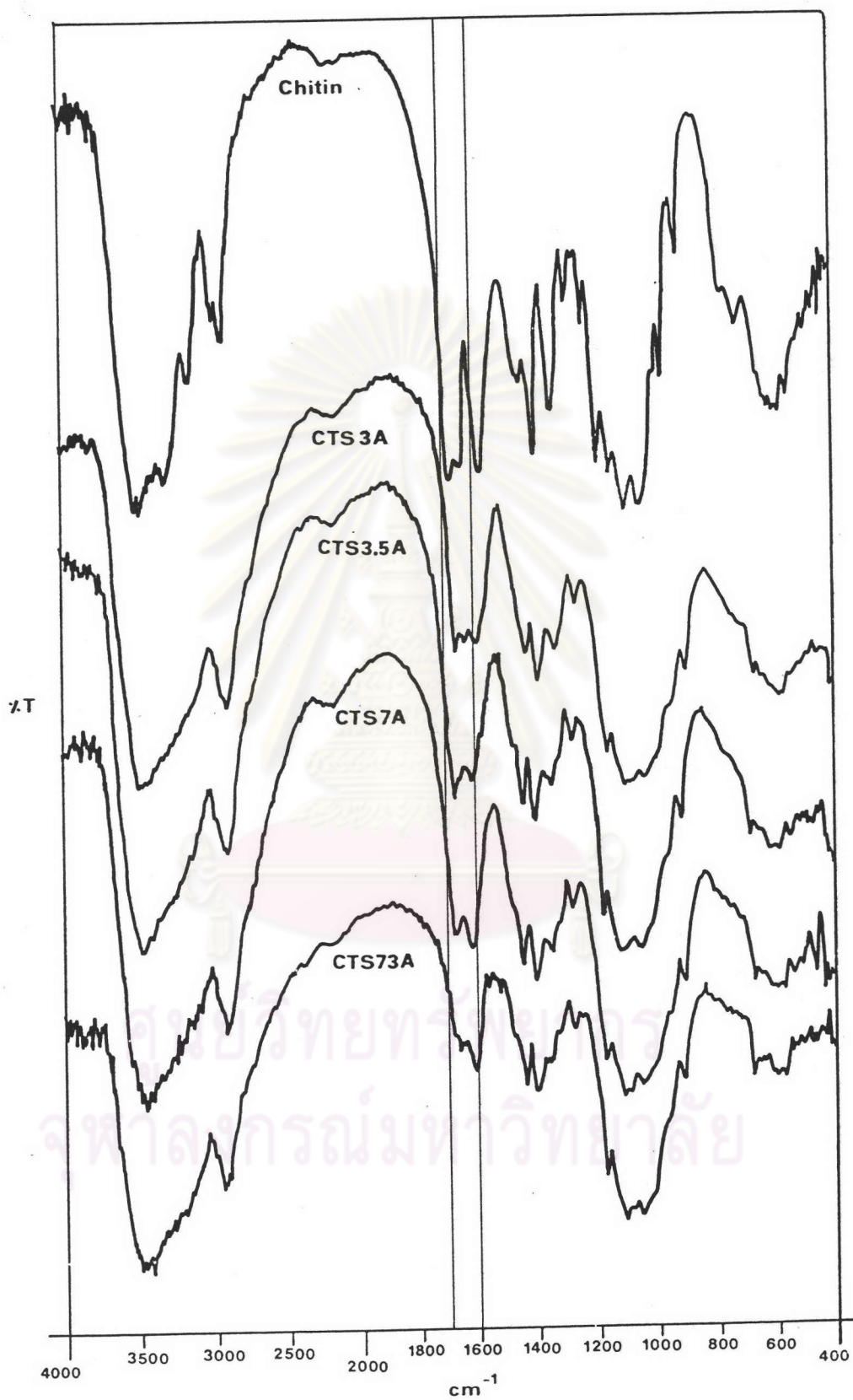
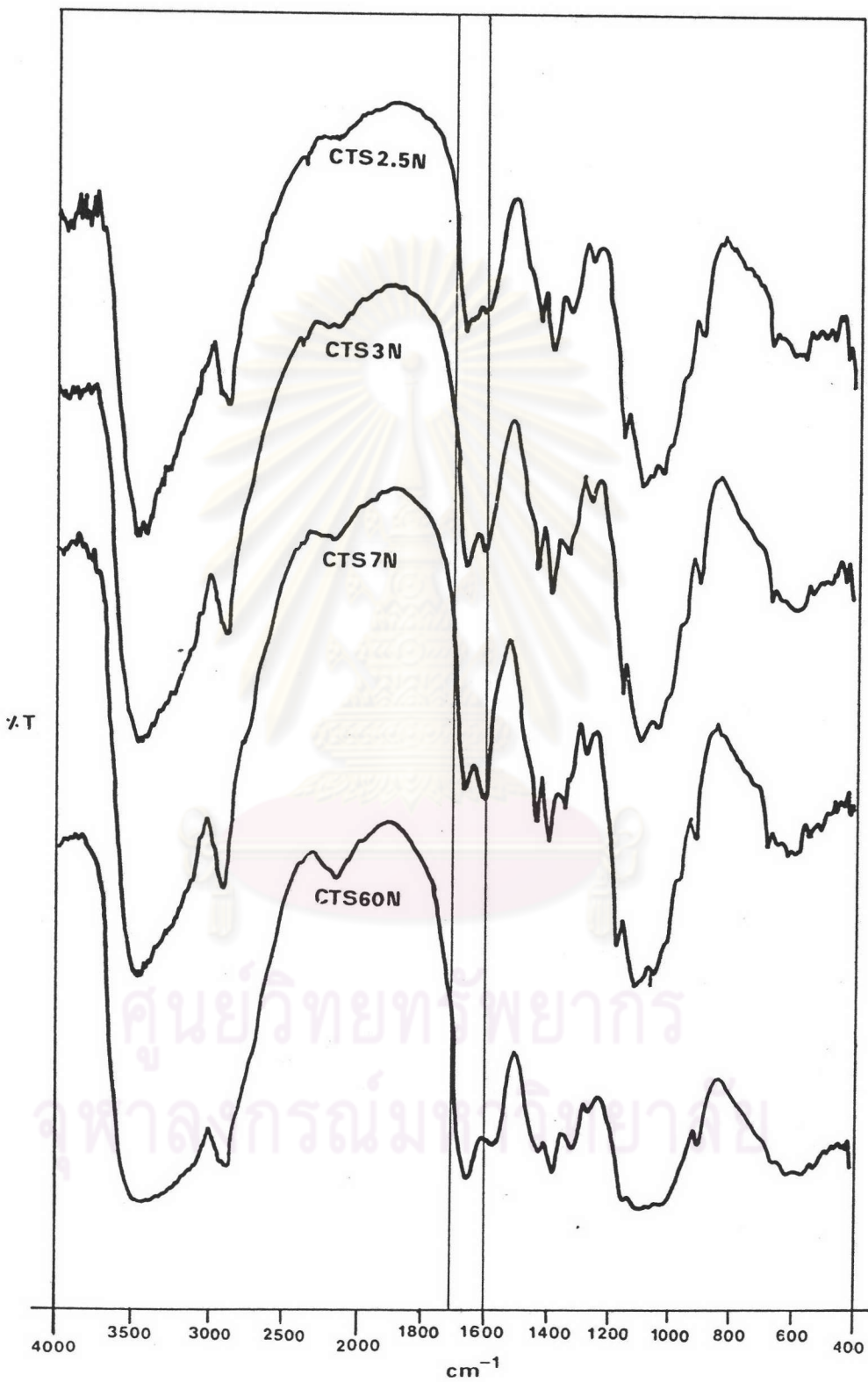Figure 4   Infrared spectra of chitin and chitosans produced by method A.

Figure 5   Infrared spectra of chitosans produced by method B and C.

1.2 Molecular weight comparison

1.2.1 Mass spectrometry

To compare the molecular weight of the polymers, mass spectrometry was performed. The mass spectra (electron impact spectra) of various polymers are distinctive and depicted as bar graphs in Appendix B.

The interpretation of this study based on the principle that the high molecular weight polymers are ionized and the opportunity that short fragments or fragments having low weight (For instance, 203 for chitin monomer, and 161 for chitosan monomer) detected is less than the low molecular weight polymers. Therefore, the spectrum of the lower molecular weight polymer exhibits the higher intensity of the peaks at about 161 and 203.

The fragments obtained were derived from the monomer units

(203)   and   (161)

Clusters of ions could be observed in the mass spectra. The fragments to which some of these ions could be attributed were proposed by Hayes (1978) and listed in Table 6.

Table 6   Mass spectra and associated ion fragments.

Peak	Fragment
29	$> CHNH_2$
31	$- CH_2OH$
36	HCl
43	$- COCH_3$
55	$> CHCH(NH_2)CH$
59	$- CHOHCHNH_2$
60	$- NHCOCH_3$
71	$> CHNHCOCH_3$
72	$- CHOHCHNH_2CH$
84	$> CHCHNHCOCH_3$

On the basis of this principle, the molecular weight of the polymers could be compared and arranged in order as follows:

Chitin > CTS3A > CTS3.5A > CTS7A

CTS73A > CTS7A

Chitin > CTS2.5N > CTS3N > CTS7N

CTS2.5N > CTS3A

CTS3N > CTS3.5A, CTS3N > CTS60N

CTS7N < CTS7A

1.2.2 Differential thermal analysis

DTA curve of chitin is depicted in Figure 6. Chitosans also exhibited the same pattern of DTA curves but different in DTA peak temperature. The DTA peak temperatures of chitin and chitosans are given in Table 7.

165 C

Figure 6   DTA curve of chitin.

Table 7   DTA peak temperature of chitin and chitosans.

Polymer	DTA peak temperature (°C)
Chitin	165
CTS3A	155
CTS3.5A	141
CTS7A	149
CTS73A	149
CTS2.5N	146
CTS3N	158
CTS7N	143
CTS60N	140

1.2.3   Viscosity measurement

Viscosity of various chitosans was measured and the values of mean and standard deviation are shown in Table 8.

The viscosities of chitosans having approximately the same degree of deacetylation produced by method B were higher than those produced by method A (Viscosity of CTS2.5N > CTS3A and CTS3N > CTS3.5A, except CTS7N that had a little lower viscosity value than of CTS7A), and by method C was the highest.   In the same method, it could be noticed that chitosan having higher degree of deacetylation (chitosan that deacetylated by using higher reaction time) exhibited lower viscosity. (CTS2.5N > CTS3A   and CTS3N > CTS3.5A, except CTS7N < CTS7A)

Table 8   Viscosity values of 1% (w/v) chitosan in 2% Acetic acid.

Polymer	Viscosity *(cps.) ± s.d.
CTS3A	3660 ± 43
CTS3.5A	839 ± 29
CTS7A	415 ± 11
CTS73A	254 ± 3
CTS2.5N	3877 ± 66
CTS3N	952 ± 7
CTS7N	363 ± 9
CTS60N	2747 ± 127

* The average of three determinations

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1.3 Morphology examination

The photomicrographs of chitin and chitosans at 100 time magnification are shown in Figure 7-15. It is apparent that the powders of chitin and chitosans possess irregular shapes. After alkali treatment with Sodium hydroxide 50%(w/w), chitosan products seemed having no differnce from starting chitin.
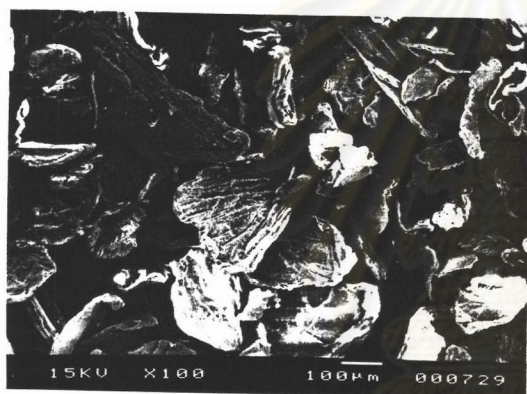
Fig. 7 Photomicrograph of chitin
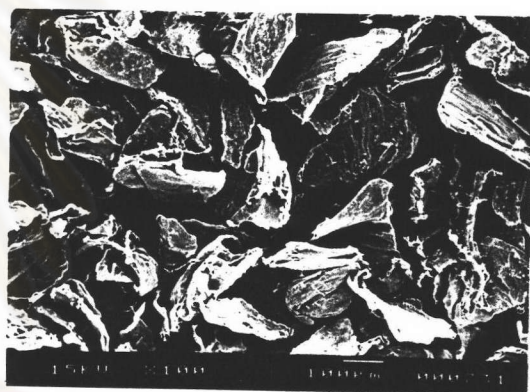
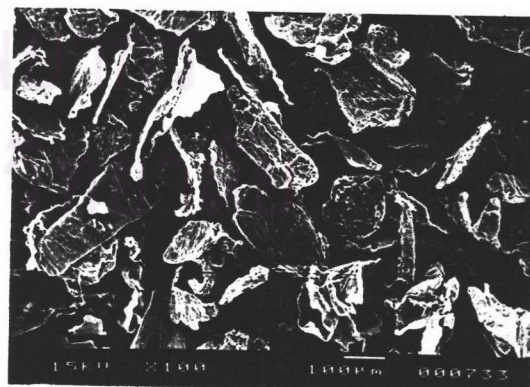Fig. 8 Photomicrograph of CTS3A

Fig. 9 Photomicrograph of CTS3.5A

Fig. 10 Photomicrograph of CTS7A

Fig. 11   Photomicrograph of CTS73A

Fig. 12   Photomicrograph of CTS2.5N

Fig. 13   Photomicrograph of CTS3N
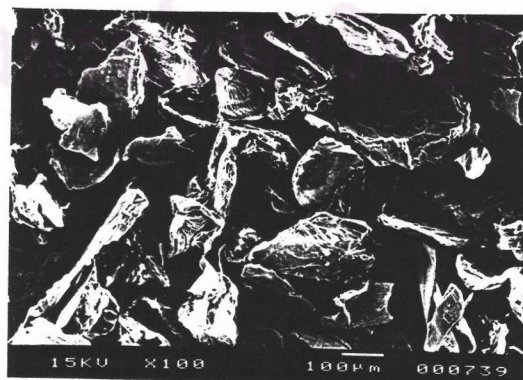
Fig. 14   Photomicrograph of CTS7N

Fig.15   Photomicrograph of CTS60N

1.4 Particle size distribution

The particle size distribution of the powders was analyzed by sieve analysis. The histograms of particle size distribution are shown in Figure 16 and the sieve analysis data are given in Table 9. It was found that the patterns of particle size distribution of chitin and chitosans were the same. The range of particle sizes was from 45 to 250 μm (60/200 mesh). The size of approximately 60 - 70 % of each polymer was about 180 - 250 μm.
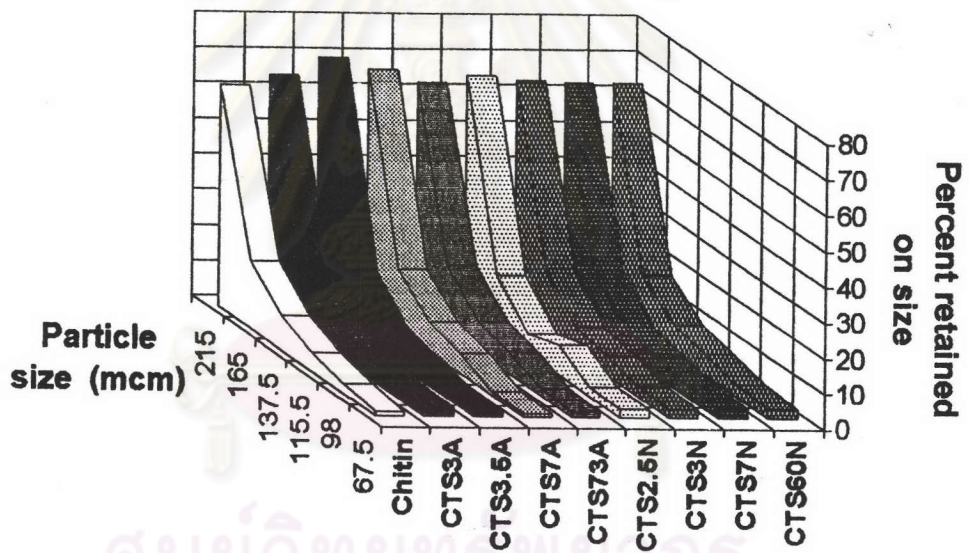
Figure 16   Histograms for the particle size distribution of chitin and chitosans.

Table 9   Particle size distribution of chitin and chitosans.

	Percent retained on sized (μm)					
	215	165	137.5	115.5	98	67.5
Chitin	62.17	19.06	9.58	5.38	2.74	1.08
CTS3A	65.31	17.40	7.09	4.86	2.82	2.53
CTS3.5A	70.06	16.37	6.19	4.39	1.60	1.40
CTS7A	67.03	17.18	8.29	5.73	0.89	0.89
CTS73A	63.30	18.54	8.74	6.21	1.84	1.36
CTS2.5N	65.61	15.71	5.48	8.36	2.42	2.42
CTS3N	64.32	17.74	7.14	5.40	2.89	2.51
CTS7N	63.75	17.52	7.55	5.31	3.17	2.70
CTS60N	63.72	15.85	8.23	6.10	3.35	2.74

1.5   True density determination

True density of chitin and chitosans was determined and given in Table 10. It could be noticed that chitin and chitosans had similar density-values about 0.33 - 0.34 gm/cm^3.

Table 10   True density of chitin and chitosans.

Polymer	True density (gm/cm^3) $\pm$ s.d.
Chitin	0.3373 $\pm$ 0.0004
CTS3A	0.3380 $\pm$ 0.0007
CTS3.5A	0.3419 $\pm$ 0.0012
CTS7A	0.3381 $\pm$ 0.0029
CTS73A	0.3377 $\pm$ 0.0008
CTS2.5N	0.3364 $\pm$ 0.0004
CTS3N	0.3328 $\pm$ 0.0003
CTS7N	0.3378 $\pm$ 0.0005
CTS60N	0.3354 $\pm$ 0.0022

1.6 Moisture determination

Moisture content of various polymers are presented as percentage of moisture content and given in Table 11.

Table 11   Percentage of moisture content of chitin and chitosans.

Polymer	% Moisture content ± s.d.
Chitin	4.05 ± 0.07
CTS3A	5.95 ± 0.05
CTS3.5A	5.81 ± 0.05
CTS7A	5.51 ± 0.23
CTS73A	4.94 ± 0.12
CTS2.5N	6.90 ± 0.23
CTS3N	4.85 ± 0.20
CTS7N	6.38 ± 0.31
CTS60N	3.00 ± 0.08

1.7 Hydration capacity

The hydration capacity of chitin and chitosans was evaluated in distilled water. The results are shown in Figure 17. It could be obtained that CTS60N had the highest hydration capacity and chitin showed a little lower than of CTS60N, whereas the others had quite low hydration capacity values and seemed having no difference among them.
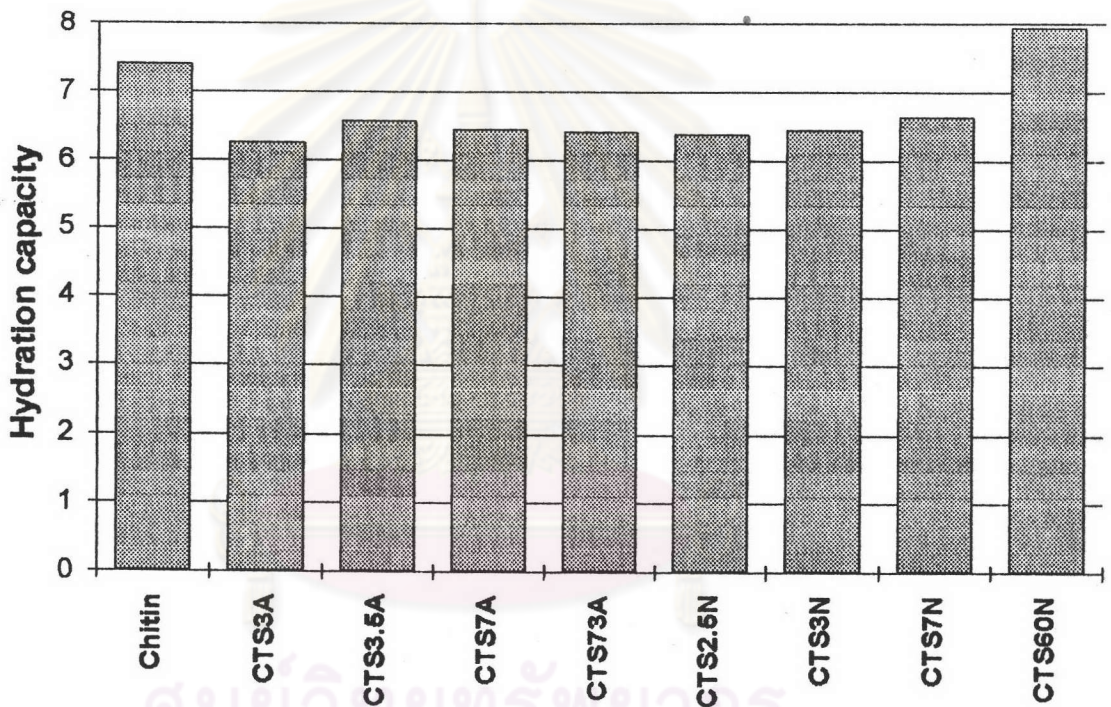
Figure 17 Hydration capacity of chitin and chitosans.

1.8 Swelling power of particle.

The swelling of chitin and chitosan powders was determined by sedimentation volume method and was performed in distilled water. The swelling volume and swelling capacity of all polymers are depicted in Figure 18.
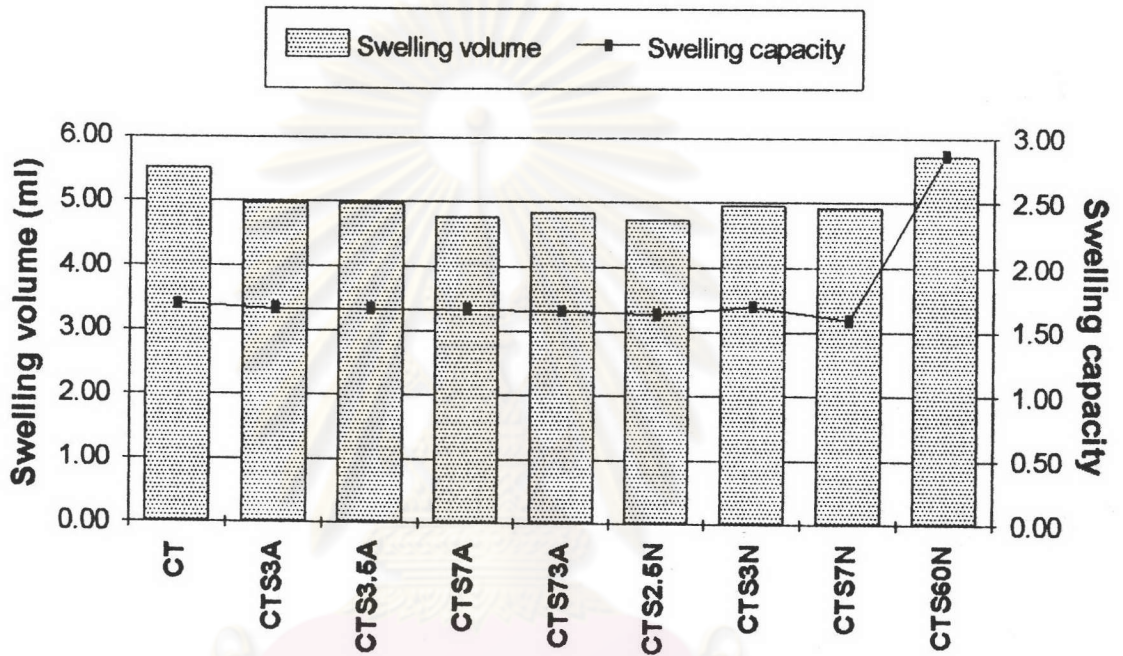

Figure 18   Swelling volume and swelling capacity of chitin and chitosans.

From Figure 17 and 18, it could be seen that the swelling volume of each polymer correlated with it's hydration capacity because both of parameters based on the initial weight. In order to compare with the initial volume (bulk volume), the swelling capacity was determined. It was found that CTS60N had the highest swelling volume and swelling capacity, and had substantially higher than the others. Besides, chitin had slightly higher swelling capacity than the others, except of CTS60N.

1.9   Rate of water uptake

Rate of water uptake of various polymers was investigated.   The volume and rate of water uptake of chitin and chitosans at various time intervals are shown in Figure 19-22. It was noticed that chitin had the fastest rate within the first two minute, whereas CTS60N had the slowest rate. (Fig.20 and 22) The results obtained shown that the rate of water uptake of various disintegrants decrease in the following order : chitin > chitosans produced by method A > chitosans produced by method B > CTS60N (chitosan produced by method C). Although CTS60N had the slowest rate of water uptake, it had the highest volume of water uptake whereas the others were considerably lower and seemed having no difference among them.
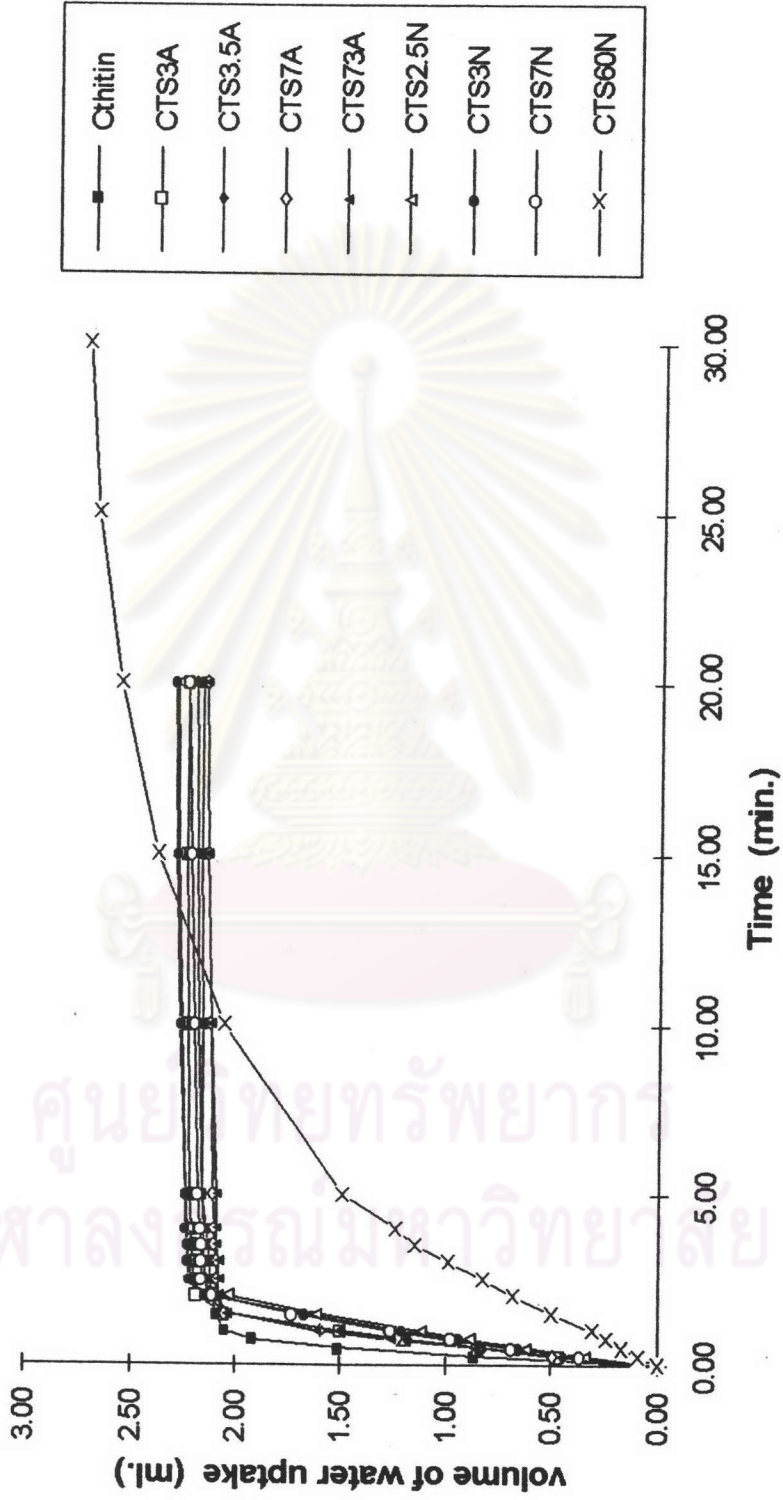
Figure 19 Volume of water uptake of chitin and chitosans at various time intervals within 30 minutes.
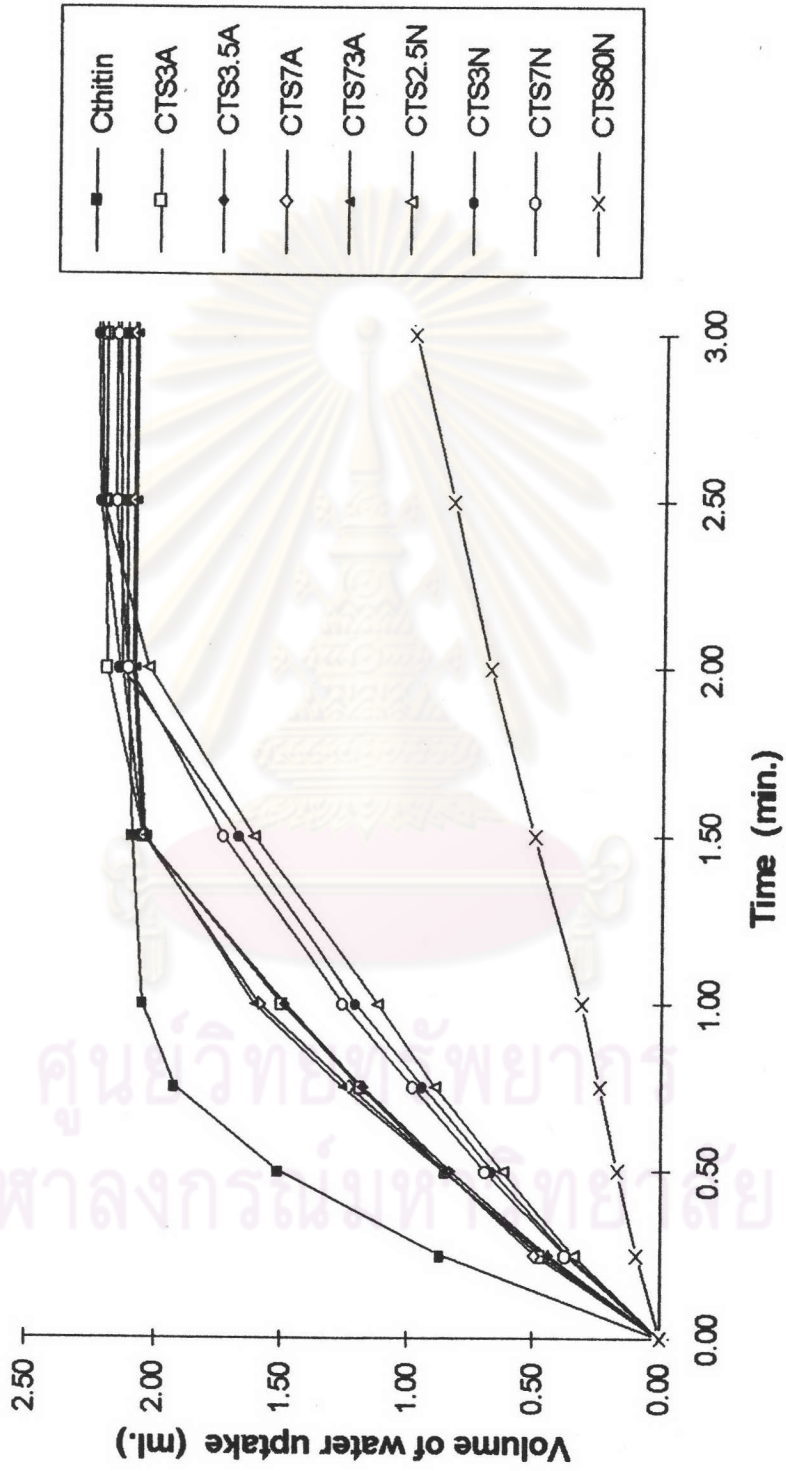
Figure 20 Volume of water uptake of chitin and chitosans at various time intervals withih the first 3 minutes.
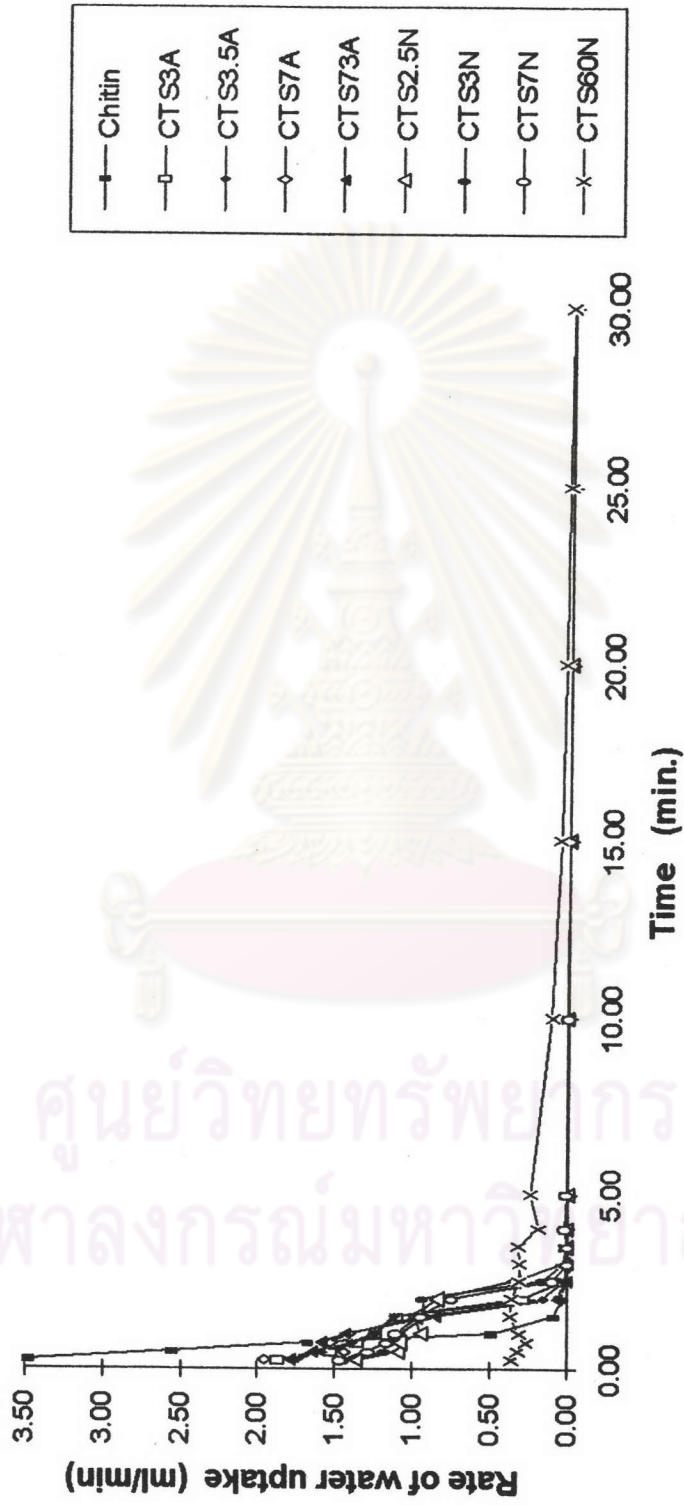
Figure 21   Rate of water uptake of chitin and chitosans at various time intervalswithih 30 minutes.
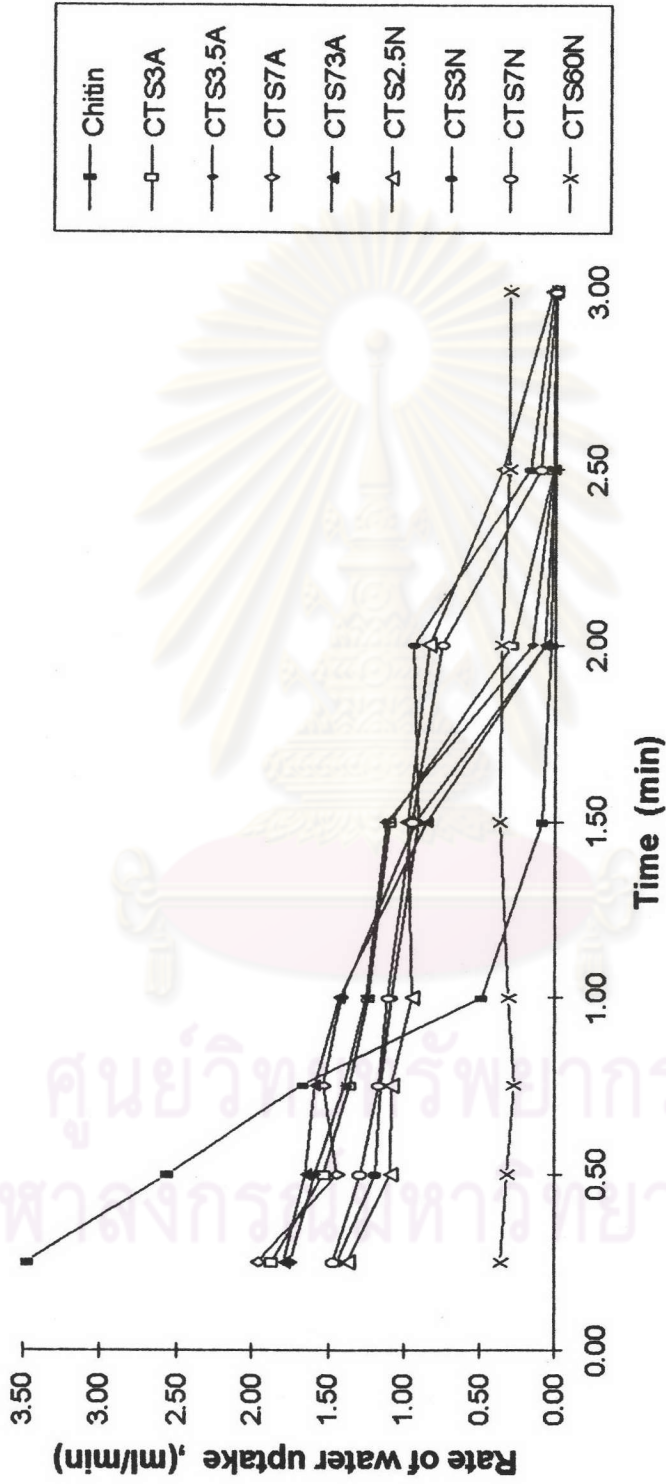
Figure 22 Rate of water uptake of chitin and chitosans at various time intervals within the first 3 minutes.

1.10 X-ray diffraction

X-ray diffractograms of chitin and all chitosans are depicted in Figure 23 and 24. All diffractograms showed the peaks at about 10° and 20°. Unlike all of chitosans, diffractogram of chitin showed lower peaks at about 12.5° and 27°. The peak at 20° of all polymers had significantly higher intensity, except of CTS60N that the intensity of the peak at 10° and 20° had no difference. In addition, it was noticed that the first peak of chitin and CTS60N slightly shifted to the left at 9°.

In this study, chitin from crab shell was used. As it was expected, x-ray diffractogram of chitin was similar to the previous diffractogram of crab shell reported by Takai, Shimizu, and Hayashi (1989).
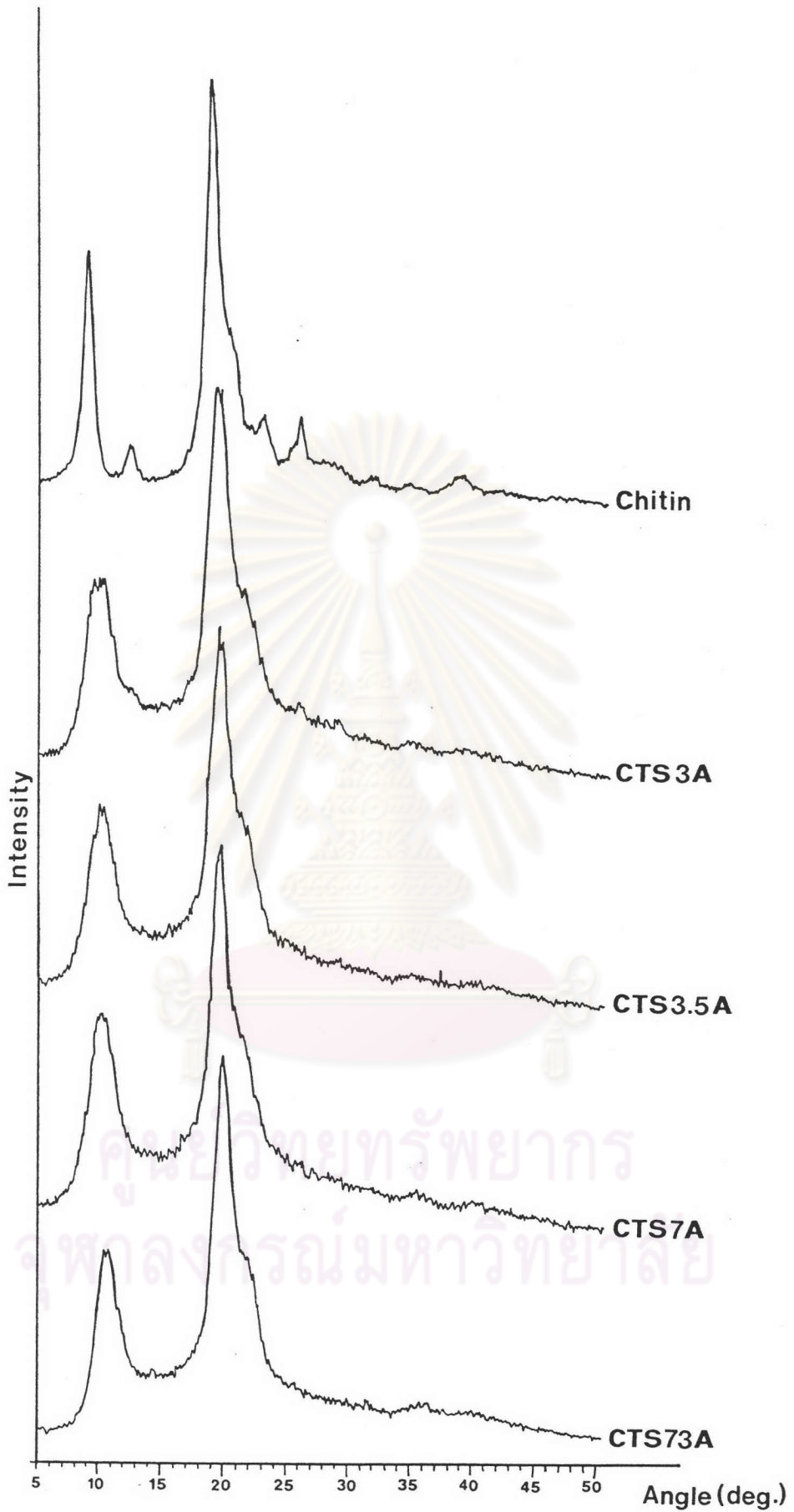
Figure 23   X-ray diffractograms of chitin and chitosan produced by method A.
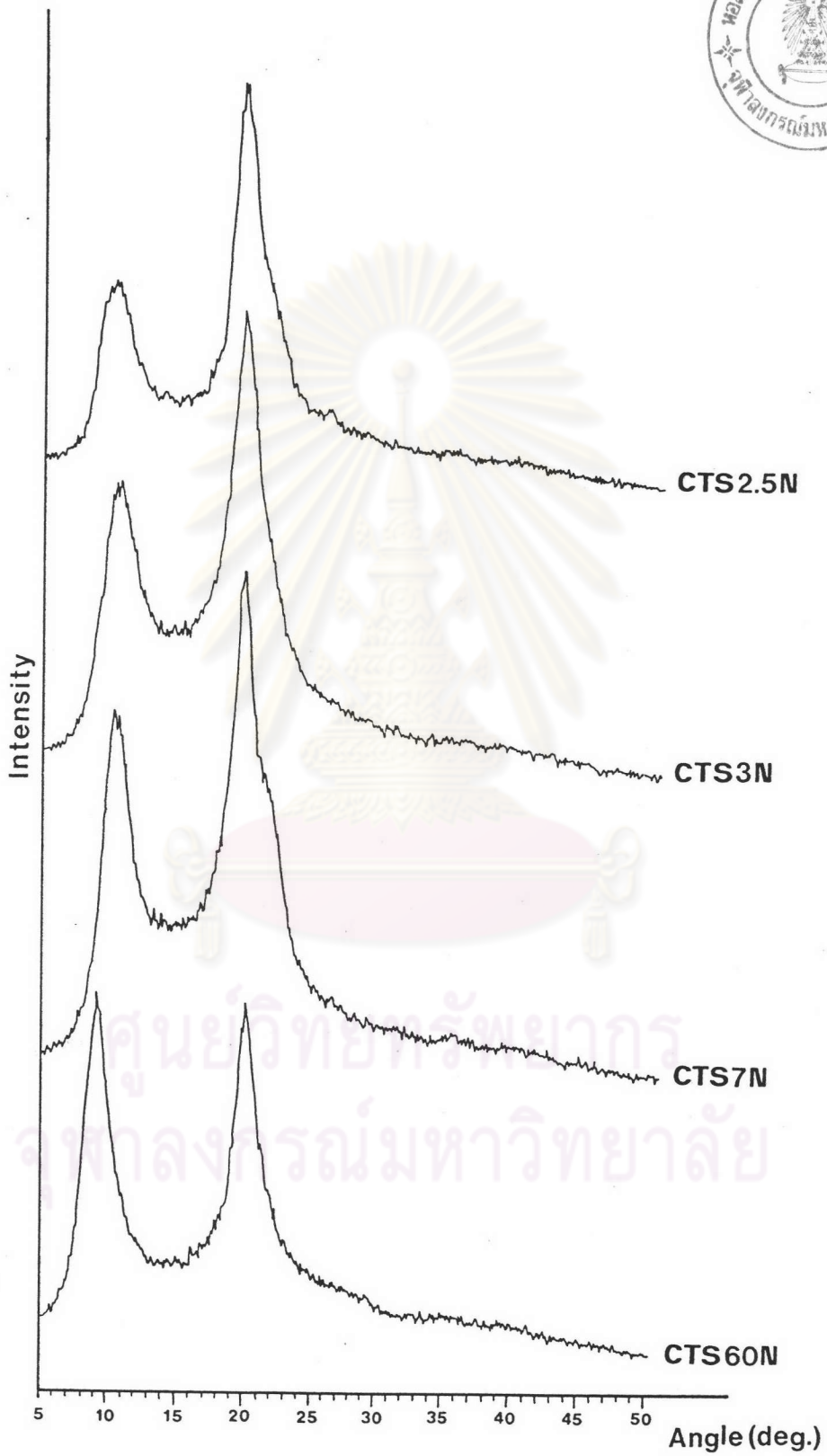
Figure 24   X-ray diffractograms of chitosan produced by method B and C.

2. <u>Evaluation of Tablet-Disintegration</u>

Paracetamol tablets prepared by wet granulation using chitin and chitosans as disintegrant, compressing at four compression pressures were observed for physical properties as follows: weight variation, thickness, hardness, and disintegration time. Data from these measurements are shown in Table 12-15.

2.1 Weight variation

The average weight and standard variation of tablets for each formulation are shown in Table 12-15. In all case, weight variation was well within the limit of USP standard. Moreover, the standard variation of each formulation was very low.

2.2 Thickness

The average weight and standard variation of tablets for each formulation are shown in Table 12-15. It was found that, thickness values tended to increase when the amount of disintegrant in formula increased. In the opposite, the decreasing of thickness values was found as compression force increased.

Table 12 Physical properties of paracetamol tablets containing various disintegrants at 3 % concentration at different compression pressure .

P (lbs)	Physical properties of paracetamol tablet		3 % Disintegrant in Paracetamol tablet								
			Chitin	CTS3A	CTS3.5A	CTS7A	CTS73A	CTS2.5N	CTS3N	CTS7N	CTS60N
2000	Weight	(mg ± s.d.)	541.0 ± 0.7	540.1 ± 1.6	540.9 ± 0.9	539.4 ± 0.4	540.3 ± 0.5	544.4 ± 0.9	542.0 ± 0.5	543.0 ± 0.5	544.2 ± 1.0
	Thickness	(mm ± s.d.)	3.848 ± 0.010	3.840 ± 0.010	3.820 ± 0.014	3.821 ± 0.005	3.834 ± 0.005	3.828 ± 0.010	3.846 ± 0.025	3.832 ± 0.011	3.810 ± 0.017
	Hardnes	(kp ± s.d.)	6.90 ± 0.24	7.02 ± 0.24	9.27 ± 0.17	8.57 ± 0.14	7.96 ± 0.06	8.66 ± 0.12	7.93 ± 0.86	8.94 ± 0.44	8.73 ± 0.30
	Disintegration time (sec ± s.d.)		27.73 ± 0.65	30.40 ± 1.04	29.34 ± 0.64	30.58 ± 0.90	29.25 ± 0.30	31.14 ± 0.86	26.18 ± 1.41	31.44 ± 1.15	23.89 ± 0.85
	range	(sec)	26.43 - 28.28	28.94 - 31.71	28.68 ± 30.04	29.28 - 31.94	28.84 - 29.54	29.78 - 32.35	24.37 - 28.47	30.13 - 33.18	22.82 - 25.25
3000	Weight	(mg ± s.d.)	542.4 ± 0.1	540.4 ± 0.5	541.1 ± 1.1	541.9 ± 0.7	542.3 ± 1.0	543.8 ± 0.9	543.9 ± 0.8	543.3 ± 0.8	543.7 ± 0.5
	Thickness	(mm ± s.d.)	3.706 ± 0.010	3.688 ± 0.006	3.716 ± 0.008	3.728 ± 0.006	3.724 ± 0.014	3.700 ± 0.009	3.680 ± 0.008	3.684 ± 0.007	3.674 ± 0.021
	Hardnes	(kp ± s.d.)	11.15 ± 0.20	11.34 ± 0.44	10.40 ± 0.41	9.61 ± 0.59	10.46 ± 0.40	11.25 ± 0.23	12.59 ± 0.36	11.95 ± 0.45	11.37 ± 0.39
	Disintegration time (sec ± s.d.)		43.36 ± 0.76	48.26 ± 1.80	44.35 ± 1.46	44.97 ± 1.52	47.14 ± 1.82	50.99 ± 1.09	48.42 ± 2.26	51.82 ± 1.08	42.78 ± 1.90
	range	(sec)	42.19 - 44.63	45.66 - 50.53	42.19 - 46.50	42.37 - 46.91	44.41 - 50.50	50.10 - 52.87	45.87 - 51.19	50.25 - 53.09	40.19 - 46.44
4000	Weight	(mg ± s.d.)	542.7 ± 0.9	542.7 ± 0.9	542.2 ± 1.1	540.7 ± 0.7	541.7 ± 1.2	542.4 ± 0.8	541.8 ± 1.1	542.4 ± 0.6	542.5 ± 0.8
	Thickness	(mm ± s.d.)	3.632 ± 0.006	3.625 ± 0.11	3.647 ± 0.006	3.639 0.006	3.639 ± 0.006	3.657 ± 0.016	3.627 ± 0.007	3.634 ± 0.007	3.611 ± 0.005
	Hardnes	(kp ± s.d.)	13.29 ± 0.48	13.20 ± 0.46	11.88 ± 0.44	11.02 ± 0.53	11.02 ± 0.53	12.88 ± 0.36	13.92 ± 0.63	14.25 ± 0.93	14.47 ± 0.24
	Disintegration time (sec ± s.d.)		65.69 ± 3.23	80.38 ± 2.93	65.11 ± 3.22	69.00 ± 2.09	69.00 ± 2.09	74.88 ± 2.89	66.74 ± 1.33	76.32 ± 1.20	62.19 ± 1.48
	range	(sec)	61.03 - 69.25	76.13 ± 84.78	60.12 - 69.81	66.35 - 71.82	66.35 - 71.82	70.91 - 78.77	65.10 - 68.65	75.22 - 78.81	60.44 - 64.91
5000	Weight	(mg ± s.d.)	540.4 ± 0.7	540.0 ± 1.3	540.6 ± 1.0	540.0 ± 1.8	540.1 ± 1.9	543.2 ± 1.2	541.9 ± 0.9	542.2 ± 1.2	543.3 ± 0.8
	Thickness	(mm ± s.d.)	3.569 ± 0.003	3.574 ± 0.010	3.553 ± 0.004	3.553 ± 0.013	3.561 ± 0.009	3.582 ± 0.006	3.645 ± 0.021	3.565 ± 0.005	3.556 ± 0.009
	Hardnes	(kp ± s.d.)	15.17 ± 0.52	14.80 ± 0.62	16.99 ± 0.76	15.93 ± 0.35	15.06 ± 0.48	14.95 ± 0.16	17.19 ± 0.29	15.96 ± 0.44	15.60 ± 0.45
	Disintegration time (sec ± s.d.)		121.01 ± 3.13	131.91 ± 2.32	122.44 ± 8.40	119.10 ± 6.85	129.34 ± 9.84	117.03 ± 5.67	109.25 ± 2.90	124.48 ± 5.56	82.81 ± 1.46
	range	(sec)	115.13 - 124.90	128.37 - 135.27	114.52 - 138.77	112.86 - 128.99	118.80 - 134.86	110.33 - 125.55	105.59 - 113.50	117.79 - 133.87	81.00 - 84.91

Table 13   Physical properties of paracetamol tablets containing various disintegrants at 5 % concentration at different compression pressure.

P (lbs)	Physical properties of paracetmol tablet		5 % Disintegrant in Paracetamol tablet								
			Chitin	CTS3A	CTS3.5A	CTS7A	CTS73A	CTS2.5N	CTS3N	CTS7N	CTS60N
2000	Weight	(mg ± s.d.)	550.1± 1.4	551.9 ± 1.0	551.6 ± 0.5	552.1 ± 1.3	550.1 ± 0.7	553.3 ± 0.6	552.6 ± 0.8	552.7 ± 1.2	554.0 ± 1.2
	Thickness	(mm ± s.d.)	3.929 ± 0.005	3.919 ± 0.011	3.920 ± 0.010	3.927 ± 0.005	3.932 ± 0.008	3.938 ± 0.016	3.873 ± 0.099	3.909 ± 0.011	3.888 ± 0.007
	Hardnes	(kp ± s.d.)	6.25 ± 0.50	6.49 ± 0.37	6.48 ± 0.25	6.68 ± 0.24	5.73 ± 0.37	7.48 ± 0.13	8.41 ± 0.24	8.78 ± 0.28	8.91 ± 0.60
	Disintegration time (sec ± s.d.)		20.14 ± 1.09	22.10 ± 0.80	22.34 ± 0.76	21.71 ± 0.77	22.09 ± 0.59	20.93 ± 0.49	20.80 ± 0.97	24.11± 1.08	20.57 ± 0.99
	range	(sec)	18.50 - 21.56	20.84 - 23.35	21.47 - 23.68	20.63 - 22.79	21.25 - 22.84	20.16 - 21.34	19.37 - 22.16	22.59 - 25.69	19.16 - 21.32
3000	Weight	(mg ± s.d.)	549.6 ± 1.3	551.9 ± 1.0	551.5 ± 0.5	551.3 ± 1.3	551.8 ± 1.3	553.2 ± 1.0	552.9 ± 0.9	553.7 ± 0.7	552.7 ± 1.1
	Thickness	(mm ± s.d.)	3.789 ± 0.007	3.787 ± 0.012	3.775 ± 0.006	3.758 ± 0.008	3.759 ± 0.007	3.798 ± 0.009	3.765 ± 0.006	3.767 ± 0.006	3.754 ± 0.009
	Hardnes	(kp ± s.d.)	9.18 ± 0.63	9.68 ± 0.66	9.27 ± 0.40	10.71 ± 0.60	10.97 ± 0.82	10.60 ± 0.20	11.68 ± 0.33	10.94 ± 0.38	11.71 ± 0.43
	Disintegration time (sec ± s.d.)		27.02 ± 1.39	31.18 ± 0.99	30.19 ± 0.59	33.10 ± 0.54	32.24 ± 1.13	30.02 ± 1.14	30.24 ± 0.63	36.83 ± 0.75	33.11 ± 1.27
	range	(sec)	25.10 - 29.29	29.50 - 32.38	29.44 - 30.97	32.47 - 34.03	30.72 - 33.69	28.62 - 31.66	29.00 - 31.04	35.78 - 37.97	31.62 - 34.97
4000	Weight	(mg ± s.d.)	551.1 ± 1.8	551.2 ± 0.9	550.7 ± 1.3	550.6 ± 0.7	549.5 ± 1.1	553.0 ± 1.3	552.6 ± 0.8	552.3 ± 0.7	552.7 ± 0.4
	Thickness	(mm ± s.d.)	3.697 ± 0.023	3.695 ± 0.008	3.694 ± 0.007	3.672 ± 0.002	3.674 ± 0.005	3.718 ± 0.006	3.701 ± 0.012	3.691 ± 0.009	3.687 ± 0.011
	Hardnes	(kp ± s.d.)	11.92 ± 0.56	12.97 ± 0.84	11.06 ± 0.48	13.30 ± 0.52	13.07 ± 1.06	13.01 ± 0.22	13.27 ± 0.60	13.47 ± 0.64	14.63 ± 0.46
	Disintegration time (sec ± s.d.)		42.34 ± 1.19	45.98 ± 1.42	45.01 ± 1.05	48.21± 0.92	48.14 ± 1.43	42.25 ± 1.37	44.07 ± 1.13	52.36 ± 1.31	46.67 ± 1.93
	range	(sec)	40.88 - 44.16	44.57 - 47.84	44.03 - 46.53	47.18 - 49.78	45.94 - 50.59	40.14 - 44.37	42.16 - 45.53	50.53 - 54.88	43.62 - 48.41
5000	Weight	(mg s.d.)	550.7 ± 1.1	5524.4 ± 0.9	550.1 ± 1.3	549.6 ± 0.5	550.4 ± 0.6	553.0 ± 1.0	553.7 ± 0.9	552.3 ± 1.0	553.0 ± 0.9
	Thickness	(mm s.d.)	3.635 ± 0.007	3.641 ± 0.010	3.624 ± 0.012	3.628 ± 0.005	3.631 ± 0.007	3.651 ± 0.012	3.648 ± 0.007	3.628 ± 0.008	3.624 ± 0.004
	Hardnes	(kp s.d.)	12.95 ± 0.28	13.43 ± 0.55	14.54 ± 0.56	13.18 ± 0.43	13.42 ± 0.85	14.54 ± 0.29	15.72 ± 0.48	16.19 ± 0.71	16.30 ± 0.38
	Disintegration time (sec s.d.)		62.25 ± 4.62	69.29 ± 4.17	64.52 ± 2.97	72.73 ± 3.38	67.59 ± 2.62	61.94 ± 2.32	68.26 ± 2.90	82.75 ± 4.91	67.59 ± 2.41
	range	(sec)	57.31 - 70.19	63.57 - 74.50	60.56 - 68.32	68.57 - 78.28	65.97 - 70.06	59.43 - 65.40	64.10 - 72.75	75.87 - 89.56	62.72 - 70.22

Table 14 Physical properties of paracetamol tablets containing various disintegrants at 10 % concentration at different compression pressure.

P (lbs)	Physical properties of paracetamol tablet	10 % Disintegrant in Paracetamol Tablet			
		CTS3A	CTS7A	CTS2.5N	CTS7N
2000	Weight (mg ± s.d.)	575.3 ± 1.3	574.5 ± 0.8	574.4 ± 0.9	573.8 ± 0.9
	Thickness (mm ± s.d.)	4.081 ± 1.7	4.112 ± 0.016	4.083 ± 0.008	4.080 ± 0.007
	Hardnes (kp ± s.d.)	7.67 ± 0.58	7.07 ± 0.58	7.24 ± 0.41	7.29 ± 0.61
	Disintegration time (sec ± s.d.)	17.75 ± 0.76	15.80 ± 0.69	16.86 ± 0.47	16.50 ± 0.78
	range (sec)	16.67 - 18.91	14.97 - 17.02	16.14 - 17.45	15.41 - 17.53
3000	Weight (mg ± s.d.)	576.0 ± 1.0	575.6 ± 1.9	574.6 ±1.1	574.2 ±1.1
	Thickness (mm ± s.d.)	3.898 ± 0.094	3.949 ± 0.008	3.946 ± 0.009	3.940 ± 0.015
	Hardnes (kp ± s.d.)	12.08 ± 0.62	11.08 ± 0.45	11.05 ± 0.39	10.93 ± 0.45
	Disintegration time (sec ± s.d.)	24.85 ± 0.74	23.94 ± 0.64	23.37 ± 0.43	23.39 ± 0.77
	range (sec)	23.97 - 25.64	22.82 - 24.80	22.69 - 23.84	22.20 - 24.56
4000	Weight (mg ± s.d.)	573.8 ± 1.3	573.9 ± 1.3	572.8 ± 1.0	574.7 ± 1.3
	Thickness (mm ± s.d.)	3.840 ± 0.020	3.851 ± 0.013	3.859 ± 0.011	3.871 ± 0.010
	Hardnes (kp ± s.d.)	13.53 ± 0.57	13.37 ± 0.75	13.12 ± 0.85	13.82 ± 0.51
	Disintegration time (sec ± s.d.)	32.24 ± 1.34	31.60 ± 0.70	31.13 ± 0.98	32.68 ± 1.18
	range (sec)	30.10 - 34.24	30.81 - 32.90	29.27 - 32.23	30.38 - 34.37
5000	Weight (mg s.d.)	574.1 ± 1.4	574.6 ± 1.3	573.0 ± 0.9	576.2 ± 0.5
	Thickness (mm s.d.)	3.782 ± 0.010	3.794 ± 0.009	3.807 ± 0.013	3.809 ± 0.009
	Hardnes (kp s.d.)	17.19 ± 0.42	17.19 ± 0.73	16.02 ± 0.87	17.08 ± 0.63
	Disintegration time (sec s.d.)	43.88 ± 1.00	42.09 ± 0.40	42.92 ± 0.47	44.09 ± 0.74
	range (sec)	42.20 - 45.46	41.54 - 42.70	41.77 - 43.82	43.05 - 45.38

Table 15 Physical properties of paracetamol tablets containing various disintegrants at 5 % concentration at different compression pressure.
(Disintegration time was determined by using 0.1 N. HCl as disintegrating medium.)

P (lbs)	Physical properties of paracetamol tablet	5 % Disintegrant in Paracetamol tablet								
		Chitin	CTS3A	CTS3.5A	CTS7A	CTS73A	CTS2.5N	CTS3N	CTS7N	CTS60N
2000	Weight (mg ± s.d.)	554.5 ± 1.4	554.2 ± 1.2	554.5 ± 1.1	553.9 ± 0.8	552.3 ± 1.1	553.6 ± 0.8	554.5 ± 0.8	553.9 ± 1.3	552.7 ± 0.5
	Thickness (mm ± s.d.)	3.918 ± 0.017	3.880 ± 0.037	3.917 ± 0.016	3.908 ± 0.010	3.928 ± 0.009	3.892 ± 0.021	3.895 ± 0.026	3.917 ± 0.035	3.929 ± 0.009
	Hardnes (kp ± s.d.)	7.67 ± 0.20	7.44 ± 0.49	7.83 ± 0.27	8.10 ± 0.45	7.05 ± 0.51	8.32 ± 0.18	8.28 ± 0.59	7.58 ± 0.39	7.50 ± 0.24
	Disintegration time (sec ± s.d.)	20.28 ± 0.95	51.19 ± 2.29	97.35 ± 5.16	> 1800	> 1800	58.14 ± 4.89	93.48 ± 11.76	> 1800	109.68 ± 6.40
	range (sec)	18.90 - 21.36	48.09 - 55.51	90.48 - 105.75	-	-	49.03 - 64.18	83.49 - 113.47	-	101.04 - 120.17
3000	Weight (mg ± s.d.)	554.1 ± 0.8	554.5 ± 0.5	552.7 ± 0.6	552.9 ± 0.8	552.6 ± 0.8	555.1 ± 1.6	554.1 ± 1.2	554.9 ± 0.7	553.2 ± 1.3
	Thickness (mm ± s.d.)	3.772 ± 0.003	3.792 ± 0.007	3.777 ± 0.008	3.764 ± 0.010	3.785 ± 0.008	3.767 ± 0.008	3.759 ± 0.014	3.775 ± 0.007	3.769 ± 0.006
	Hardnes (kp ± s.d.)	10.15 ± 0.25	10.57 ± 0.36	10.14 ± 0.22	10.67 ± 0.27	9.79 ± 0.60	10.32 ± 0.39	9.94 ± 0.44	10.59 ± 0.39	10.07 ± 0.47
	Disintegration time (sec ± s.d.)	33.29 ± 0.96	50.12 ± 1.45	107.76 ± 4.75	> 1800	> 1800	62.35 ± 3.65	95.21 ± 5.47	> 1800	115.18 ± 6.94
	range (sec)	32.02 - 35.02	47.99 - 52.64	102.01 - 114.47	-	-	55.79 - 66.31	87.72 - 103.61	-	106.42 - 127.34
4000	Weight (mg ± s.d.)	552.7 ± 0.8	554.3 ± 1.3	552.9 ± 0.8	552.9 ± 1.2	552.9 ± 0.5	553.0 ± 1.0	552.5 ± 0.8	552.3 ± 1.9	551.7 ± 1.0
	Thickness (mm ± s.d.)	3.696 ± 0.014	3.719 ± 0.009	3.702 ± 0.004	3.704 ± 0.006	3.717 ± 0.009	3.676 ± 0.008	3.688 ± 0.016	3.712 ± 0.009	3.703 ± 0.007
	Hardnes (kp ± s.d.)	12.18 ± 0.36	12.06 ± 0.40	12.55 ± 0.37	12.77 ± 0.73	12.22 ± 0.55	12.70 ± 0.90	12.44 ± 0.62	12.09 ± 1.33	11.49 ± 0.76
	Disintegration time (sec ± s.d.)	49.05 ± 1.47	64.75 ± 2.22	112.63 ± 4.77	> 1800	> 1800	74.23 ± 5.94	111.97 ± 7.37	> 1800	114.77 ± 5.75
	range (sec)	47.13 - 51.68	60.15 - 66.50	108.41 - 122.84	-	-	62.88 - 82.70	97.78 - 121.67	-	105.27 - 121.23
5000	Weight (mg s.d.)	554.1 ± 1.4	553.3 ± 0.8	554.0 ± 1.4	553.1 ± 1.1	552.1 ± 1.2	553.5 ± 1.3	552.7 ± 1.3	553.6 ± 1.2	552.1 ± 1.4
	Thickness (mm s.d.)	3.636 ± 0.010	3.635 ± 0.009	3.652 ± 0.016	3.638 ± 0.012	3.645 ± 0.013	3.649 ± 0.016	3.625 ± 0.018	3.630 ± 0.012	3.629 ± 0.011
	Hardnes (kp s.d.)	12.83 ± 0.48	14.24 ± 0.53	14.14 ± 0.53	13.80 ± 0.62	14.37 ± 0.78	14.29 ± 0.79	14.28 ± 0.22	14.11 ± 0.62	14.25 ± 0.35
	Disintegration time (sec s.d.)	70.30 ± 2.95	99.71 ± 5.07	189.30 ± 12.89	> 1800	> 1800	114.34 ± 5.46	140.88 ± 9.74	> 1800	199.25 ± 12.73
	range (sec)	66.45 - 74.34	92.29 - 108.02	178.34 - 215.89	-	-	107.97 - 122.15	127.38 - 156.34	-	185.66 - 220.43

2.3   Hardness

The average hardness and standard deviation of tablets are given in Table 12-15. From pressure-hardness profiles in Figure 25-28, it was observed that increasing compression pressure will increase hardness of paracetamol tablets, except for tablets containing 5% CTS7A at compression pressure 5000 lb. (Hardness at 4000 and 5000 lb. was 13.30 and 13.18 kp.,respectively that seemed having no difference.) At the same compression pressure, the hardness of each formulation was slightly different from the hardness of the others.
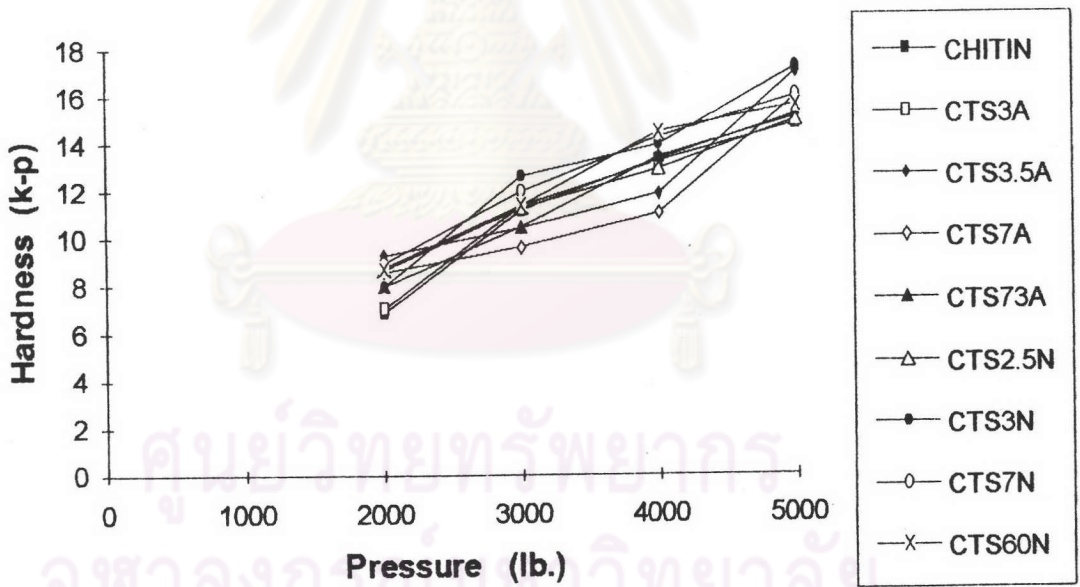
Figure 25   Pressure - hardness profile of paracetamol tablets containing 3% disintegrant.
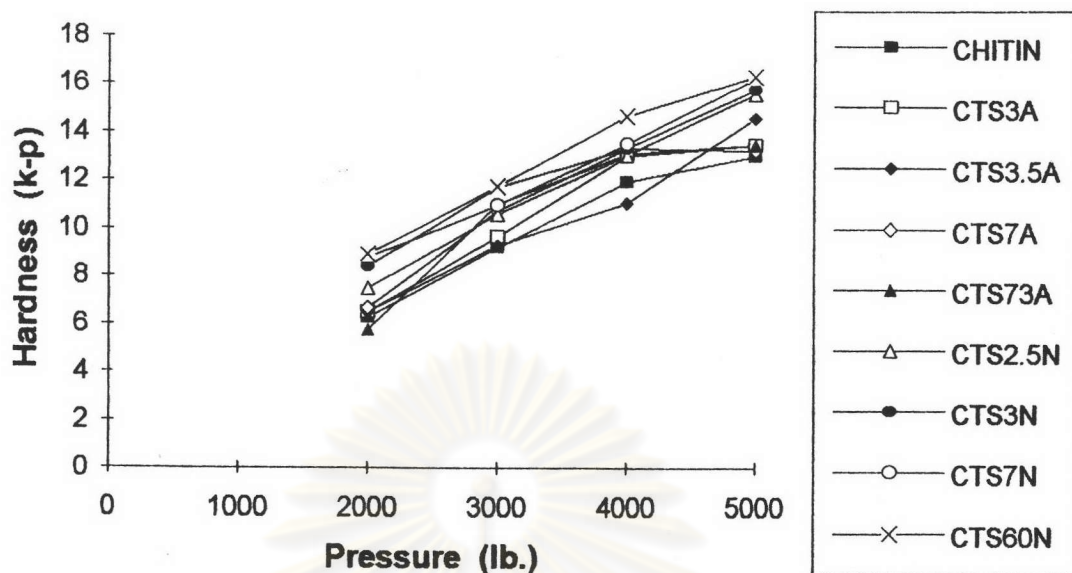
Figure 26   Pressure - hardness profile of paracetamol tablets containing
5% disintegrant that disintegration time evaluated in deionized
water.
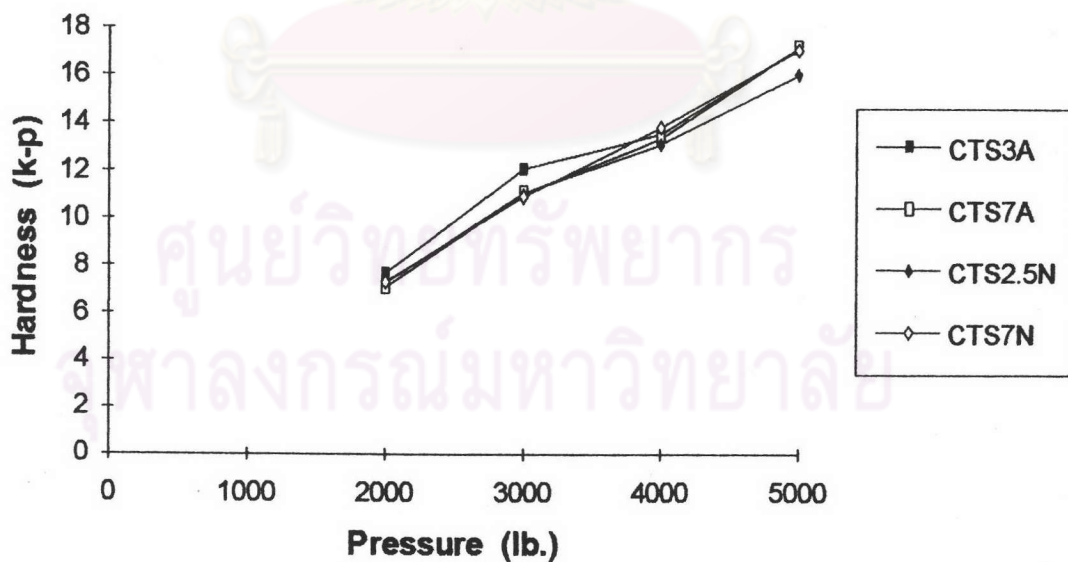
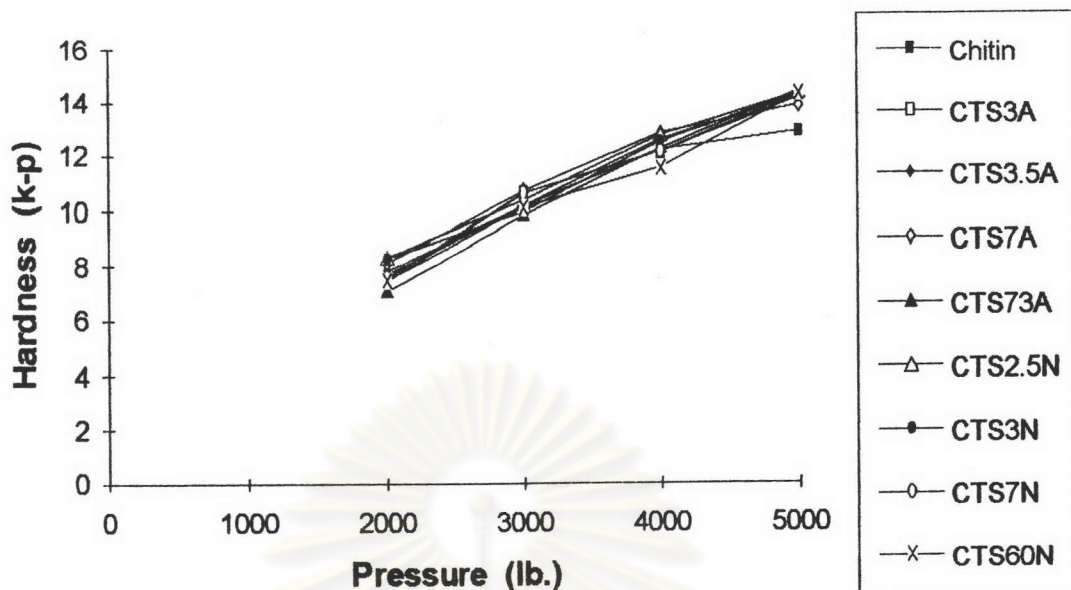Figure 27   Pressure - hardness profile of paracetamol tablets containing
10% disintegrant.

Figure 28   Pressure - hardness profile of paracetamol tablets containing
              5% disintegrant that disintegration time evaluated in 0.1 N. HCl.

2.4   Disintegration time

At the first time, paracetamol tablets of each formulation containing 3 and 5% disintegrant were prepared in order to evaluate physical properties, especially disintegration time in deionized water. The disintegration time of the paracetamol tablets containing various disintegrants (3 and 5%) at the same compression force appeared to have no difference. After that, the concentration of chitin and chitosan in paracetamol tablets was increased to 10%, and in this case, chitosans used as disintegrants were CTS3A, CTS7A, CTS2.5N, and CTS7N. No difference of disintegration time was observed. Finally, tablets containing 5% disintegrant were prepared in order to investigate disintegration time of tablet in 0.1 N. HCl.

Disintegration times of paracetamol tablets containing various disintegrant at 3, 5, and 10% concentration, and compressed at 2000-5000 lb. are given in Table 12-15. To compare disintegrating properties of each disintegrant in paracetamol tablets, data are depicted as three-axis graphs as shown in Figure 29-32. (The individual plot of each disintegrant is depicted in Appendix G.) From these figures, the disintegrating properties were easily compared by considering disintegration time at the same pressure and hardness. (Every points in the line that paralleled to disintegration-time axis have equal pressure and hardness value)

At the same compression pressure, it could be observed that the disintegration times in deionized water of each formulation were slightly different from the others (not more than 20 seconds at 3 and 5 % disintegrant level and not more than 10 seconds at 10% level), but these excepted for tablets containing 3% CTS60N that had significantly lower disintegration time than the others at the same amount of disintegrant (Figure 29), and tablets containing 5% CTS7N that had noticeably higher than the others especially at 5000-lb. compression pressure. (Figure 30)
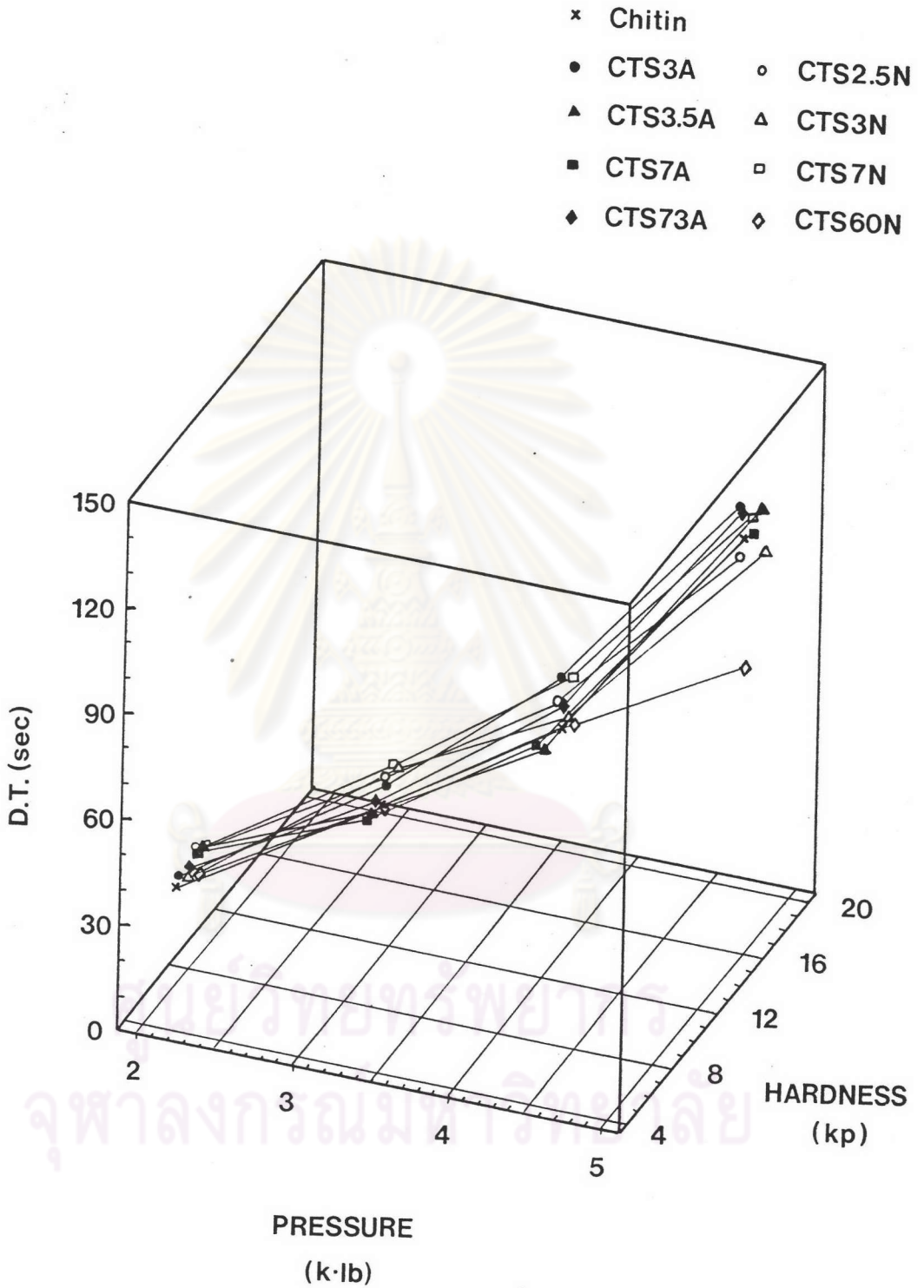
Figure 29 Disintegration time of paracetamol tablets containing 3% disintegrant at various pressure and hardness.
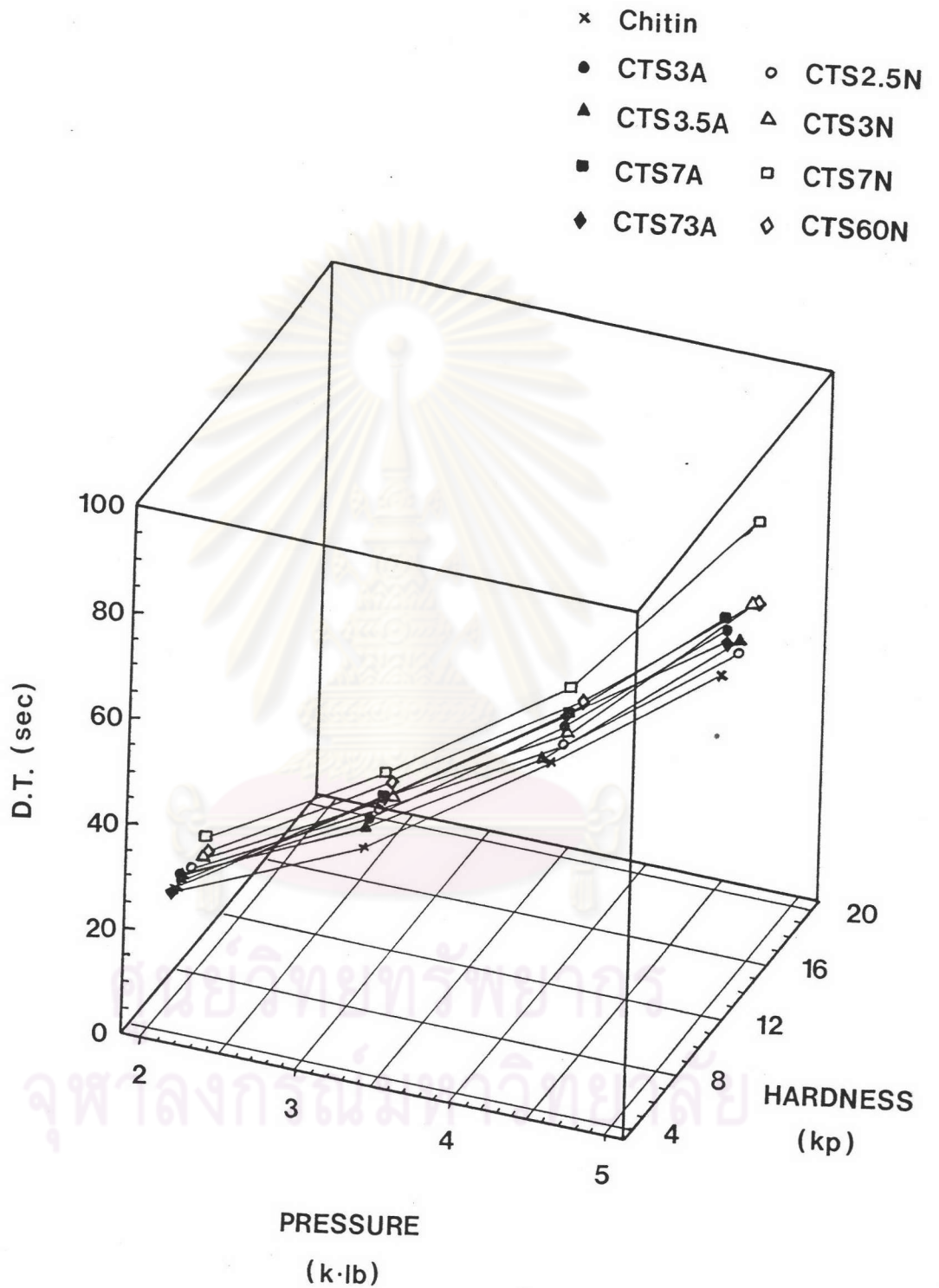
Figure 30   Disintegration time of paracetamol tablets containing 5% disintegrant at various pressure and hardness.
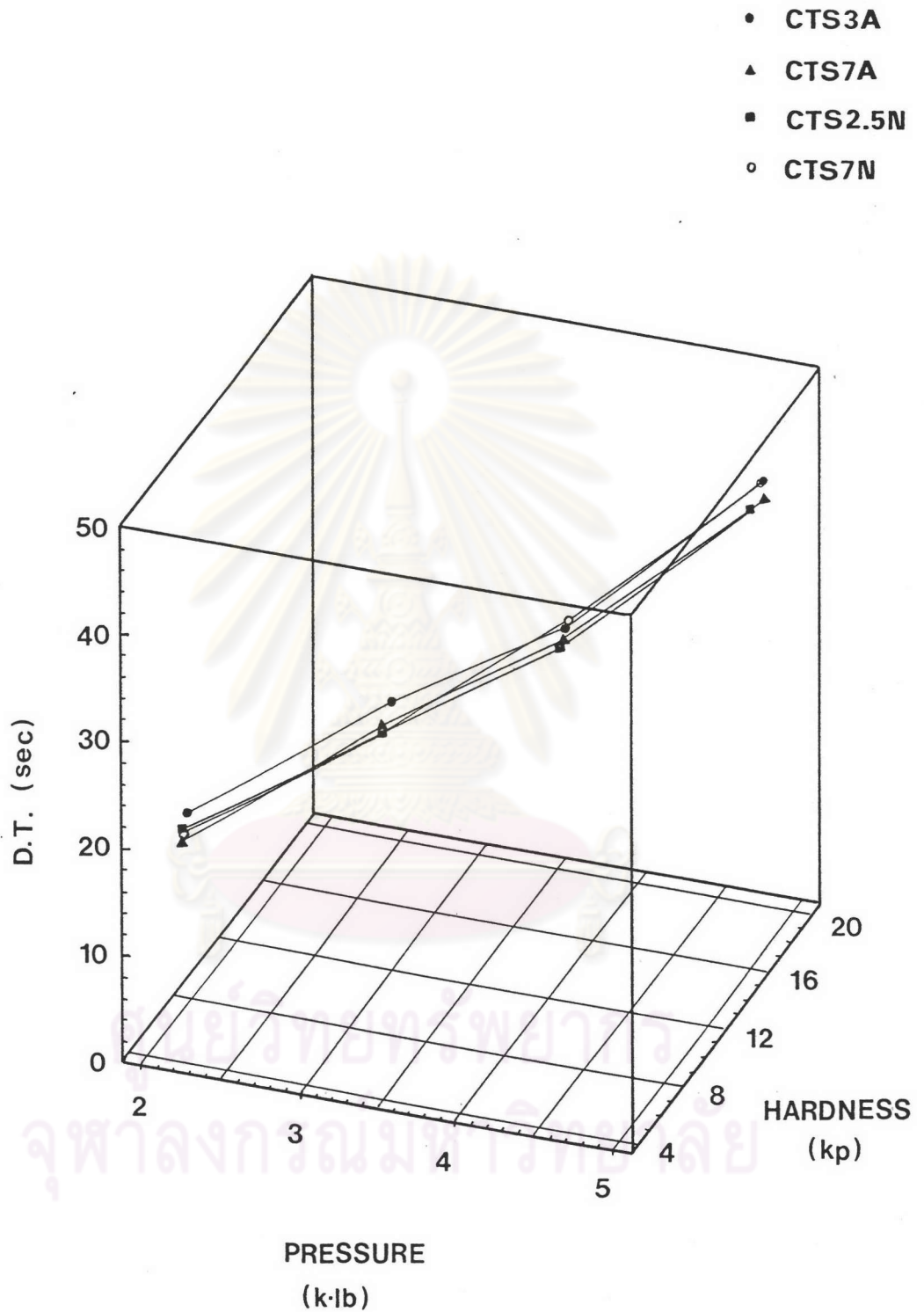
Figure 31 Disintegration time of paracetamol tablets containing 10% disintegrant at various pressure and hardness.
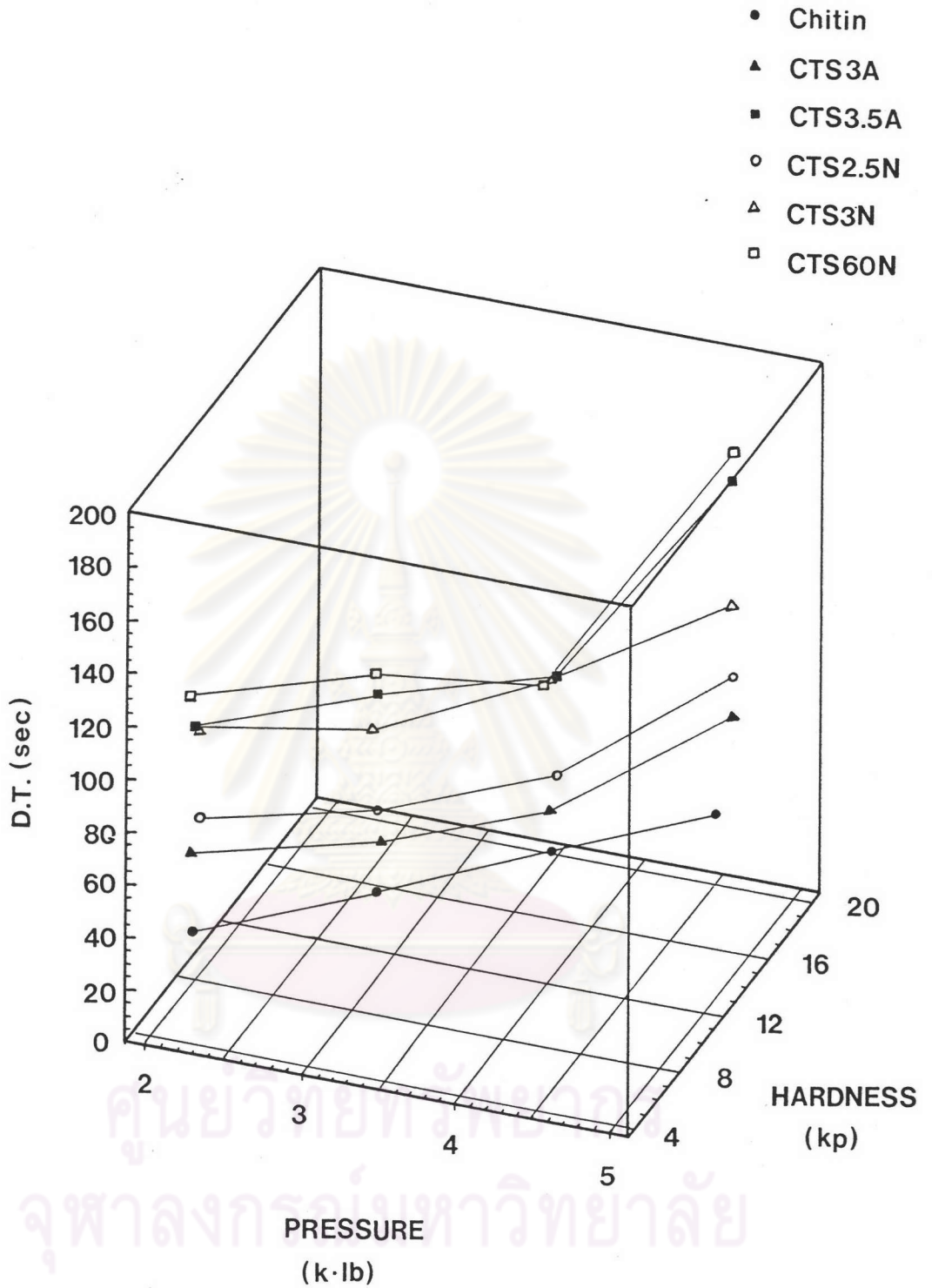
Figure 32   Disintegration time of paracetamol tablets containing 5% disintegrant
            at various pressure and hardness.(Disintegration time was evaluated
            in 0.1 N. HCl)

For disintegration time in 0.1 N. HCl , it was clearly observed that at the same compression pressure, disintegration time of each formulation was substantially different from the others. These differences correlated with the degree of deacetylation of each chitosan. It was found that disintegration times of tablets containing chitin in deionized water and in 0.1 N. HCl were not different. However, disintegration times of tablets containing chitosan in deionized water were lower than in 0.1 N. HCl. The tablets containing chitosan with higher degree of deacetylation had longer disintegration time as in the following order: disintegration time of CTS3A > CTS3.5A > CTS7A, CTS73A and CTS2.5N > CTS3N > CTS7N. Besides, disintegration time of tablets containing CTS7A, CTS73A, and CTS7N was more than 30 minutes.

Tablets containing CTS60N compressed at 2000-4000 lb. exhibited the disintegration time values closed to those of CTS3.5A and CTS3N, and those compressed at 5000 lb. showed similar disintegrating properties the same as of CTS3.5A.