

CHAPTER V

EFFECT OF VARIATION OF MOLECULAR STRUCTURE ON PHYSICO-CHEMICAL PROPERTIES OF MODIFIED TAPIOCA STARCH

It is generally accepted that the starches are not soluble in cold water. Carboxymethylation of starch resulted in an increase in solubility of starch product accompanied by increase in viscosity. One of the most important problem of modified carboxymethyl tapioca starch to be used as tablet disintegrant was its dissolution in water to form a viscous gel which retarded the tablet disintegration. To overcome this problem the carboxymethylated starch should be modified by alteration of molecular structure using crosslinking treatment to reduce its solubility and also decrease in viscosity resulting poor gel formation. The reduction of solubility of crosslinked carboxymethyl starch is obtained by the steric effect of crosslinked molecules. Huttenrauch (1973) suggested the criterion for a good disintegrant are poor solubility, poor gel formation, high swellability and great ease of hydration. Of course the development of tapioca starch as a new super disintegrant must be followed this criterion. However, modification of the molecular structure may change the physico-chemical properties of modified starch.

The effect of variation of degree of substitution and crosslinking on the disintegration efficiency of carboxymethyl potato starch have been studied by Bolhuis, et al.(1984). They reported that carboxymethylation of potato starch resulted in an increase in solubility accompanied by increased swelling capacity and viscosity when it was brought into contact with water. With increasing degree of substitution, increasing in electrostatic repulsion, the carboxymethylated starch

becomes gradually more soluble in cold water accompanied by an increased viscosity. They suggested that minor changes in molecular structure did not affect the disintegration efficiency when the disintegrant was used in a concentration of 4%.

Rudnic, Kanig and Rhodes(1983) have investigated the effect of molecular structure on the function of sodium starch glycolate in wet granulation systems. They concluded that lower levels of cross-linkage and substitution were favored when compared to higher levels of cross-linkage and substitution. In addition, their study clearly showed that it is necessary to maintain strict control over the molecular structure of the commercial product to maintain consistent quality. Furthermore, they have studied the effect of molecular structure variation on the disintegrant action of sodium starch glycolate. The results indicated that the relative small change in molecular structure caused substantial modification of disintegrant properties (Rudnic, Kanig and Rhodes, 1985).

Purpose of the study

As the modification of tapioca starch for the purpose to be used as a super disintegrant had not been investigated. Therefore, the optimum degree of substitution and degree of crosslinking must be developed and also the effects of variation of degree of substitution and crosslinking on physico-chemical properties of modified tapioca starch are evaluated, particularly its disintegrating property. In this part of studies, the various degree of substitution and crosslinking of tapioca starch derivatives were produced.

Materials and Methods

Materials

Tapioca starch	(Thai wah, Co., Ltd. Thailand)
Chloroacetic acid	(Sigma Chem. Co., USA)
Methanol	(BDH Lab., England)
Sodium hydroxide	(Eka Nobel, Sweden)
Acetic acid	(Riedee de Hain, Germany)
Sodium trimetaphosphate	(Sigma Chem. Co., USA)
Sodium carbonate	(BDH Lab., England)
Silver nitrate	(E Merck, Germany)
Ammonium thiocyanate	(Fluka Chem., Switzerland)
Sodium chloride	(E Merck, Germany)
Ammonium thiocyanate	(Fluka Chem., Switzerland)
Sodium chloride	(E Merck, Germany)
Standard phosphorus solution	(Sigma Chem. Co, USA)
Ammonium vanadate	(Farmitalia Carlo Erba, Italy)
Ammonium molybdate	(Sigma Chem. Co., USA)
Dicalcium phosphate	(Mendell, Co. Inc., USA)
Lactose direct compressed	(The Lactose Company of New Zealand, New Zealand)
Magnesium stearate	(Durham Chem., Ltd., England)

Methods

1. Preparation of carboxymethyl tapioca starch with various degree of substitutions.

From the previous study in chapter IV, the important factors affected the degree of substitution were reaction time and temperature. As a result the

preparation of various degree of substitution of carboxymethyl starch could be done by varying the time and temperature of reaction.

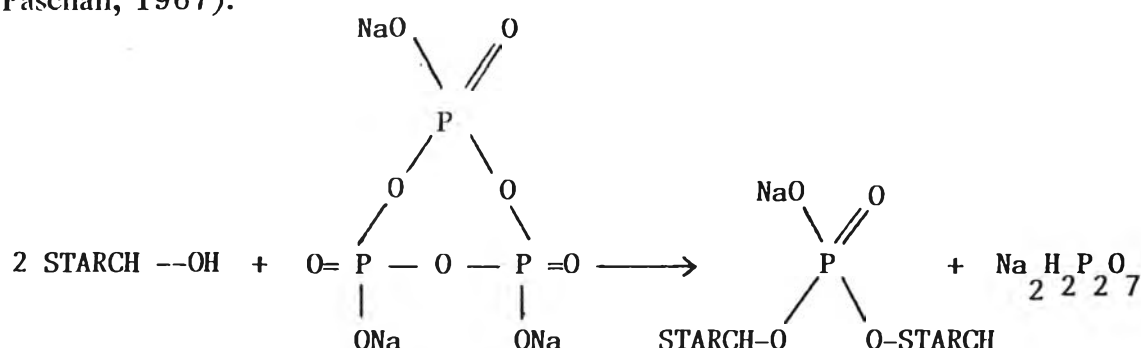
The different degree of substitution (DS) of carboxymethyl tapioca starch have been selected for this study were 0, 0.1, 0.17 and 0.22. The reasons for selecting DS in the range of 0.1 to 0.22 were based on the previous studied in chapter IV. As sedimentation volume in 0.1 N HCl which more closely resembled the gastric fluid showed the carboxymethyl tapioca starch with DS between 0.1- 0.22 could swelled in 0.1 N HCl. While those of lower 0.1 DS exhibited no swelling both in 0.1N HCl and water as shown in Figure 19 and the DS above 0.22 produced a hard gel formation both in water and 0.1 N HCl.

2. Preparation of cross-linked carboxymethyl tapioca starch (modified tapioca starch, MTS).

The carboxymethyl tapioca starches with different levels of degree of substitution (0, 0.1, 0.17 and 0.22) were crosslinked by food grade crosslinking agent, sodium trimetaphosphate in the presence of alkali, pH~11.2, the reaction was held at 50°C (Kerr and Cleveland, 1957).

The reason for selecting sodium trimetaphosphate as a crosslinking agent was that it has been approved for use in food starches by The Food Additive Regulations (Hamilton and Paschall, 1967).

The reaction of crosslinking the starch by water soluble trimetaphosphate salts was shown as the following equation (Hamilton and Paschall, 1967).



The percentage distribution of phosphate groups esterified in the C-2, C-3, and C-6 positions of the starch phosphate molecule was calculated to be 28%, 9% and 63%, respectively (Gramera, Heerema, and Parrish, 1966).

A quantitative determination of starch esters is determination of degree of substitution. With starch phosphate the degree of substitution is calculated from the phosphorous content (Van der Bij, 1976).

The crosslinking of carboxymethyl starch was performed by modification of Kerr and Cleveland's method (Kerr and Cleveland, 1957).

A 110.0 g of carboxymethyl starch with various degree of substitution was suspended in 330.00 ml of aqueous alcoholic solvent into which had been dissolved 3.3 g of sodium trimetaphosphate and sufficient sodium carbonate buffer to adjust pH of the starch slurry to 11.2. The slurry was heated to 50°C with continuously stirring and held at this reaction temperature for the time to be studied and then adjusted pH to 6.5 with 2 N HCl. The product was washed several times with 80% methanol until free of phosphate and finally with 100% of methanol, dry the product in hot air oven at 50°C overnight to ensure the removal of the trace solvent.

The reaction time intervals selected for this study were varied in the range of 0, 6, 12 and 24 hours. The reason for selecting the maximum reaction time of 24 hours was that the residual phosphate content was in the limitation that approved by The Food Additives Regulations when the reaction time was within 24 hours.

The Food Additives Regulations provided the safe use of a food starch modified by treatment with sodium tripolyphosphate and sodium trimetaphosphate that the residual phosphate in the starch is not to exceed 0.4% calculated as phosphorous (Hamilton and Paschall, 1967).

Sixteen derivatives of modified tapioca starches (MTS) were selected for evaluation of their disintegrating property and their composition were represented in the grid by the sample number in Table 12.

Table 12 Chemical Modification of Modified Tapioca Starch Studied.

Crosslinking Times (hr.)	%PO ₄	DS			
		0	0.10	0.17	0.22
0	0	1	2	3	4
6	0.64	5	6	7	8
12	0.95	9	10	11	12
24	1.04	13	14	15	16

3. Evaluation of the physico-chemical properties of modified tapioca starch.

3.1 Chemical evaluation.

3.1.1 Determination of degree of substitution of carboxymethyl tapioca starch (CMTS).

The methods to determine the DS of CMTS were explained in 3.1.1 and 3.1.2 of Chapter IV.

3.1.2 Qualitative and relative quantitative evaluations of carboxymethyl tapioca starch with various DS.

The qualitative and relative quantitative evaluations of CMTS were conducted by using infrared spectrophotometer. The infrared spectra of tapioca starch and modified tapioca starch were evaluated.

3.1.3. Determination of phosphate contents

The phosphate contents were determined by determination of the percentage of phosphorous in the sample. The small amount of phosphorous in samples of modified tapioca starch were determined by using spectrophotometry. This method was employed by Corn Industries Research Foundation (Lyne, 1976).

Weighed 10.0 g of starch sample into evaporating dish, add 10.00 ml of 2% calcium acetate solution in a fine steam. Distribute the solution uniformly in the sample and then evaporate to dryness on hot plate and carbonized the sample. Place the dish in the muffle furnace at 650°C until free of carbon. Then cool to room temperature and wet the ash with 15.00 ml of water. Slowly wash down the sides of the dish with 5.00 ml of 29% nitric acid, quantitatively transfer to a 200-ml volumetric flask, rinsing the dish with three 20-ml portions of distilled water. Dilute to the volume with distilled water and mix thoroughly.

Transfer 2.50 ml of prepared sample to 100-ml volumetric flask, add 50.00 ml of water to another flask to serve as blank. To each flask, add 10.00 ml of 29% nitric acid and 10.00 ml of 0.25% ammonium vanadate, and then add 10.00 ml of 5% ammonium molybdate, mixing thoroughly after addition of each reagent. Dilute to volume with distilled water, mix thoroughly and allow to stand for 10 minutes.

Determine percent transmission of sample at 460 nm, using the blank as a reference solution at 100% transmission. The phosphorous content were calculated from the transmission concentration curve which was performed by using standard phosphorous solution.

$$\% \text{ phosphorous} = \frac{(\text{P} \times \text{dilution volume in ml} \times 100)}{(\text{Aliquot volume in ml} \times \text{sample weight in g} \times 1000)}$$

where P is phosphorous content (mg/100 ml) from calibration curve (Appendix 3).

$$\% \text{ phosphate} = \% \text{ phosphorous} \times 3.065$$

3.1.4 Determination of sodium chloride contents.

The sodium chloride contents were performed as the method explained in 3.1.3 of Chapter IV.

3.2 Physical property evaluations

The physical properties of carboxymethyl tapioca starch (MST): water uptake, bulk swelling, sedimentation volume, hydration capacity, cold water soluble fraction and viscosity, were performed as the methods described in 3.2 of Chapter IV.

4. Evaluation of the disintegrant property of MTS.

Dicalcium phosphate and lactose direct compressed tablets were used as model to represent poorly soluble and very soluble tablet systems, respectively.

4.1 Preparation of dicalcium phosphate and lactose tablets.

The experimental formulation of dicalcium tablets and lactose tablets had been described in chapter III. Various MTS were used as tablet disintegrant at the concentration of 4%. The tablets were compressed by hydraulic press with pressure about 3000 pounds, using flat face, 11/32 inches punch.

4.2 Evaluation of tablets

4.2.1 Disintegration times

The disintegration time (DT) of tablets were determined in both deionized water and 0.1N HCl, using Hanson Research Tablet Disintegration Tester (model 64-700-156). The mean of six determinations for each batch was calculated.

4.2.2 Hardness of tablets

Five tablets were randomly selected and subjected to a hardness tester (Schleuniger-2E, model 2E/205). The mean and standard deviation were calculated.

Results and Discussion

1. Chemical evaluations

1.1 Determination of DS of carboxymethyl tapioca starch (CMTS).

The DS of synthetic CMTS were shown in Table 13 and Figure 22. The S1, S2 and S3 were the synthetic CMTS with DS of 0.10, 0.17 and 0.22, respectively.

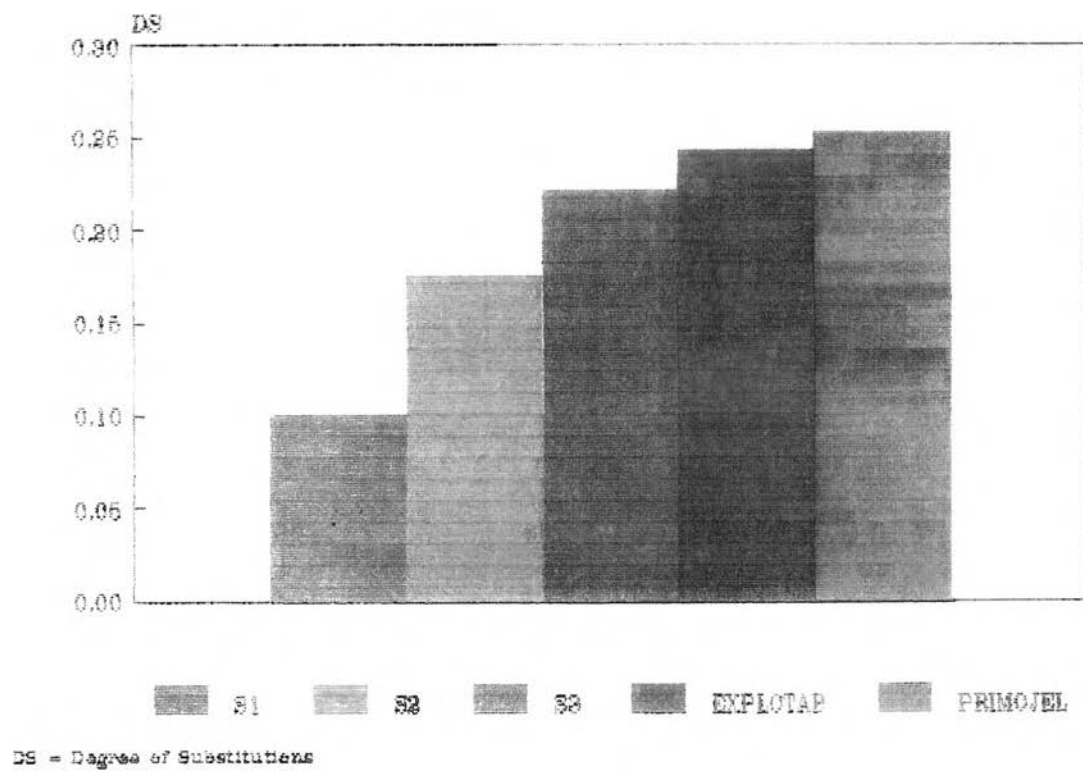


Figure 22 Degree of Substitutions of Prepared CMTS.

Table 13. Degree of Substitutions of Synthesized CMTS.

Types	Degree of Substitutions (DS)	
	carboxyl method	USP method
S ₁	0.08 (0.01)	0.10 (0.01)
S ₂	0.16 (0.01)	0.17 (0.00)
S ₃	0.22 (0.01)	0.22 (0.01)
Explotab ^R	0.21 (0.00)	0.24 (0.01)
Primojel ^R	0.25 (0.00)	0.25 (0.00)

Standard deviation in parentheses

1.2 Qualitative evaluation of CMTS.

The qualitative evaluation of CMTS was conducted by using Fourier Transform IR-spectrophotometer (model 1760x, Perkin Elmer, USA). The infrared spectrum were shown in Figure 23.

Figure 23 showed the infrared spectrum of tapioca starch and carboxymethyl starch with various degree of substitutions. A carboxymethyl substitution are characterized by a specific absorption band at 1610 cm⁻¹ and 1422 cm⁻¹. The absorption peak at 1610 cm⁻¹ represented the ionized carboxyl group, $-\overset{\text{O}(-)}{\parallel}{\text{C}}-\text{O}^-$, from carboxymethyl group $[-\text{CH}_2-\overset{\text{O}^-}{\parallel}{\text{C}}=\text{O}]$ and at 1422 cm⁻¹ represented the tertiary alcohol (Pecsok, et al., 1976).

1.3 Relative quantitative evaluation of CMTS.

The relative quantitative evaluation of CMTS was performed by using infrared spectrophotometry. The infrared spectrum of CMTS with various DS were illustrated in Figure 23. The peak height ratios were used to determine the relative quantitative of carboxymethyl substitutions.

Using the absorption peak at about 996 cm⁻¹ as a reference, measured the peak height at 1610 cm⁻¹. The peak height ratios of carboxymethyl

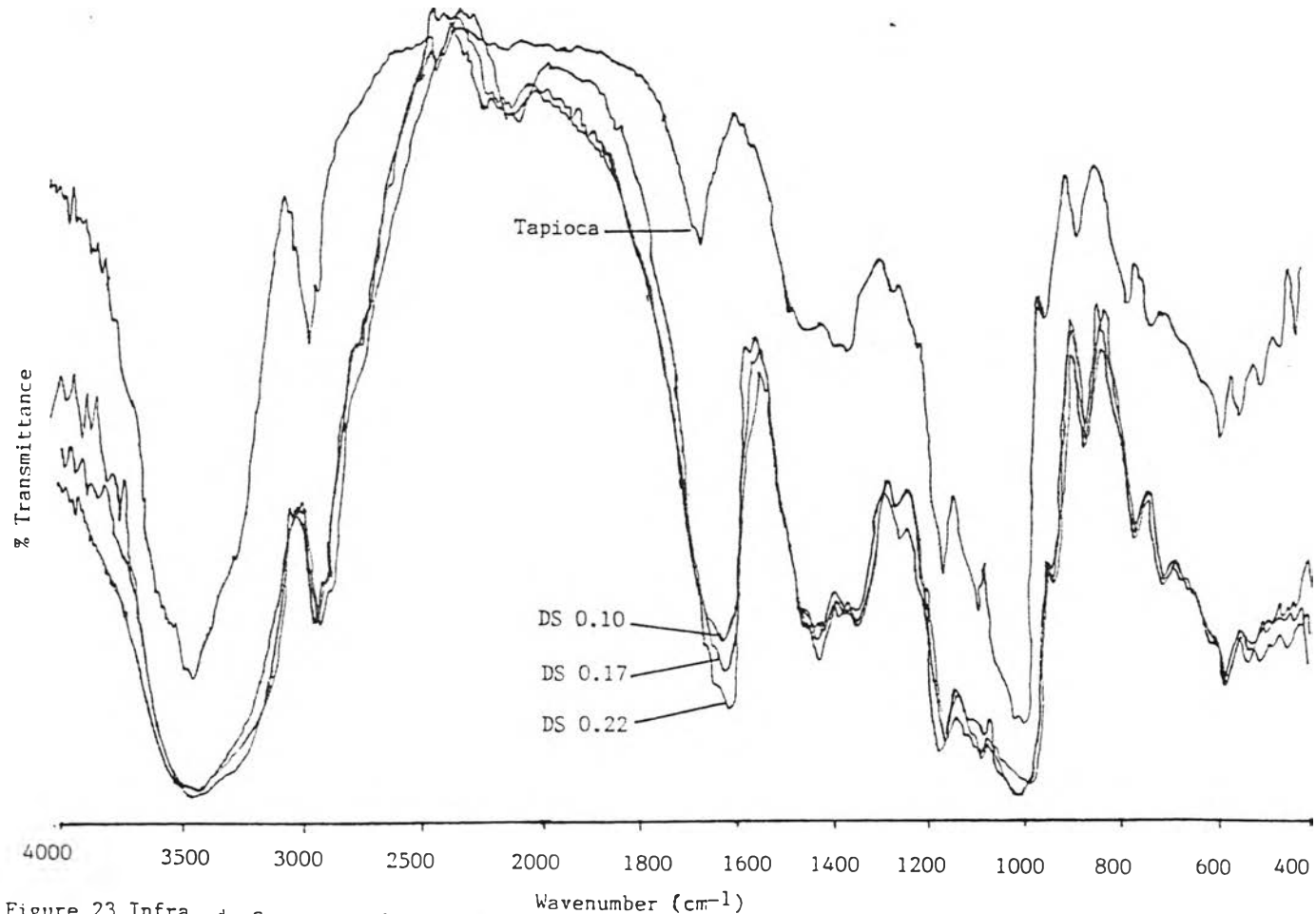


Figure 23 Infrared Spectrum of Carboxymethyl Tapioca Starches.

substitution of CMTS with DS of 0.1, 0.17 and 0.22 were 1:1.09:1.17. Similarly, the peak height ratio at 1422 cm^{-1} , were 1:1.04:1.13. This could be concluded that the carboxymethyl substitutions were taken place, which were characterized by a specific absorption band at 1610 cm^{-1} and 1422 cm^{-1} , with various degree of substitutions.

1.4 Qualitative determination of phosphate in modified tapioca starch (MTS)

The qualitative determination of phosphate in MTS were conducted by using infrared spectroscopy. The infrared spectrum were shown in Figure 24. A generally characteristic absorption band of starch phosphate ester was illustrated at $1240\text{--}1200\text{ cm}^{-1}$ (Van der Bij, 1976) which represented the covalent phosphate ($-\text{CH}_2\text{-O-P-O}$). In fact, at the $1240\text{--}1200\text{ cm}^{-1}$ were covered by C-OH stretching vibrations and a broad C-O stretching band centered at 1242 cm^{-1} (Pecsok et al., 1976). However the qualitative determination could be performed at $1371\text{--}1365\text{ cm}^{-1}$ which represented the phosphorous in the form of $-\overset{\text{||}}{\text{P}}=\text{O}$, the relative quantitative determination of phosphorous content in sample could not determine. However, the quantitative determination of phosphate content might be performed by chemical methods.

1.5 Determination of phosphate contents. The phosphate content were determined using spectrophotometric method. The results were presented in Table 14 and Figure 25.

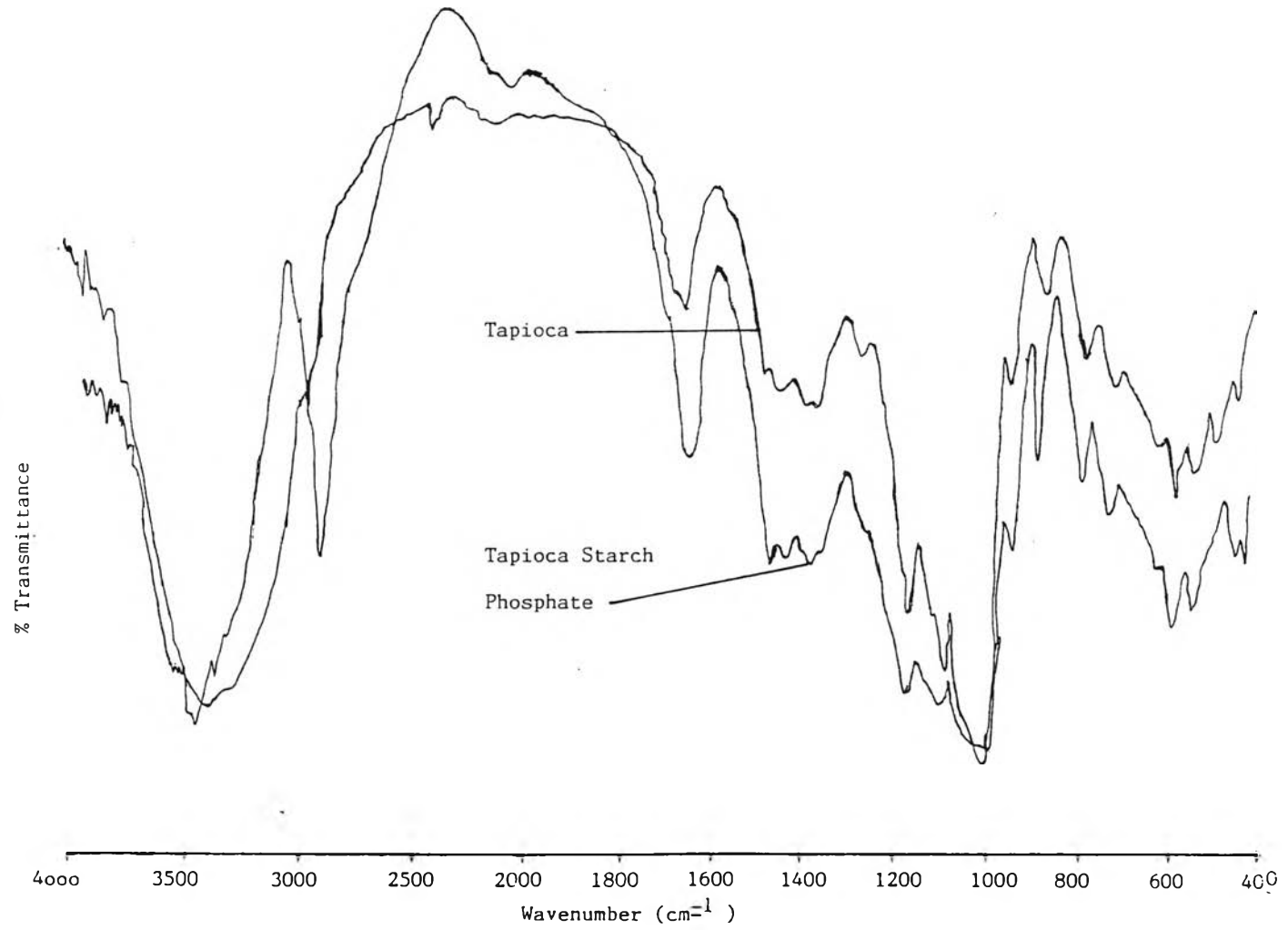


Figure 24 Infrared Spectrum of Tapioca Starch Phosphate.

Table 14 Phosphate Contents of Native Tapioca Starch before and after Modification in Comparison to Modified Potato Starches.

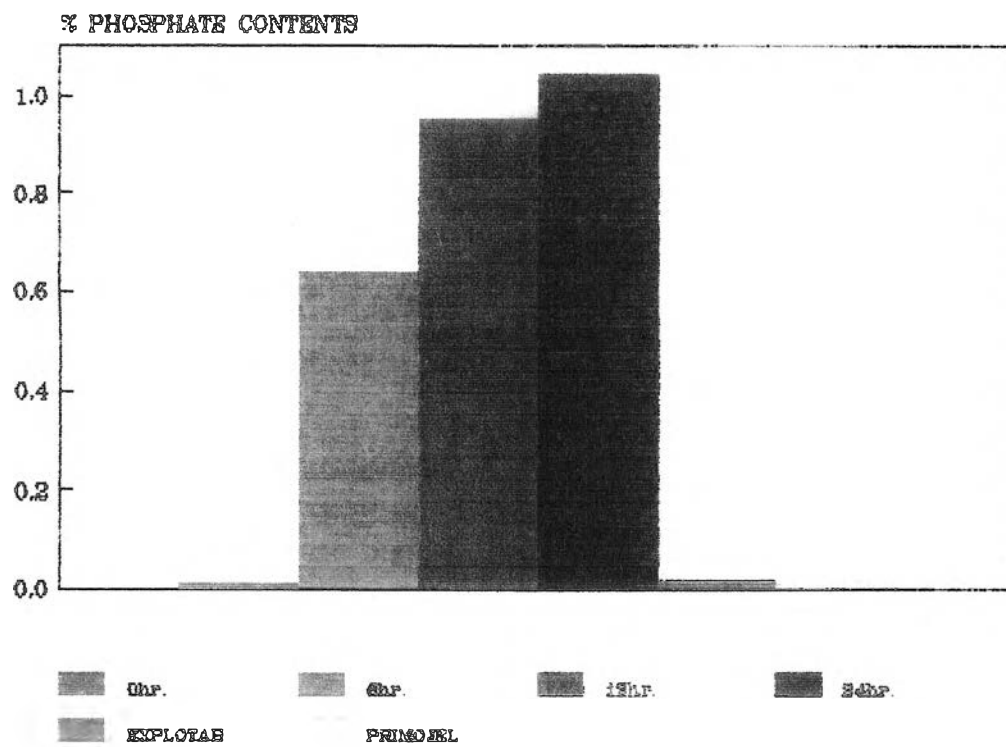
Types	% Phosphorous	% Phosphate
Sample No.1	0.0028 (0.0003)	0.0086 (0.0008)
Sample No.5	0.2108 (0.0133)	0.6374 (0.0415)
Sample No.9	0.3121 (0.0039)	0.9479 (0.1131)
Sample No.13	0.3422 (0.0029)	1.0403 (0.0082)
Explotab ^R	0.0041 (0.0002)	0.0127 (0.0007)
Primojel ^R	0.0042 (0.0001)	0.0135 (0.0011)

Standard deviations are in parentheses.

Sample NO. 1, 5, 9 and 13 were tapioca starches which were crosslinked for 0, 6, 12, and 24 hours, respectively. When the crosslinking time increased, phosphate contents gradually increased. Figure 25 exhibited that phosphate contents of Explotab^R and Primojel^R were relatively low when compared with the modified tapioca starch which was crosslinked with sodium trimetaphosphate. Explotab^R and Primojel^R are the modified potato starch prepared by substitution with carboxymethyl substituent but the type of crosslinking agent was not reported.

1.6 Determination of sodium chloride contents.

As sodium chloride content affected disintegrant properties of modified starch by both decreases in water uptake and swelling capacity (Bolhius et al., 1984). Hence sodium chloride content had been evaluated. The sodium chloride contents of MTS of 16 samples were illustrated in Figure 26. MTS sample No.1, 5, 9 and 13 which were native tapioca starch with various degree of crosslinking showed lower sodium chloride contents than MTS with higher DS. As sodium chloride was the byproduct occurred during carboxymethyl reaction.



**Figure 25 Phosphate Contents of Crosslinked Carboxymethyl
Starch,**

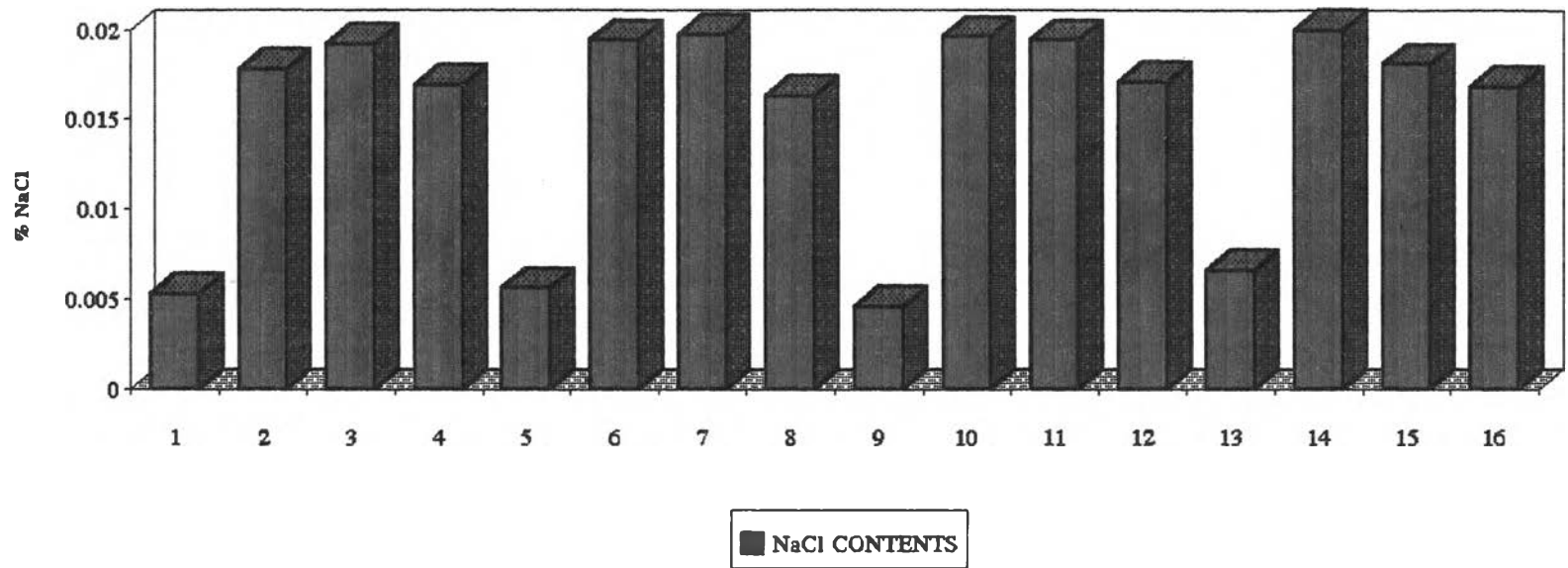


Figure 26 Sodium Chloride Contents of Modified Tapioca Starches.

2. Evaluation of Physical properties

The physical properties of modified tapioca starch were demonstrated in table 15. As water uptake of disintegrant plays an important role in tablet disintegration. Water penetration hardly occurred in products with zero DS and zero crosslinking. All of the carboxymethylated products showed a large water uptake at moderate degree of crosslinking. The highest value was found for the sample No.11 with DS of 0.17 and crosslinking of 0.95% phosphate.

The effect of degree of substitution on water uptake of modified tapioca starch was shown in Table 15 and Figure 27. The water uptake of tapioca starch decreased when tapioca starch was substituted with carboxymethyl substituent. In fact, an increase in degree of substitution increased water uptake and also increased solubility produced a high viscosity. This can be attributed that carboxymethylation of tapioca starch facilitated the dissolution of carboxymethyl starch in cold water due to hydrophilicity of carboxymethyl anion which preferred to form hydrogen bonding with water and produced viscous gel barrier which retarded water to be drawn up to the powder bed. As a result, the water uptake of carboxymethyl tapioca starch studied were apparent values.

The effect of crosslinking on water uptake of tapioca starch was shown in Table 15 and Figure 28. The water uptake gradually increased when the degree of crosslinking increased as shown in sample No. 5 (% $\text{PO}_4=0.64$) and sample No. 9 (% $\text{PO}_4=0.95$). It was due to phosphate ion preferred to form hydrogen bond with water and the starch were crossed bond by phosphate ion to form network which facilitated to uptake the water by capillary action. Conversely, as the cross-bonding reaction progressed the water uptake reached a peak and then declined to a low value as shown in sample No. 13 (% $\text{PO}_4=1.04$) due to the steric effect of phosphate ion of higher molecular weight and more complex of starch polymer.

Table 15 Effect of Substitution and Crosslinking on Physical Properties of MTS.

PO ₄ %	DS = 0						DS = 0.10						DS = 0.17						DS = 0.22					
	WU ml/g	BS %	HC g/g	SV ml	CWS gx10 ⁻²	VIS Cp	WU ml/g	BS %	HC g/g	SV ml	CWS gx10 ⁻²	VIS Cp	WU ml/g	BS %	HC g/g	SV ml	CWS gx10 ⁻²	VIS Cp	WU ml/g	BS %	HC g/g	SV ml	CWS gx10 ⁻²	VIS Cp
0	0.37	6.67	2.58	1.40	0.73	1.35	0.07	ND*	69.17	20.00	74.98	46.14	0.08	ND*	94.07	20.00	100.00	66.66	0.08	ND*	81.14	20.00	100.00	3348
0.64	0.62	ND	2.50	1.60	2.46	1.41	9.11	833	22.38	17.75	8.73	1.78	9.58	633	19.53	14.20	5.31	2.52	11.56	1450	31.41	20.00	7.46	2.76
0.95	0.63	ND	2.46	1.65	6.26	1.23	6.09	450	14.57	12.25	4.81	1.60	13.20	1500	28.37	18.30	4.74	2.03	9.83	700	19.29	14.60	7.97	1.78
1.04	0.57	ND	2.30	1.60	5.47	1.23	5.66	400	13.34	11.35	4.24	1.54	6.69	500	14.45	11.95	4.42	1.60	8.11	500	14.47	11.90	3.54	1.54

WU = Water uptake

BS = Bulk swelling

HC = Hydration capacity

SV = Sedimentation volume

CWS = cold water soluble fraction

VIS = Viscosity

ND = Non detectable due to forming viscous gel barrier

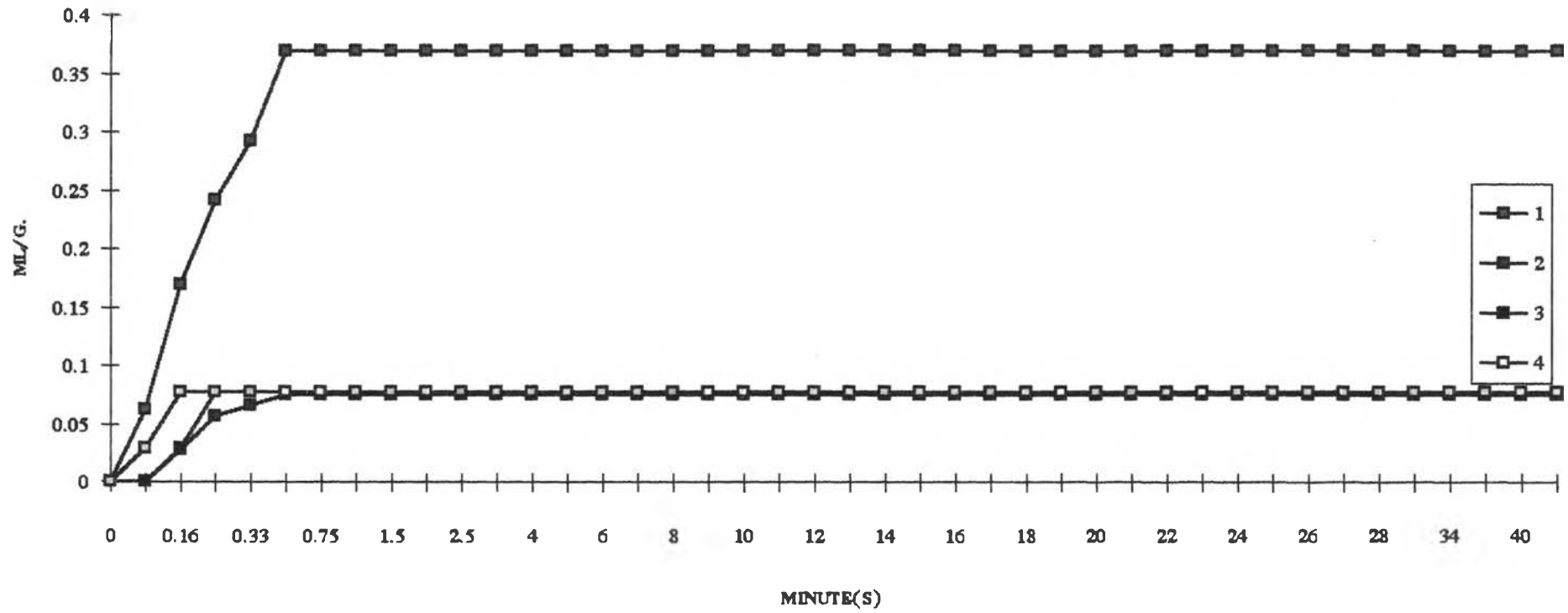


Figure 27 Effect of Degree of Substitutions on Water Uptake of Tapioca Starch.

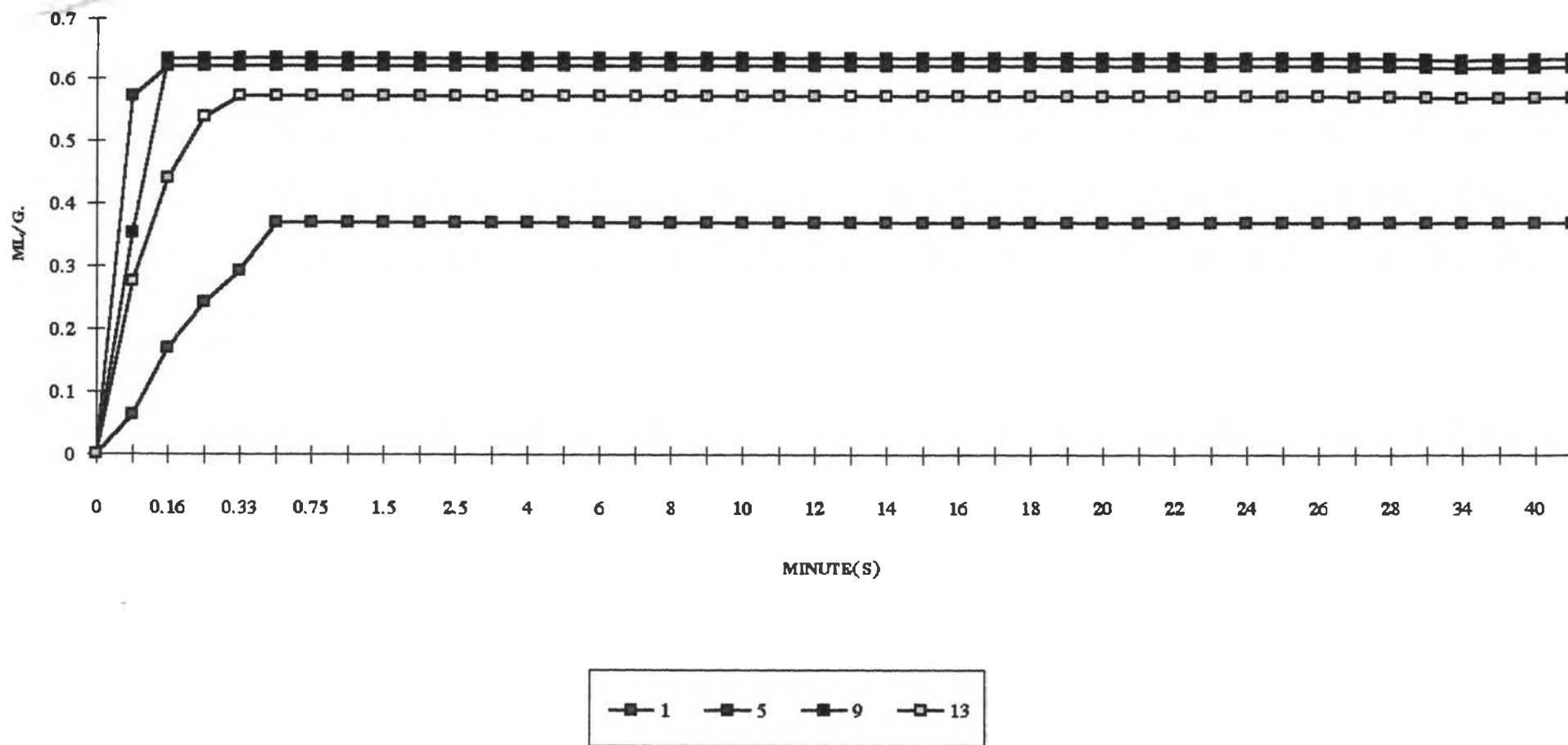


Figure 28 Effect of Crosslinking on Water Uptake of Tapioca Starch.

The effect of both substitution and crosslinking on water uptake of tapioca starch were shown in Figure 29. The carboxymethyl substitution caused starch hydrophilic and more soluble in cold water while phosphate crosslinking caused the starch molecule to form network which water was facilitated to drawn up into the structure. As a result, both optimal substitution and crosslinking caused the water uptake of modified starch very high as shown in sample No.11 (DS of 0.17, PO₄ 0.95%) the water uptake about 35 times of native tapioca starch (sample No. 1).

To determine the optimum degree of substitution and crosslinking of MTS which provided maximum water uptake property. The various degree of substitution and crosslinking of MTS were plotted against their water uptake in three dimension and the results were shown in Figure 30, the maximum water uptake was obtained by modification of tapioca starch with degree of substitution of 0.17 and crosslinking 12 hours (%PO₄=0.95) as presented in sample NO.11.

Figure 31 exhibited the evaluation of the effect of degree of substitution and crosslinking on water uptake of MTS on different graphical displays from Figure 30. The sample No.11 with DS of 0.17 and crosslinking time 12 hour showed the highest water uptake value.

Perhaps the most widely accepted general mechanism of tablet disintegration is swelling (Kanig and Rudmic, 1984). As DS increased, the swelling property increased since carboxymethylated products were more hydrophilic and increased water uptake into molecular structure. The molecular structure expanded by mutual repulsion of carboxymethyl anion when exposed to water, hence swelling before dissolving occurred. Increasing the degree of crosslinking, decreased the swelling due to steric effect and more complex structure lattice.

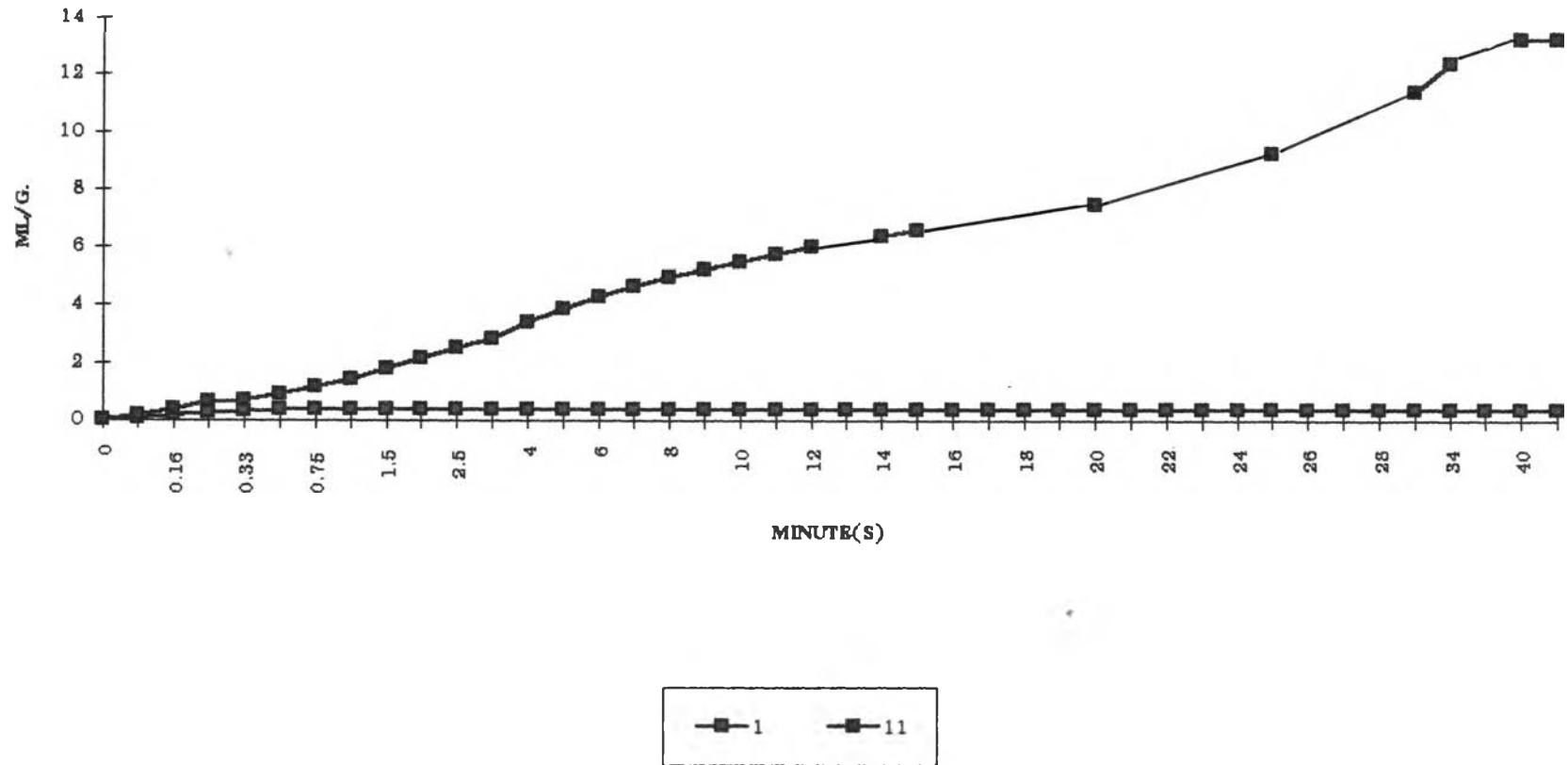


Figure 29 Effect of Substitution and Crosslinking on Water Uptake of Tapioca Starch.

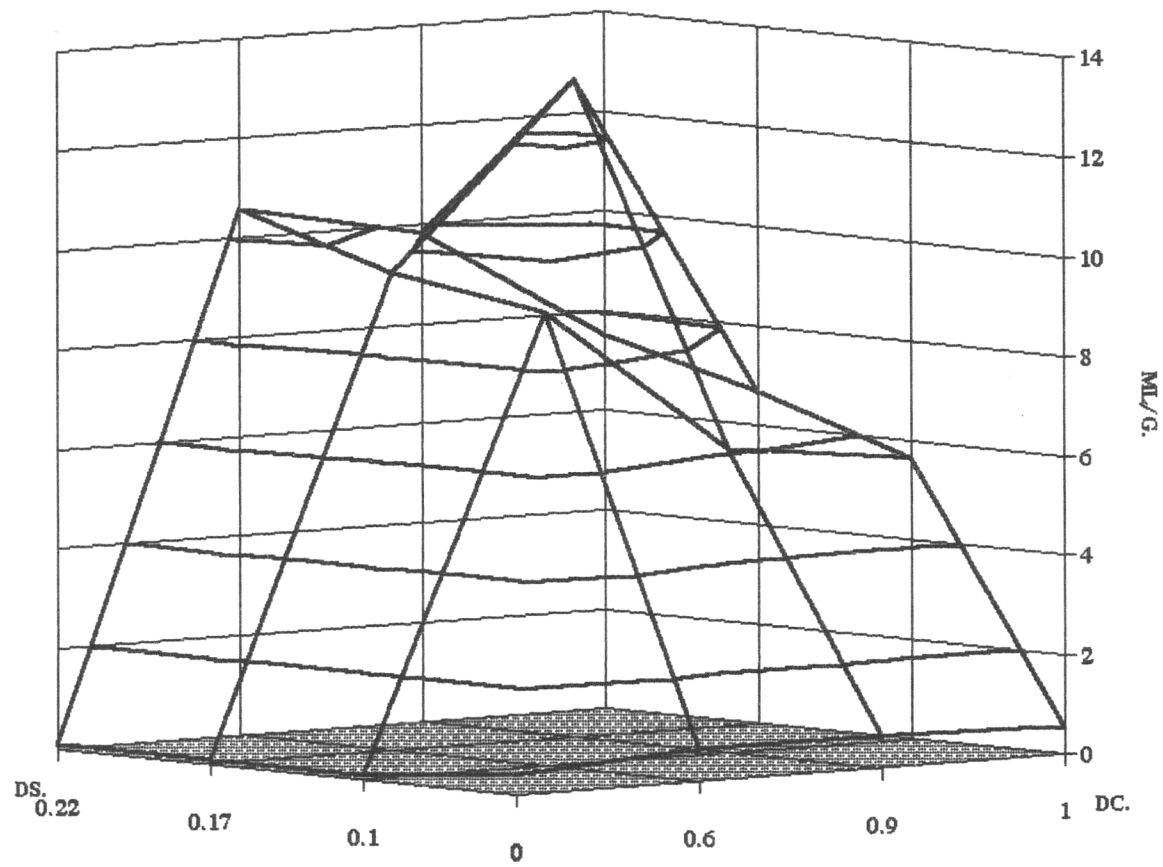


Figure 30 Effect of Substitutions and Crosslinkings on Water Uptake of MTS.

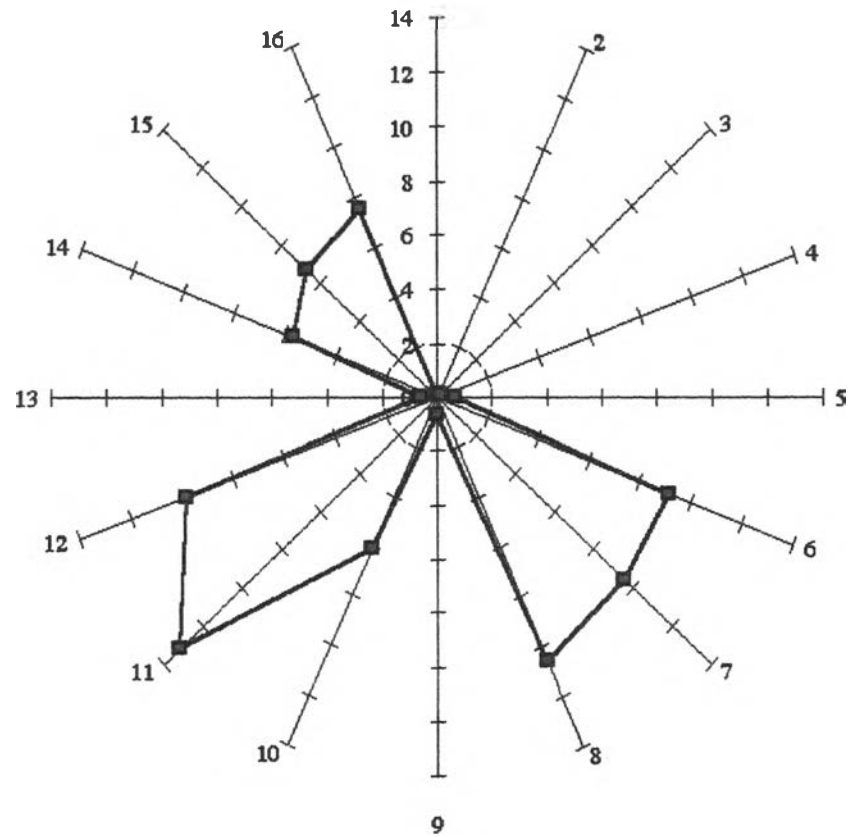


Figure 31 Effect of Substitutions and Crosslinkings on Water Uptake of MTS.

To obtain the optimum DS and crosslinking of MTS which provided the maximum swelling property, the various DS and crosslinking of MTS were evaluated. The bulk swelling of MTS studied were shown in Table 15 and Figure 32. The effect of substitution and crosslinking on bulk swelling of MTS were shown in Figure 33 and 34. It was found that there were three peak of bulk swelling of MTS with MTS sample No. 6 (DS=0.1, 0.64%PO₄), sample No.8 (DS=0.1, 0.64%PO₄) and sample No.11(DS=0.17, 0.95%PO₄). However, the maximum swelling was shown in sample No.11 as demonstrated by radar plotting of the bulk swelling as shown in Figure 34.

The hydration capacity, as shown in Figure 35 and sedimentation volume both in water and 0.1 N HCl as shown in figure 36 were correlated with bulk swelling properties. As DS increased, the hydration capacity and sedimentation volume increased while degree of crosslinking decreased the hydration capacity and sedimentation volume, except sample No.11 which provided the highest value of bulk swelling, hydration capacity and sedimentation value both in water and 0.1 N HCl. The cause of this occurrence has been previously described in the chapter IV.

From table 15 all carboxymethylated starches showed a strong increase in cold water solubility at no or low degree of crosslinking when compared to non-substituted products. A high cold water solubility of sample was accompanied by are increased in value of the viscosity of an aqueous dispersion as shown in Figure 37 and Figure 38.

3. Evaluation of the disintegrating property of MTS.

The efficiency of the MTS as tablet desintegrant was evaluated by incorporation of these products into an insoluble (dicalcium phosphate) and a soluble (lactose) tablet system.

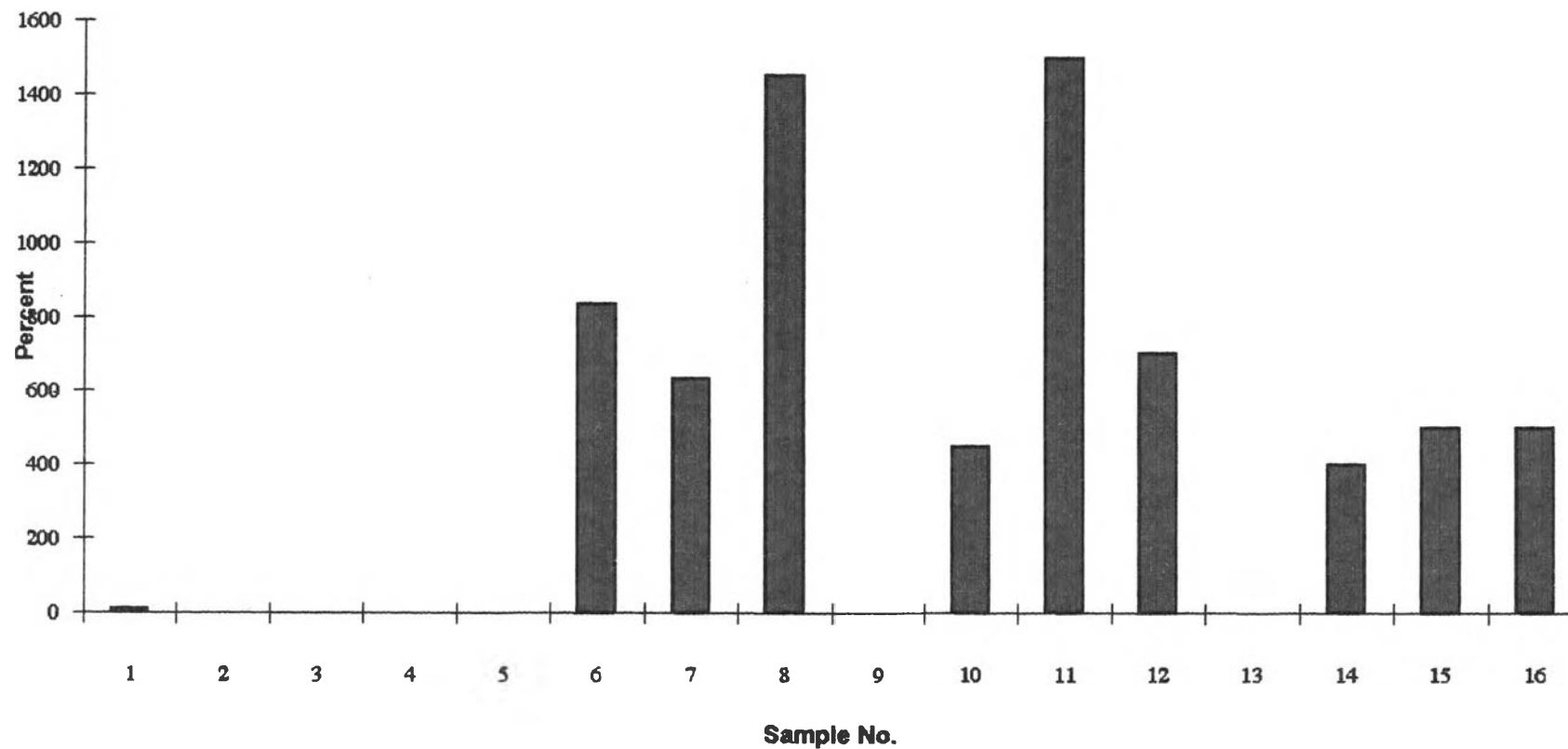


Figure 32 Bulk Swelling of MTS.

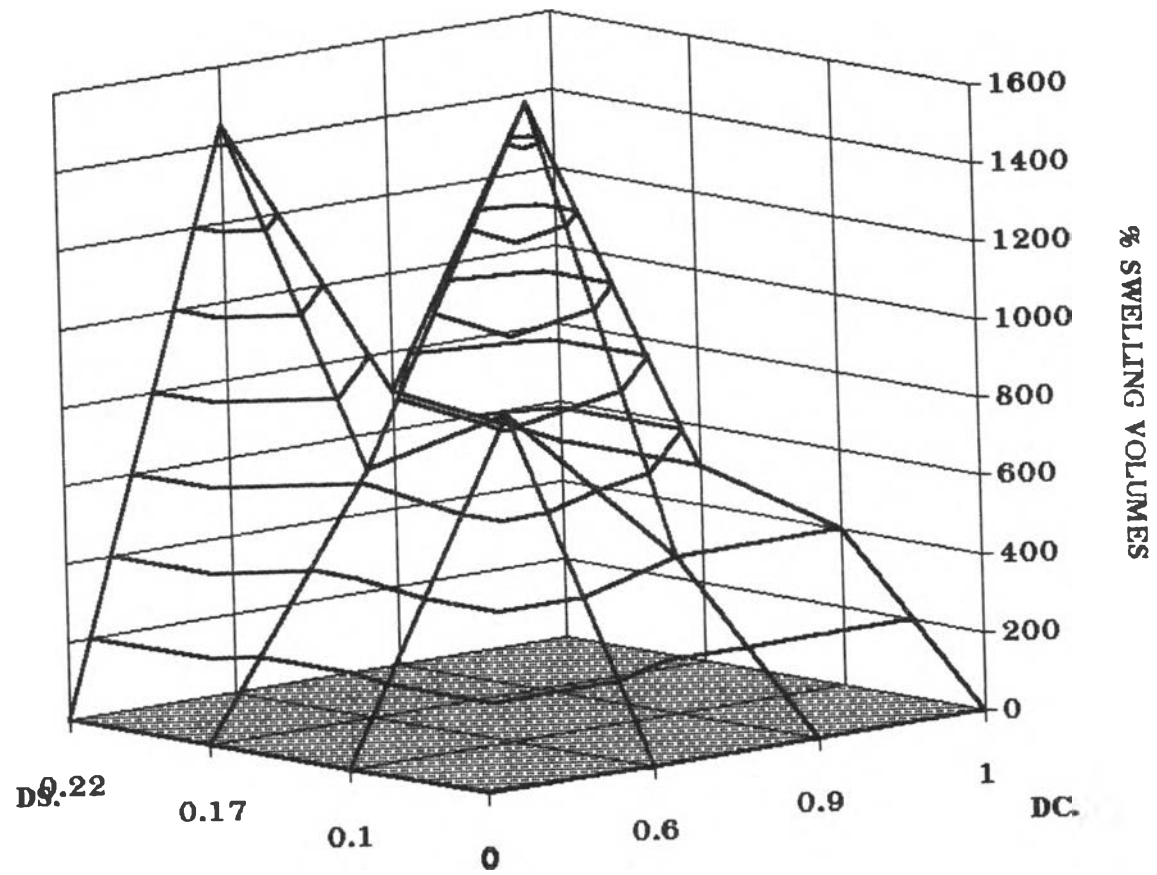


Figure 33 Effect of Substitutions and Crosslinkings on Bulk Swelling of MTS.

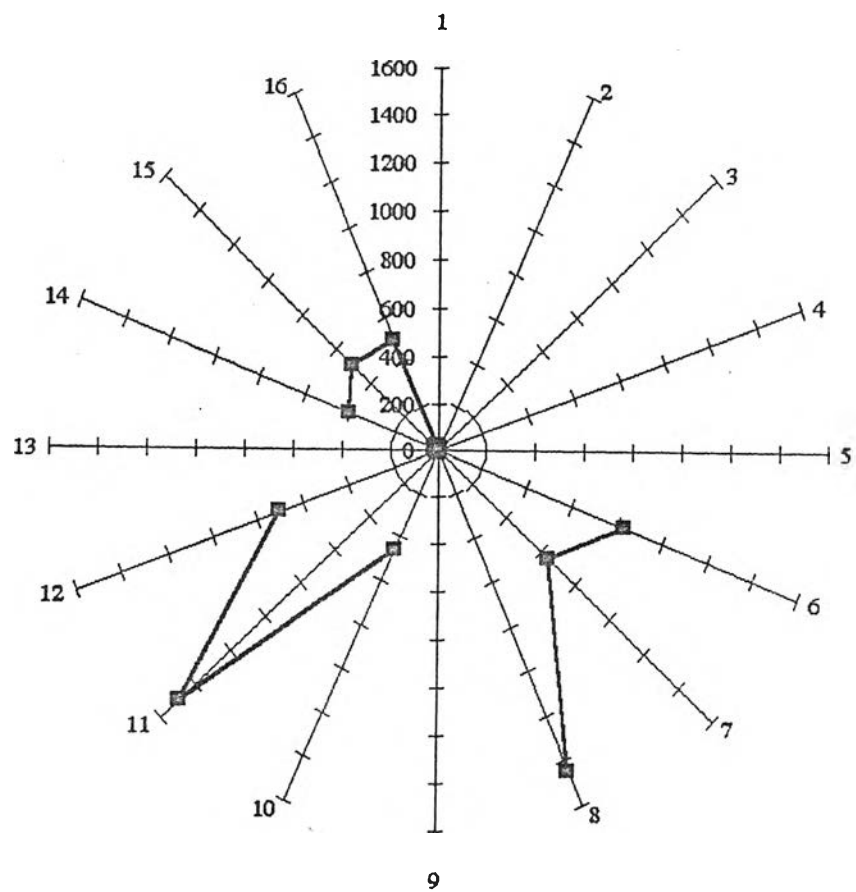


Figure 34 Effect of Substitution and Crosslinkings on Bulk Swelling of MTS.

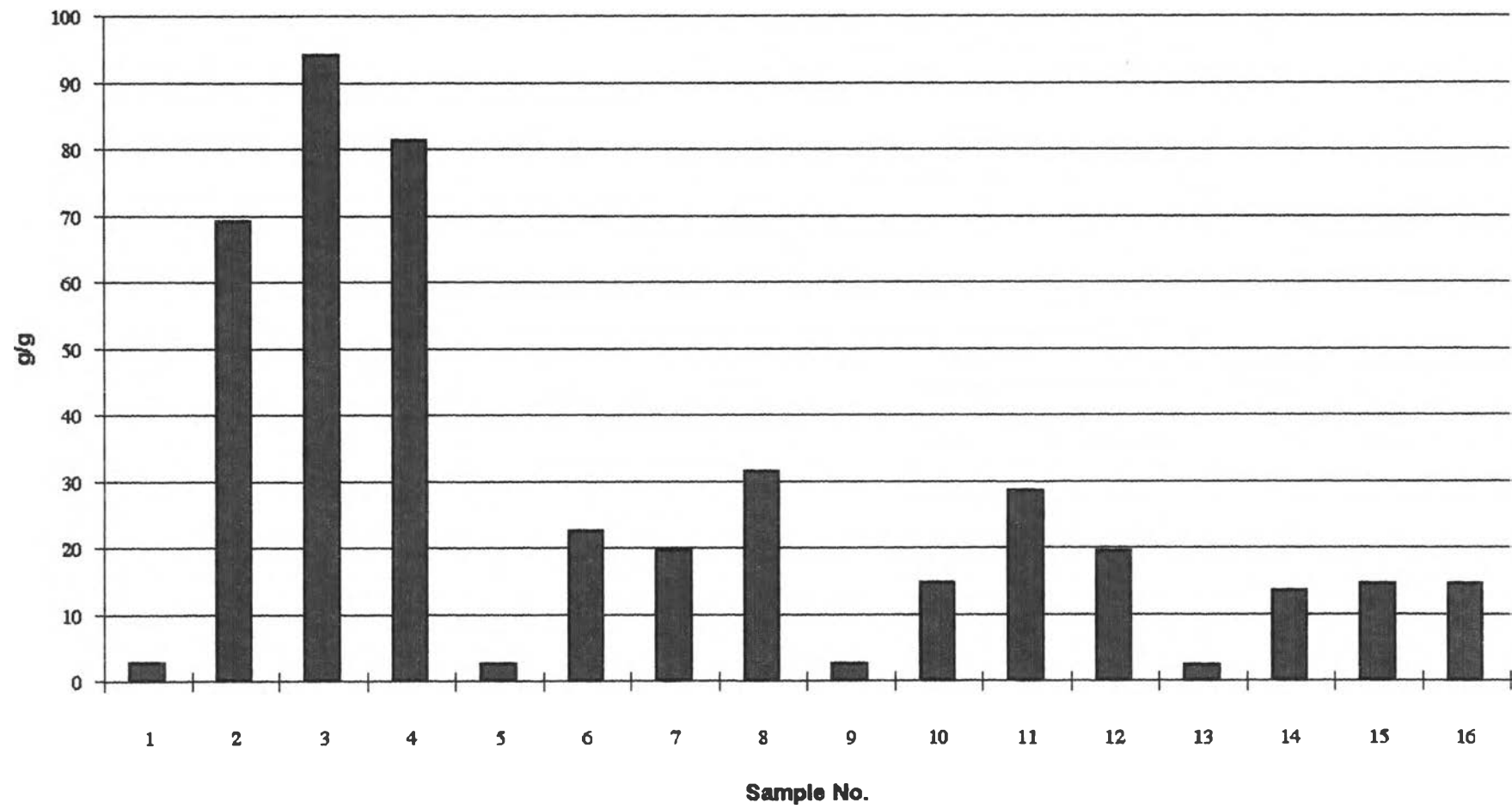


Figure 35 Hydration Capacity of MTS.

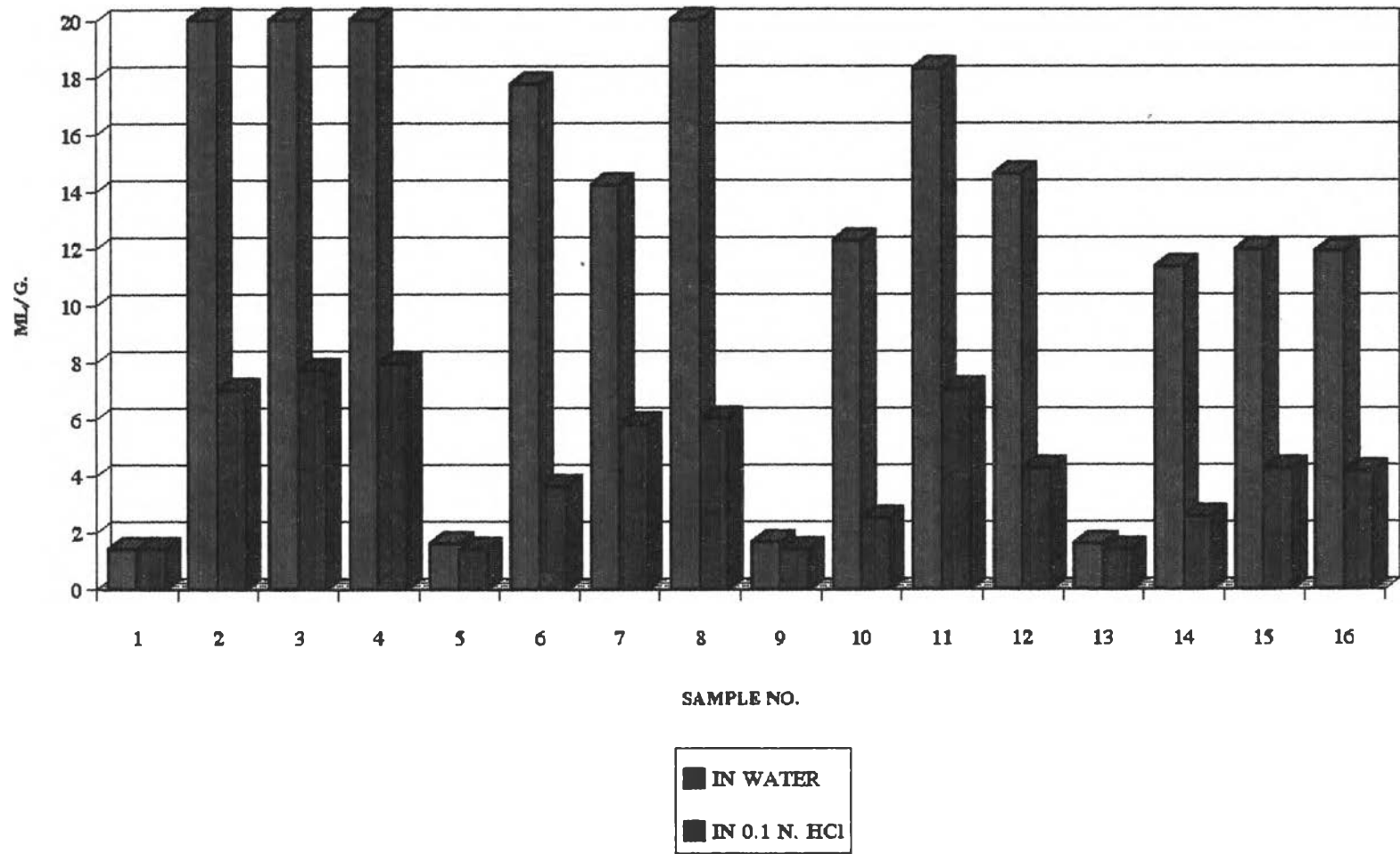
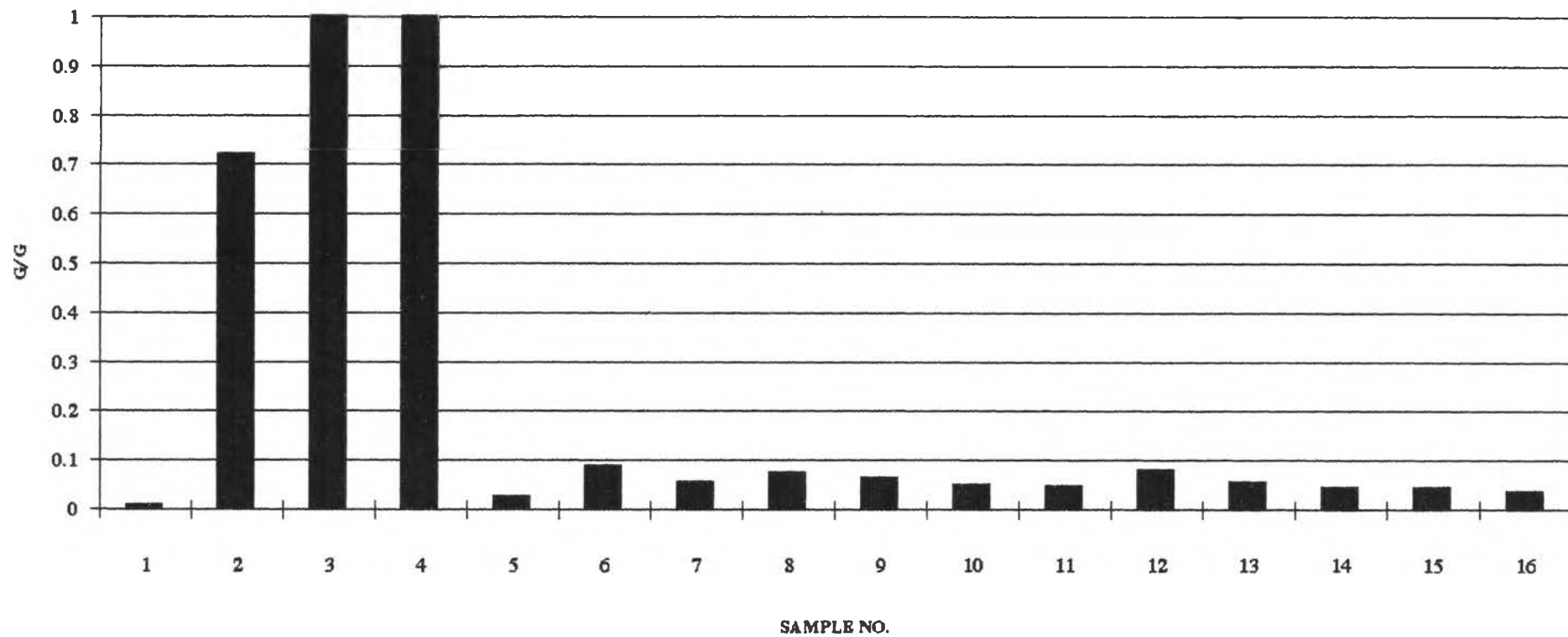


Figure 36 Sedimentation Volumes of MTS.



NOTE : SAMPLE NO. 2 , 3 , 4 GEL FORMS.

Figure 37 Cold Water Soluble Fraction of MTS.

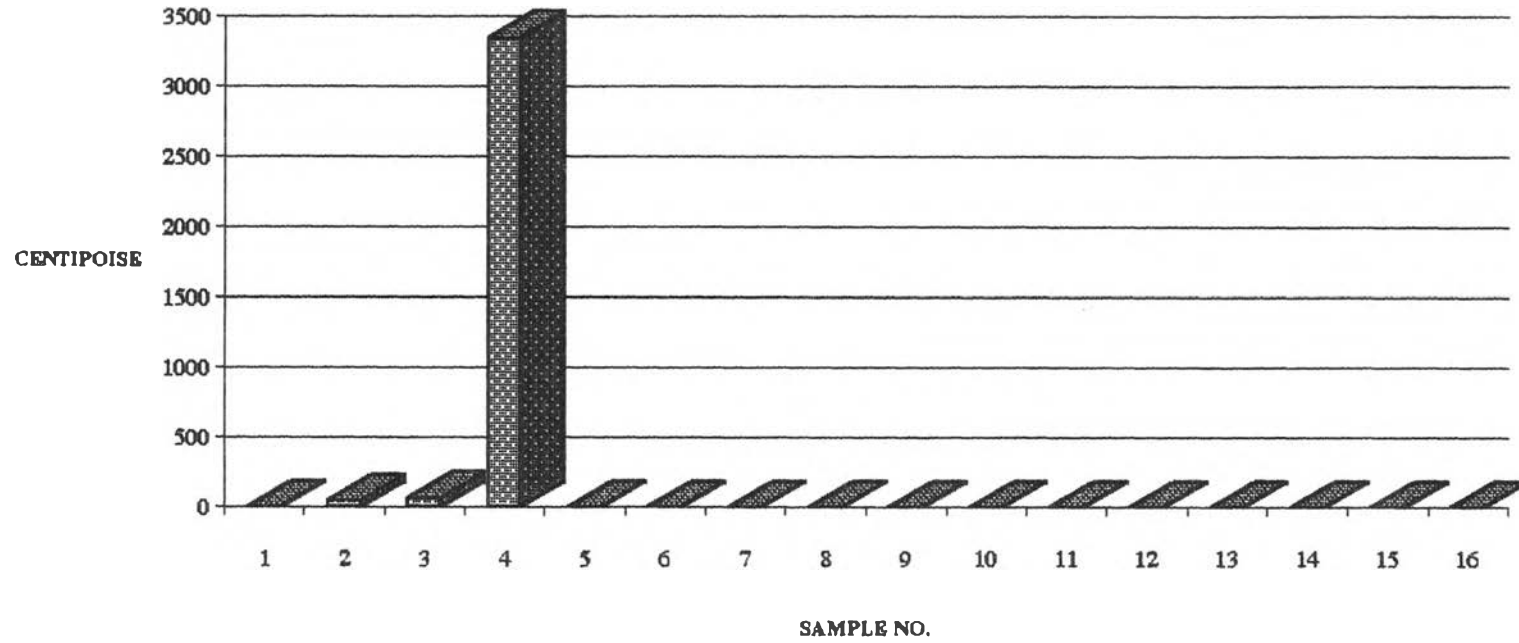


Figure 38 Viscosity of MTS.

The disintegration times of dicalcium phosphate tablets were characterized in Table 16 and Figure 39.

Table 16 Disintegration Times of Dicalcium Phosphate Tablets Containing 4 % Various MTS as Disintegrants.

% PO ₄	DT sec		Hard ness Kp	DT sec		Hard ness Kp	DT sec		Hard ness Kp	DT sec		Hard ness Kp
	H ₂ O	O.IN HCl		H ₂ O	O.IN HCl		H ₂ O	O.IN HCl		H ₂ O	O.IN HCl	
	0	25.86	15.83	11.46	21.33	13.66	12.30	19.66	12.66	11.33	12.50	11.16
0.64	12.83	10.66	12.86	6.66	6.66	12.22	9.33	8.33	12.26	8.66	7.66	12.53
0.95	10.33	10.16	12.00	6.83	6.83	12.03	6.50	6.66	12.80	6.66	6.66	11.97
1.04	11.66	10.00	12.47	6.66	6.83	12.66	6.83	5.66	12.90	6.66	6.33	12.97

DT = Disintegration Time

Kp = Kilopound

The modified tapioca starches with zero DS and zero crosslinking exhibited low disintegration properties. The disintegration time decreased both in water and 0.1 N HCl when DS increased. This can be attributed to carboxymethylated starches were hydrophilic which facilitated water uptake and swelled after absorption of water. As a result, the tablets containing carboxymethyl starch without crosslinking exhibited short disintegration time due to capillary action and swelling mechanism.

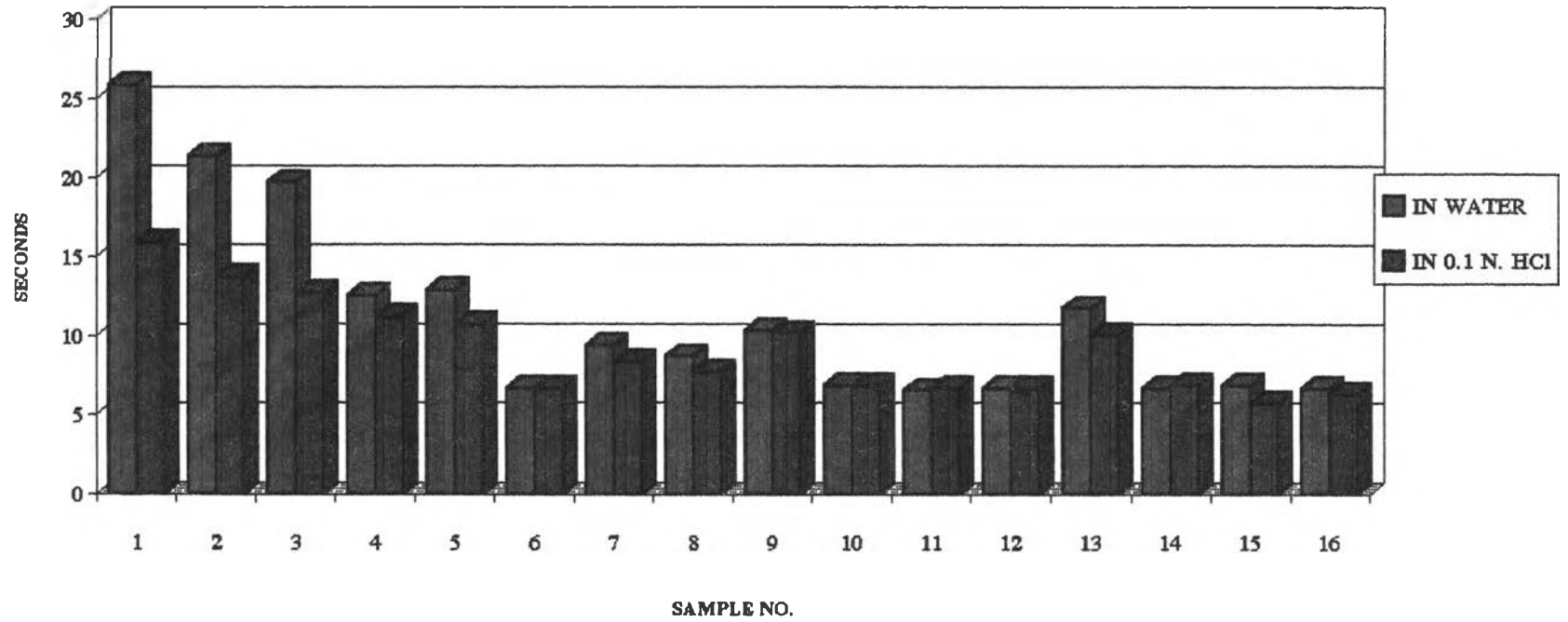


Figure 39 DT. of Dicalcium , Phosphate Tablets Containing 4 % Various MTS as Disintegrant.

The carboxymethylated starch at high degree of crosslinking gave short disintegration time. The crosslinking caused markedly decrease in disintegration time due to the presence of optimum amount of ionizable esterified phosphate group which assisted swelling by mutual electric repulsion, hence rapid disintegration of tablet.

The disintegration times of lactose tablets were illustrated in Table 17 and Figure 40.

Table 17 Disintegration Times of Lactose Tablets Containing 4 %Various MTS as Disintegrant.

% PO ₄	DS = 0			DS = 0.10			DS = 0.17			DS = 0.22		
	DT (sec)		Hardness (Kp)	DT (sec)		Hardness (Kp)	DT (sec)		Hardness (Kp)	DT (sec)		Hardness (Kp)
	H ₂ O	O.IN		H ₂ O	O.IN		H ₂ O	O.IN		H ₂ O	O.IN	
		HCl		HCl		HCl		HCl		HCl		
0	37.83	35.50	7.03	49.50	161.17	7.13	287.0	104.50	8.07	98.67	44.50	8.20
0.64	38.83	34.83	8.10	40.33	34.00	8.30	40.50	36.17	8.37	38.33	35.67	7.97
0.95	39.50	34.00	8.13	39.17	34.83	7.80	39.66	35.67	7.57	38.50	36.50	7.87
1.04	39.33	34.66	7.60	39.83	34.33	8.26	39.83	35.83	7.50	39.00	36.00	8.23

DT = Disintegration Time

Kp = Kilopound

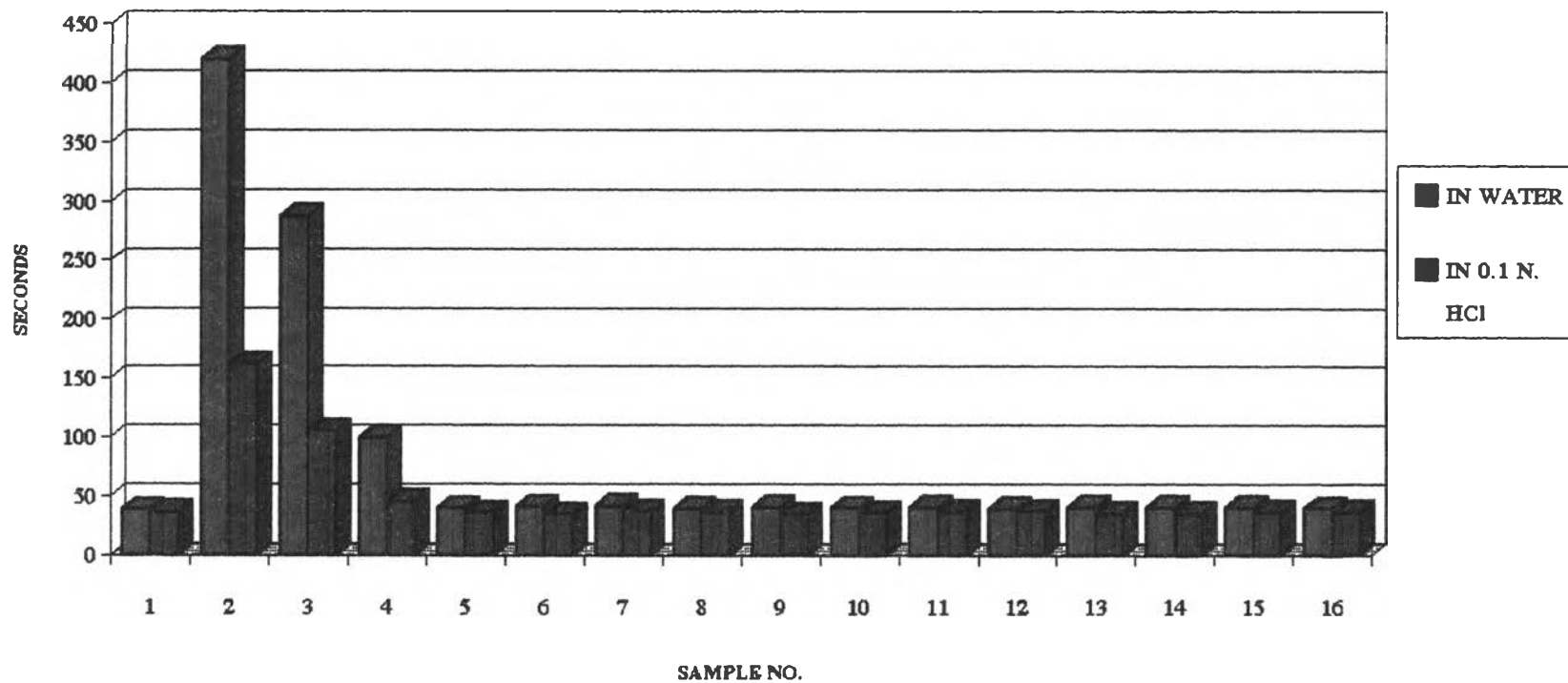


Figure 40 DT. of Lactose Tablets Containing 4 % Various MTS as Disintegrant.

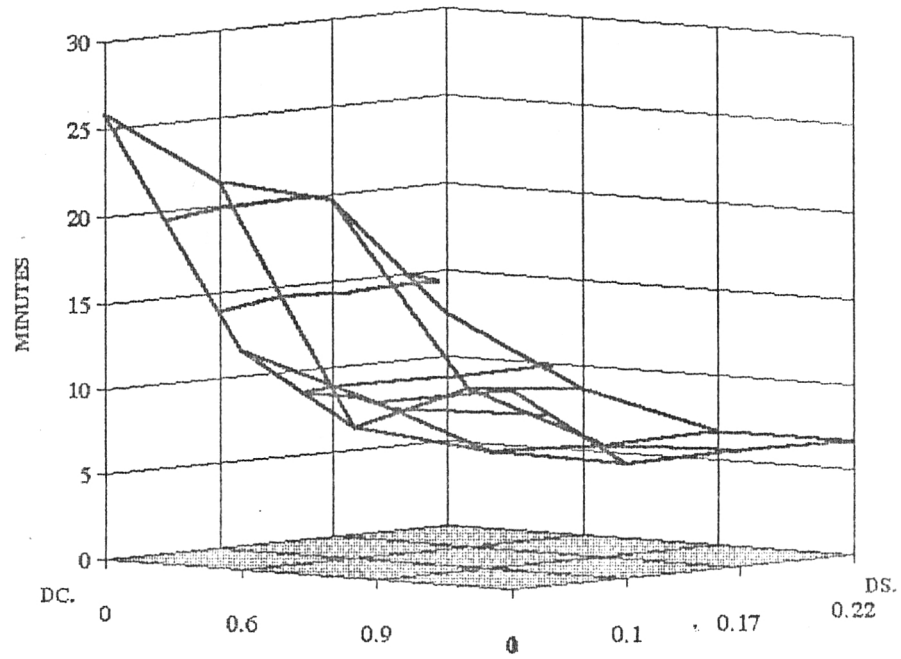


Figure 41 Effect of Substitution and Crosslinking of MTS. on DT. of Dicalcium Phosphate.

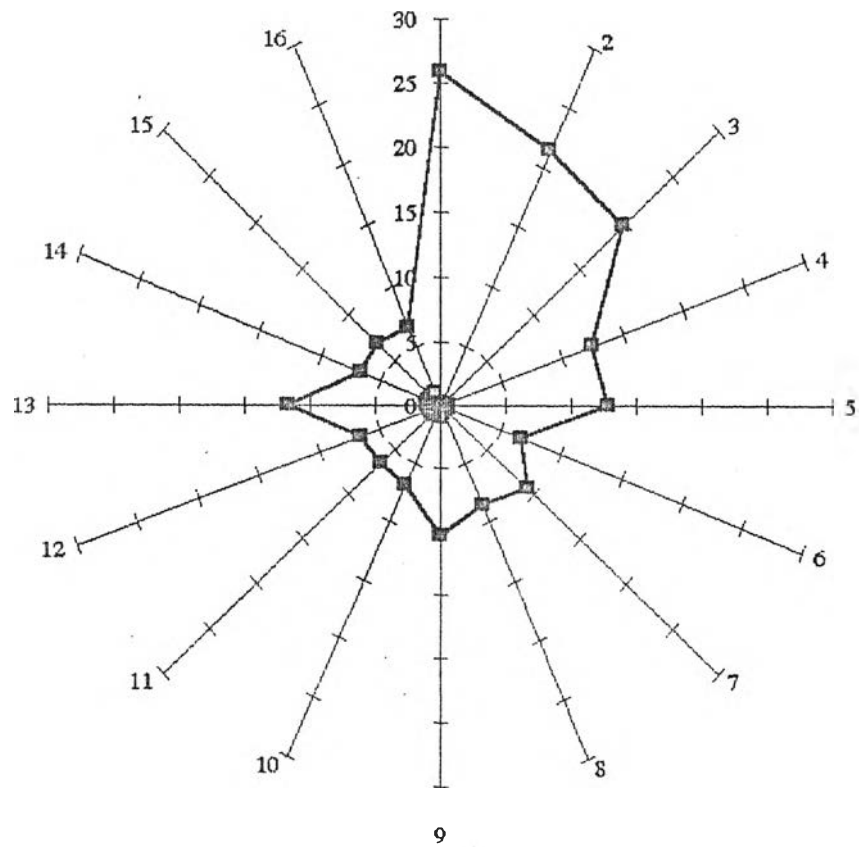


Figure 42 Effect of Substitution and Crosslinking of MTS. on DT. of Dicalcium Phosphate Tablets.

For the lactose tablets containing MTS with zero DS the crosslinking did not affect disintegration times. Conversely, the crosslinking at the various DS (DS=0.10-0.22) caused markedly decrease in disintegration time when they were compared with non-crosslinked product at the same DS. It was due to mutual repulsion of phosphate ions which promoted swelling characteristics. However, the extents of crosslinking (0.64-1.04%PO₄) did not affect disintegration time of all carboxymethylated starches with DS of 0.10 to 0.22.

The disintegration times of both dicalcium phosphate and lactose tablets containing MTS with zero degree of crosslinking in 0.1 N HCl were less than those in water because in acid medium modified starch were less soluble and also less viscous gel barrier forming which retarded disintegration. Crosslinking of the modified starch produced low water solubility and low viscous gel formation caused both dicalcium phosphate and lactose tablets rapidly disintegrated.

To obtain the optimum DS and crosslinking of MTS which provided the shortest disintegration time, the effects of substitution and crosslinking on disintegration time of dicalcium phosphate were evaluated. The results were presented in Figure 41 and 42. The tablets containing MTS with high DS (DS=0.17-0.22) and high degree of crosslinking (0.95-1.04%PO₄) exhibited short disintegration times. Figure 42 (radar plotting) illustrated the value of disintegration time of dicalcium phosphate tablets containing MTS with various DS and crosslinking. It was found that the starch sample No. 10, 11, 12, 14, 15 and 16 gave the short disintegration time which corresponded the results to be demonstrated in Figure 41.

The criterion for a good disintegrant suggested by Huttenrauch(1973). The important properties of a good disintegrant are poor solubility, poor gel formation, high swellability and great ease of hydration. These criteria were used to consider the optimum degree of substitution and crosslinking of modified

tapioca starch which used as a super disintegrant. It was found that modified tapioca starch sample No.11 with DS of 0.17 and crosslinking of 0.95% phosphate exhibited the highest water uptake (13.20 ml/g), maximum swelling property (bulk swelling of 1500%) and shortest disintegration time when it was incorporated into dicalcium phosphate tablet as disintegrat with concentration of 4.0% (DT=6.50 seconds).

Consequently, the MTS sample No.11 was selected to represent the crosslinked carboxymethylated tapioca starch for further study as highly effective disintegrant.

Conclusions

The unmodified tapioca starch exhibited very low swelling and practically undissolved in cold water due to the inter-and intra molecular hydrogen bonds between the polysaccharide macromolecules, resulting in a formation of crystalline structure which hardly dissolved. By chemical modification, carboxymethyl substitution of tapioca starch caused modified starch more hydrophilic. An increase in degree of substitution increased the solubility accompanied by viscous gel formation which retarded tablet disitegration. To overcome this problem the phosphate crosslinking was used. Crosslinking of carboxymethylated tapioca starch resulted in a decrease in swelling capacity, cold water solubility and viscosity. To obtain the modified tapioca starch with provided a high efficiency of disintegrating property, the effect of variation of molecular structure on physico-chemical properties of modified tapioca starch have been studied. It was found that the modified tapioca starch with optimum degree of substitution of 0.17 and crosslinking of 0.95% phosphate exhibited the best disintegrating properties.

In conclusion, the optimum degree of substitution and crosslinking of modified tapioca starch which provided a good disintegrating property was degree of substitution of 0.17 and crosslinking of 0.95% phosphate.