CHAPTER VI

COMPARATIVE STUDY OF PHYSICO-CHEMICAL PROPERTIES OF MODIFIED TAPIOCA STARCH

The most widely accepted that starch firstly used as tablet disintegrant was potato starch (Shet, 1980) and still using today. In spite of known limitation and trend toward predicting drug bioavailability from the drug dissolution rather than from the tablet disintegration. During the past 20 years, the dissolution rate was improved by manipulating the drug particles through crystallization, micronization, solid solution and has often overlook the role of tablet disintegrant. One of the limitation of starch disintegrant was the lack of a clearly demonstrable theory explaining the disintegrant mechanism. The most accepted general mechanism of starch as tablet disintegrant is capillary action and swelling when it was exposed to water. Unfortunately, many substances swell and also form gel producing viscous barrier that may slow down rather than accelerate tablet disintegration. The first successful attempt to improve on a plain starch was the development of sodium carboxymethyl starch from potato starch. Starch grains may be chemically modified so that they swell in water without losing their integrity, thus decreasing secondary gelling effect (Shangraw, et al., 1980)

A number of papers have appeared in the literature comparing the disintegrant characteristics of sodium carboxymethyl starch with other commonly used disintegrants. Khan and Rodes(1973) have studied the efficiency of disintegrating agents in tablet formulations by comparing disintegrant properties of sodium starch glycolate with a cation exchange resin in a variety of tablet systems. Extreme efficiency, even at low concentrations was demonstrated for both compounds.

Bavitz, et al. (1974) studied disintegratability characteristics of new tablet excipients which included a water insoluble, anionic, polymer derived from cellulose (D1), a carboxymethyl substituted starch (D2) and a complex of aminoacetic acid and sodium carbonate (D3) were compared with starch USP (D4). The experimental resulted clearly indicated the following rank order D1>D2>D4>D3.

A comparative study of physical properties of disintegrating agents such as water uptake and swelling have been evaluated. It was found that carboxymethyl starch, hydroxypropyl cellulose and crosslinked carboxymethylcellulose showed the same kinetic of water uptake. In case of carboxymethyl starch it was not possible to carry on the measurement of swelling after four minutes on account of a fast disintegration which happened after the swelling (Gissinger and Stamm, 1980).

A comparative evaluation of the properties of some tablet disintegrant have been studied by Gissinger and Stamm (1980). They suggested that disintegration times could not be explained with only the formation of a porous capillary net-work in tablet, but many other factors must also be considered such as water absorption capacity and swelling capacity.

Rudnic, et al. (1981) have studied some effects of eight tablet disintegrants on a direct compression system. They concluded that new disintegrants : Explotab®, Polyplasdone®-XL, Ac-Di-Sol®, Amberlite IRP-88, Sta-RX®1500 Starch, CLD® and Guar Gum have relatively little effect on such parameters as weight, weight variation, thickness and hardness; disintegration times were reduced significantly when low levels of disintegrant were used.

There were a few papers which explained about studying of the effect of molecular structure on the functions of carboxymethyl starch. Rudnic, et al.

(1983) suggested that a lower cross-linked and carboxymethylated of potato starch was favored to use as tablet disintegrant. Further study, Bolhius, et al. (1984) suggested that an increase in disintegrating efficiency of carboxymethyl starch might be done by purification of the commercial carboxymethyl potato starch. Visavarungroj and Remon (1990) have evaluated the different types of crosslinked starch and pregelatinized-crosslinked starch to be used as disintegrating agent in comparison to potato starch and a number of super disintegrants such as Ac-Di-Sol^{R}, Explotab^{R} and Polyplasdone^{R} XL. They concluded that potato starch and crosslinked starch showed the lowest granule swelling power, but pregelatinized or pregelatinized-crosslinked starch provided the highest swelling power but both rate and amount of water uptake were low. The disintegration time of tablet using pregelatinized-crosslinked starch was influenced by the types of filler and lubricant. In addition, Visavarongroj and Remon (1991) suggested that pregelatinized hydroxypropyl starch showed some good disintegrating properties and could be used as a binder in wet granulation.

Sodium carboxymethyl starch appeared to be most effective at levels between 4% and 8%. Levels above 8% generally results increased in disintegration times, possibly due to viscosity-producing effects (Shangraw, et al., 1984).

The two brands, modified potato starches (Explotab^{R} and Primojel^{R}) and a new modified tapioca starch could behave different in disintegrating properties for a number of reasons : the raw material starch was different, the chemical reaction may be run in different solvents under different conditions, different of crosslinking agent may be used, or different purification steps may be used. It is no doubt that the modified tapioca starch developed in this study possess different property from other modified starch products. Therefore, it is essential to characterize its physico-chemical property which was found to have

relation with the outcome of its disintegrating property such as water uptake, bulk swelling, hydration capacity, viscosity, etc.

Purpose of the study

The scope of the study in this chapter is to evaluate some physico-chemical properties of modified tapioca starch compared to the commercial carboxymethyl potato starch. The disintegrating properties of modified starch was studied and the factors affected efficiency of disintegrating properties were also evaluated.

Materials and Methods

Materials

Tapioca starch (Thai Wah, Co., Ltd., Thailand)

Methanol (BHD Lab., England, Lot No. 226K 17948870)

Silver nitrate (E Merck, Germany, Lot No. K20368112)

Ammonium thiocyanate (Fluka Chem., Switzerland, Lot. No. 299876491)

Dicalcium phosphate (Mendell Co. Inc. USA, Lot. No. K27A)

Lactose direct compressed (The Lactose Company of New Zealand, New Zealand, Lot. No. 203114)

Magnesium stearate (Durham Chem., Ltd., England)

Erythromycin stearate (GP. Group, Lot. No. EST 103/93)

Explotab^{R} (Mendell, NY., USA, Lot. No. E4222)

Primojel^{R} (AVEBE, Holland)

Ac-Di-Sol^{R} (FMC. Corporation, USA, Lot. No. T 934)

Polyplasdone^{R} XL (GAF., USA)

Methods

1. Determination of sodium and sodium chloride contents.

The sodium and sodium chloride contents were conducted according to USP method (USPXXII). The mean of three determinations was calculated.

2. Determination of iron and heavy metal contents.

The iron and heavy metal content were determined according to USP method (USPXXII). The mean of three determinations of each sample was calculated.

3. Loss on drying

The percent loss of drying was performed by modified USP method (USPXXII).

4. Determination of pH

The starch concentration of 5% were stirred in water to the suspension, and then the pH of the suspension was determined electrometrically.

5. Water uptake

The amount of water uptake of modified starch was determined by modified Nogami's apparatus (Nogami, et al., 1969). The procedure of experiment was described chapter IV.

6. Bulk swelling

The bulk swelling was meansured during water uptake determination. The bulk swelling of sample was calculated according to the equation suggested by Rudnic, et al. (1982) as shown in chapter IV.

7. Sedimentation volume

The sedimentation volume was determined using cylindrical method. The starch sample concentration of 5% were used. The procedure of experiment was described in chapter IV.

8. Hydration capacity

The hydration capacity was measured by the procedure described by Kornblum and Stoopak (1973) as demonstrated in chapter IV.

9. Cold water soluble fraction

Cold water soluble fraction was determined from the dry matter content of the clear upper layer of a 1% aqueous dispersion at 37°C after centrifugation at 2350 rpm for 15 minutes.

10. Viscosity

The viscosity was determined in one percent aqueous dispersion using Brookfield's cone and plate viscometer.

11. Sorption isotherm

The sorption isotherm of modified starch was performed as the method described in Handbook of Pharmaceutical Excipients (1986).

A sample was dried to constant weight at temperature 55°C for 2 hours. Six 1.0 g sample of each were weighed into each of six dishes of approximately 5.0 cm. diameter. The sample were placed in a desiccator containing the saturated salt solution of known relative humidity. The desiccator was maintained at a constant temperature 25 $\pm$ 1°C. After 7 days intervals, the dishes were quickly removed from desiccator and rapidly weighed

and the weight change was recorded. Weighing continued until there was no further change in weight. The weight gain represented the amount of water absorbed and the percentage of moisture gain was plotted versus percentage of relative humidity. The experiments were performed in duplicates.

The materials used to prepare saturated salt solution for control of relative humidity at 25°C were :

Salts materials	% Relative humidity
$KC_2H_3O_2$	22.0
$MgCl_2.6H_2O$	32.8
K_2CO_3	43.6
$Mg(NO_3)_2.6H_2O$	52.0
$NaNO_2$	63.3
$NaC_2H_3O_2$	71.3

12. Bulk density and tapped density

Bulk density and tapped density were determined as the procedure described in chapter IV and percentage of compressibility were calculated as follow as the equation : (Cham and Lin, 1988)

$$\text{The compressibility} = \frac{\text{(Tapping bulk density-bulk density)}}{\text{Tapping bulk density}} 100\%$$

13. Evaluation of disintegrant property

Dicalcium phosphate and lactose direct compressed were used as model poorly soluble and soluble tablet systems, respectively and erythromycin stearate was selected as a model drug of disintegration study due to its practical

water insoluble and hardly disintegrate when compressed into tablet.

13.1 Preparation of dicalcium phosphate and lactose tablets

Preparation of dicalcium phosphate and lactose tablets were described in chapter IV.

13.2 Preparation of erythromycin stearate tablets

The experimental formulation of erythromycin stearate tablet was

Rx	Erythromycin stearate equivalent to	250 mg
	Lactose powder	150 mg
	PVP 30K(10% in alcohol)	80 mg
	Disintegrant	4%
	Magnesium stearate	3 mg
	Aerosil®	6 mg

The drug and diluent employed in each formulation were passed individually through a 40 mesh screen. The accurate amount of drug and other excipients used in formulation were weighed and mix thoroughly by Kenwood mixer for 10 minutes. The mixture was kneaded into damp mass with binding agent for 5 minutes. The damp mass was passed through 16 mesh screen. The granules were tray dried in oven for 6 hours at 50°C. The dried granules were again passed through a 20 mesh screen. The tablets were compressed on single punch tablet machine with strain gauge using flat face, 20/32 inches punch. The pressure was kept about 2800 pounds.

13.3 Hardness of tablets

The hardness of tablets were determined on crushing strenght tester (Schleunniger, model 2E/205). The mean of five determinations were calculated.

13.4 Disintegration time

The disintegration times of tablets were determined using Hanson Research Tablet Disintegration Tester(model 64-700-156, USA). The mean of six determinations for each batch was calculated.

Results and Discussion

1. Physico-chemical specifications

Table 18 illustrated the sodium, sodium chloride content, heavy metal, iron content, pH and loss of drying of commercial modified potato starch, Explotab^R and Primojel^R, and modified tapioca starch (MTS). It was found that a specification of newly modified tapioca starch (crosslinked-carboxymethylated tapioca starch) was in the limitation of both USP and BP.

2. Water Uptake.

Water uptake of modified tapioca starch powder compared to the modified potato starches, Explotab^R and Primojel^R, were shown in Figure 43.

Primojel^R and modified tapioca starch (MTS) exhibited the same extent of water uptake (Primojel^R = 13.08 $\pm$ 0.38 mg/g and MTS = 13.20 $\pm$ 0.59 mg/g) while the extent of water uptake of Explotab^R =8.11 $\pm$ 0.34 ml/g and native tapioca starch = 0.37 $\pm$ 0.00 ml/g. However, at the first 20 seconds, rate of water uptake of MTS was highest value about 2.55 $\pm$ 0.26 ml/min while the native tapioca starch showed the lowest rate of water uptake as shown in table 19.

Table 18. Specification of Carboxymethyl Starch (Sodium Starch Glycolate).

Types	Explotab^{R}	Primojel^{R}	MTS	USP (NF)	BP
Sodium (%)	2.50 (0.39)	3.45 (0.00)	3.34 (0.06)	2.8 - 4.2	2.8 - 4.5
NaCl(%)	4.24 (0.00)	3.57 (0.00)	0.02 (0.01)	< 10.0	10.0
Heavy metal (%)	< 0.002	< 0.002	< 0.002	< 0.002	< 0.002
Iron (%)	< 0.002	< 0.002	< 0.002	< 0.002	< 0.002
pH	4.00 (0.00)	4.00 (0.00)	6.95 (0.071)	3.0 - 5.0 5.5 - 7.5	5.5 - 7.5
Loss of dying (%)	11.40 (0.58)	11.82 (0.01)	5.93 (0.10)	< 10.0	< 10.0

Standard deviation are in parentheses.

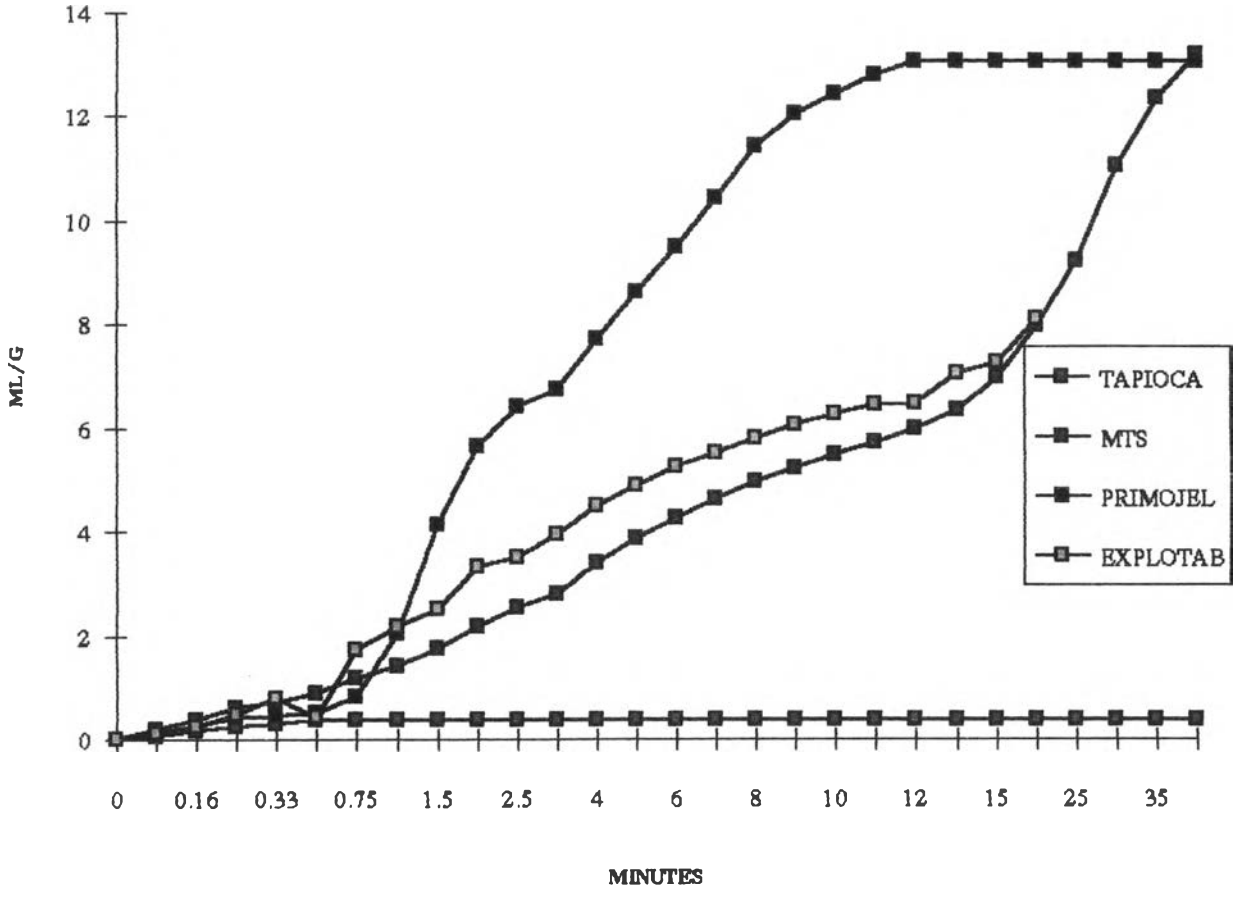


Figure 43 Water Uptake of Disinitegrant Powders.

Table 19 Rate and Extent of Water Uptake of Various Disintegrant Powders.

Disintegrants	Rate of Water Uptake, ml / min.	Water Uptake ml / g
Tapioca	1.06 (0.09)	0.36 (0.00)
MTS	2.54 (0.26)	13.20 (0.59)
Explotab^R	2.17 (0.18)	8.10 (0.34)
Primojel^R	1.53 (0.08)	13.08 (0.38)

Standard deviation are in parentheses.

After 20 seconds, Primojel^R exhibited higher rate and extent of water uptake than Explotab^R and MTS. It was due to MTS and Explotab^R produced viscous gel barrier which abated the water uptake. The viscosity of 1% aqueous MTS and 1% aqueous Explotab^R were 2.02 $\pm$ 0.08 centipoises and 2.08 $\pm$ 0.17 centipoises respectively, while the viscosity of 1% aqueous Primojel^R was 1.65 $\pm$ 0.08 centipoises. However, within 36 minutes the volume of water uptake of MTS and Primojel^R powders were paralleled as shown in table 19.

The water uptake of dicalcium phosphate tablets containing 4% various disintegrants were shown in Figure 44.

It was shown that in the first 20 seconds the tablets containing MTS as disintegrant evinced the highest rate and extent of water uptake which corresponding to the disintegration time. The disintegration time of tablets containing 4% MTS as disintegrant was shortest about 6.50 $\pm$ 0.54 seconds in water, while the tablets containing 4% Explotab^R and 4% Primojel^R exhibited the disintegration times to be 24.83 $\pm$ 0.75 seconds and 21.33 $\pm$ 1.03 seconds, respectively. After 20 seconds the rate of water uptake was slow down. It was due to the tablet disintegrated apart the water could not be

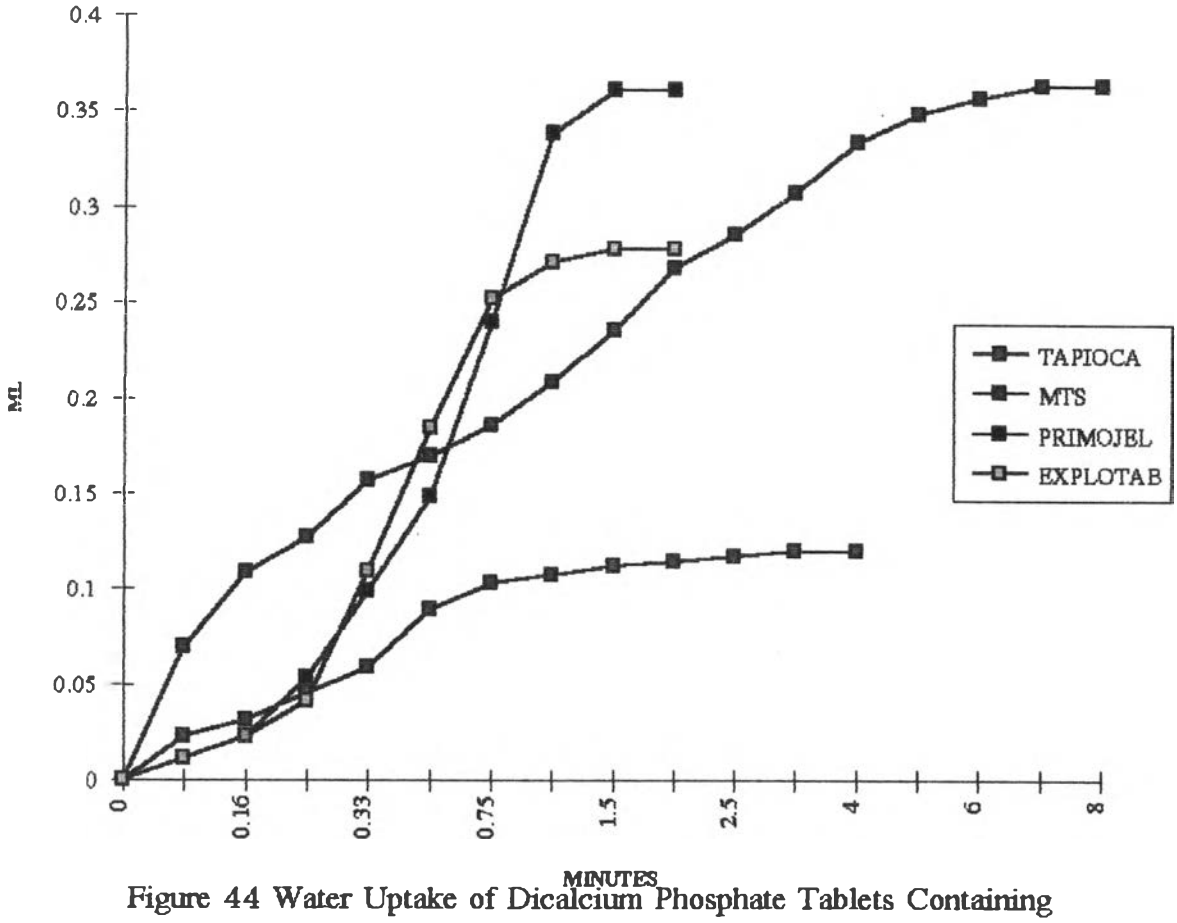


Figure 44 Water Uptake of Dicalcium Phosphate Tablets Containing 4% Various Disintegrants.

facilitated withdrawn into tablet matrix as the first. Nevertheless, the extent of water uptake of dicalcium phosphate containing 4% MTS and those containing 4% Primojel[R] more closely resembled. The extent of water uptake of dicalcium phosphate tablets containing 4% MTS and 4% Primojel[R] were 0.36 ± 0.00 ml and 0.36 ± 0.03 ml, respectively as the extent of water uptake of tablets containing 4% Explotab[R] was 0.27 ± 0.36 ml. This results were corresponding to the results achieved from the pure disintegrant powders.

The water uptake of lactose tablets containing 4% various disintegrants was shown in Figure 45.

It was found that the tablets containing 4% Primojel[R] exhibited the highest rate of water uptake while the tablets containing 4% Explotab showed the maximum extent of water uptake. The lactose tablets containing 4% MTS, 4% Explotab[R] and 4% Primojel[R] exhibited no difference in the disintegration times. The disintegration times of lactose tablets were less affected by these disintegrants at the concentration of 4%. This is due to the soluble nature of lactose which tends to produce tablets which dissolve from the outside inward rather than disintegrate rapidly.

3. Bulk swelling

The bulk swelling properties of various modified starches were shown in Figure 46. The MTS exhibited the highest extent of swelling (1500%), while Explotab[R] and Primojel[R] showed the bulk swelling to be 1113% and 1330% respectively. The modified tapioca starch (MTS), both substituted and crosslinked, markedly increased the swelling capacity when compared to plain tapioca starch (bulk swelling 6.67%).

The magnitude of force produced by disintegrants, as described by List and Muazzam (1979) the rate at which that force developed, dF/dt, was also

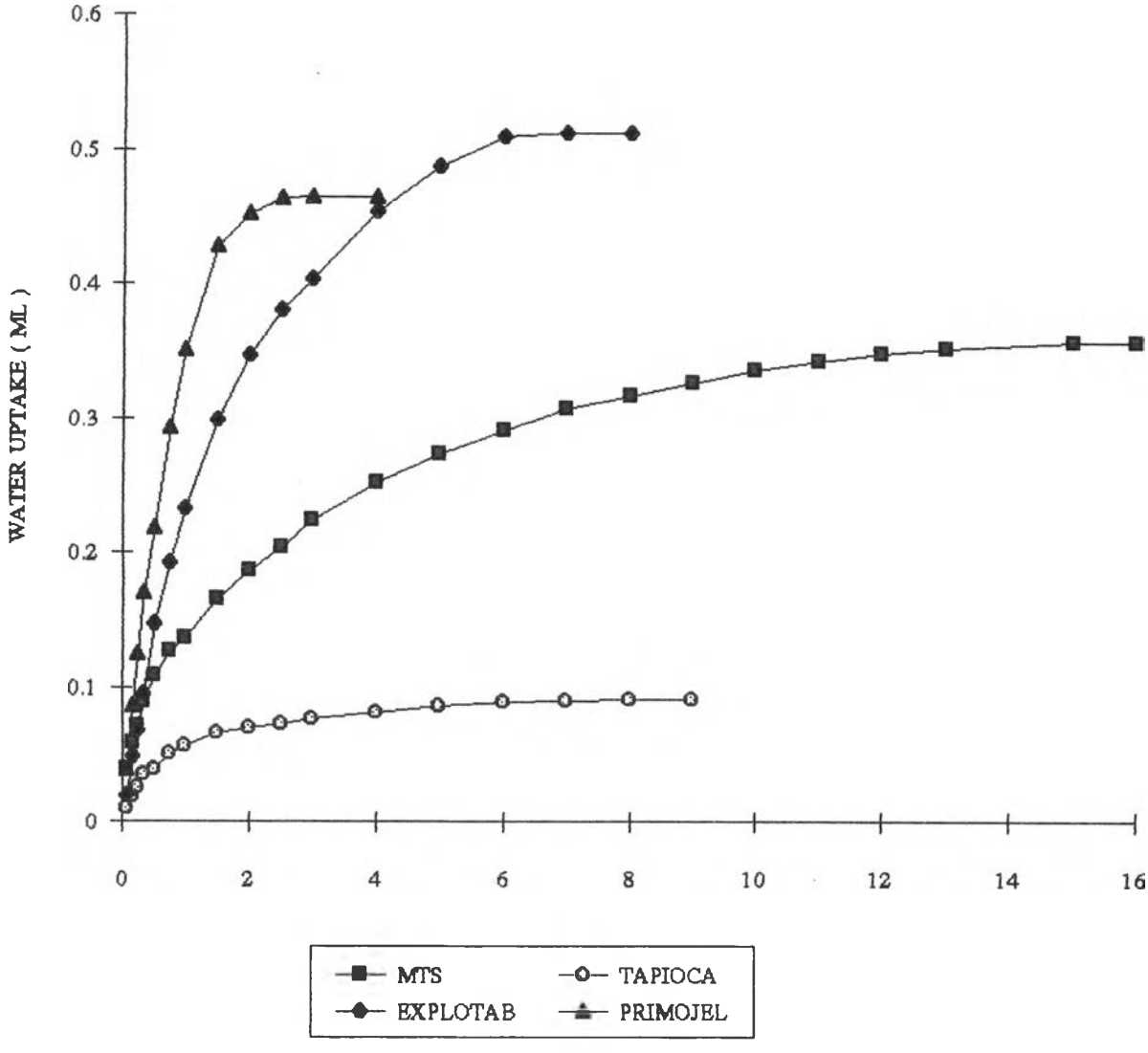


Figure 45 Water Uptake of Lactose Tablets
Containing 4% Varios Disintegrants.

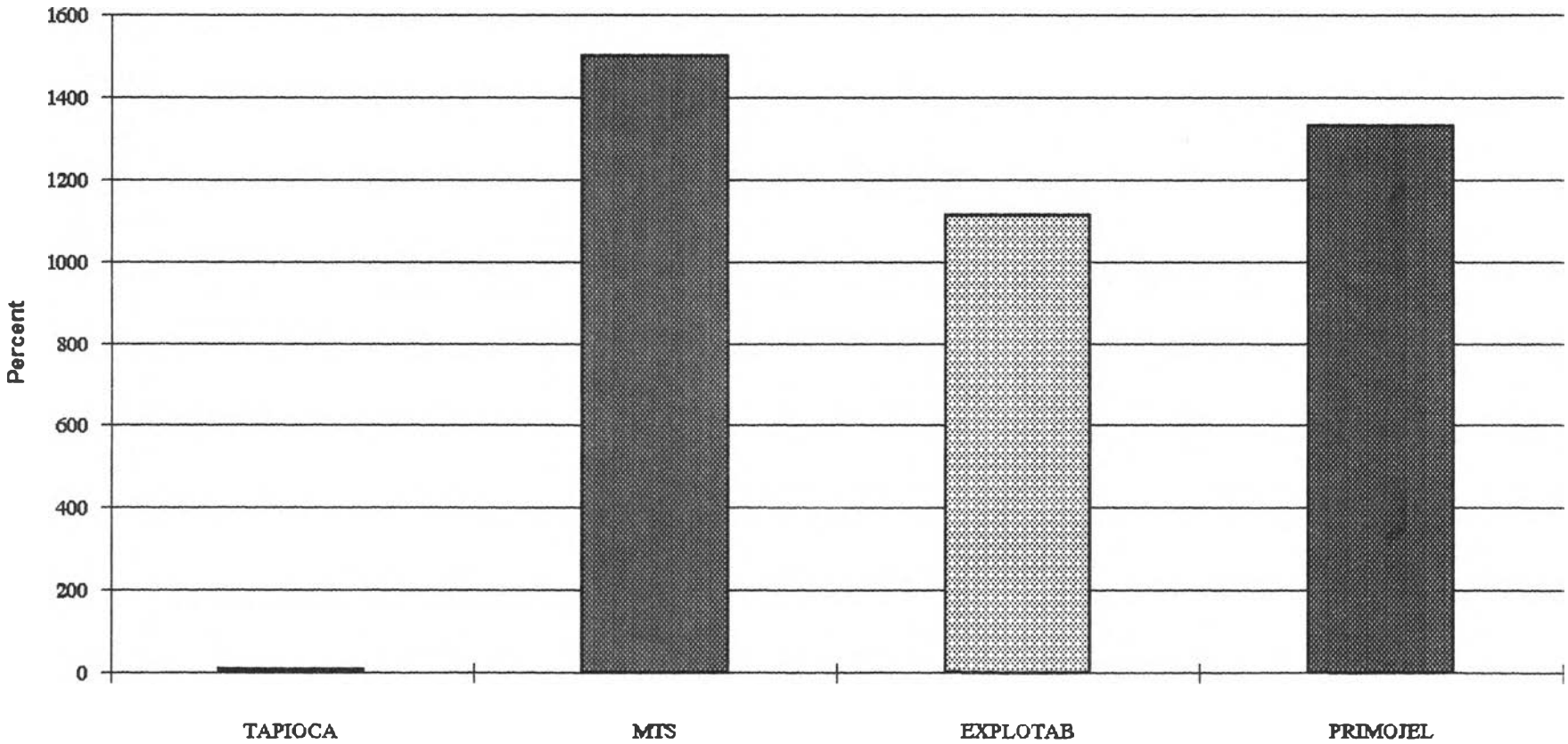


Figure 46 Bulk Swelling of Various Modified Starches.

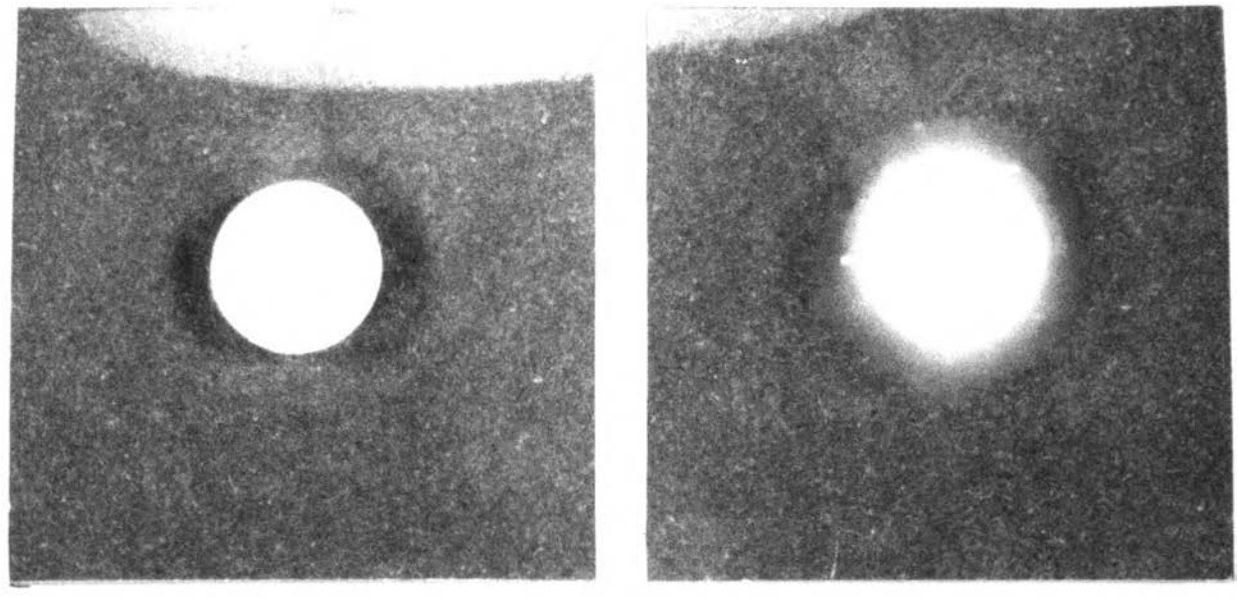
likely to be a factor involved in governing disintegrant action. They proposed the rate of swelling of disintegrant was related to the rate at which disintegrant force developed.

$$dF/dt = K\, dV/dt$$

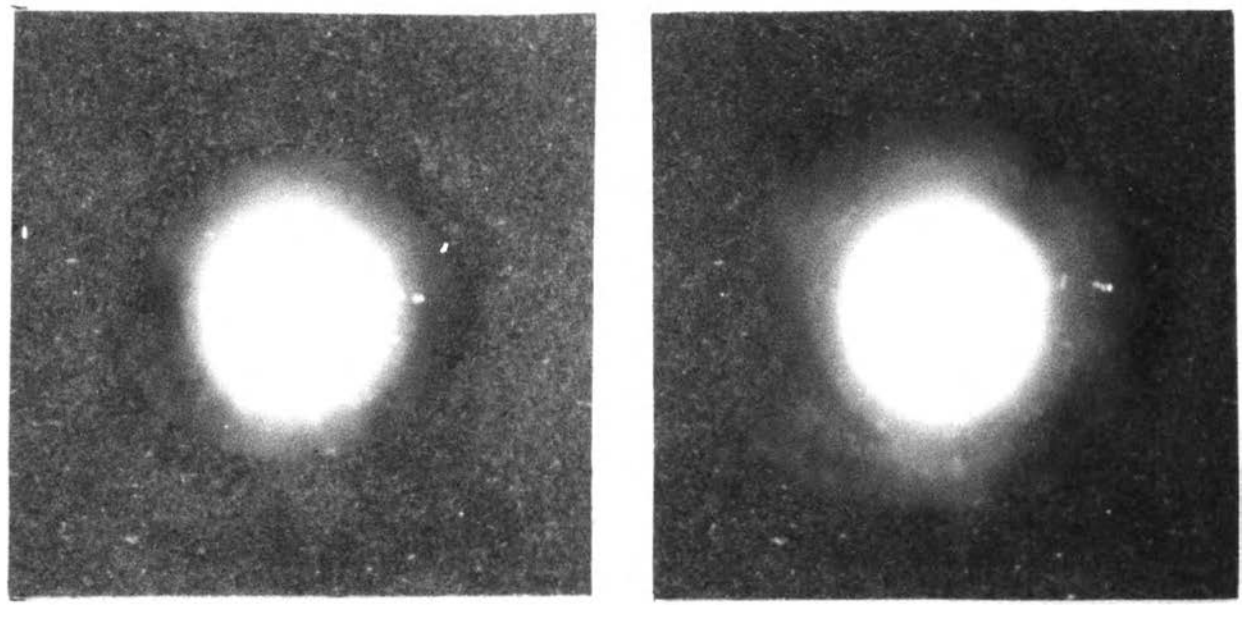
where dV/dt is a rate of swelling and K is a constant for any given matrix of formulation at constant porosity value. If the porosity of tablet is high, dV/dt will be governed by the properties of the disintegrant. If the porosity is low, dV/dt could be primarily controlled by the rate at which water can reach the disintegrant. Due to the tablet were only compressed in one dimension, it was probably unjustifiable to define the matrix as isotropic. The compaction process would result in stress in the plane of compaction. The tablets were more likely to disintegrate in the plane of compaction than the plane of non-compaction and not all disintegrants swelled equally in all dimensions. Crosslinked carboxymethylcellulose increased in radius but provided little change in length when exposed to water. This vectorial dysymmetry in swelling might perhaps be of relevance in disintegrant action the disintegration force might be non-vectorial (Rudnic, et al., 1982)

A comparative study of the swelling capacity of MTS, Explotab^{R} and Primojel^{R} at various time intervals by photography was demonstrated as the following :

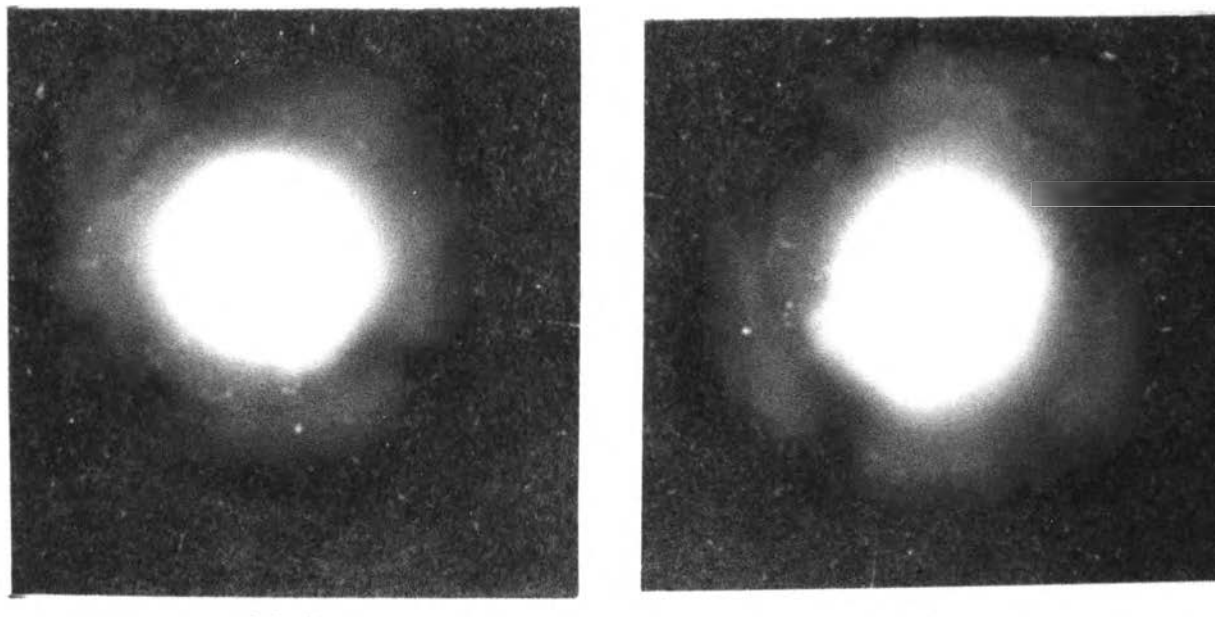
Figure 47 showed swelling characteristics of plain tapioca starch at various time intervals. It was shown that plain tapioca starch exhibited low degree swelling characteristics. Contrastly, the MTS provided the most prodigious swelling capacity and swelled into three dimensions which could be seen in Figure 48a, 48b as a top view and Figure 49 as a side view. This result was corresponding to bulk swelling of these disintegrant powders which determined by using modified Nogami's apparatus. It was found that there



0 Min. 5 Min.

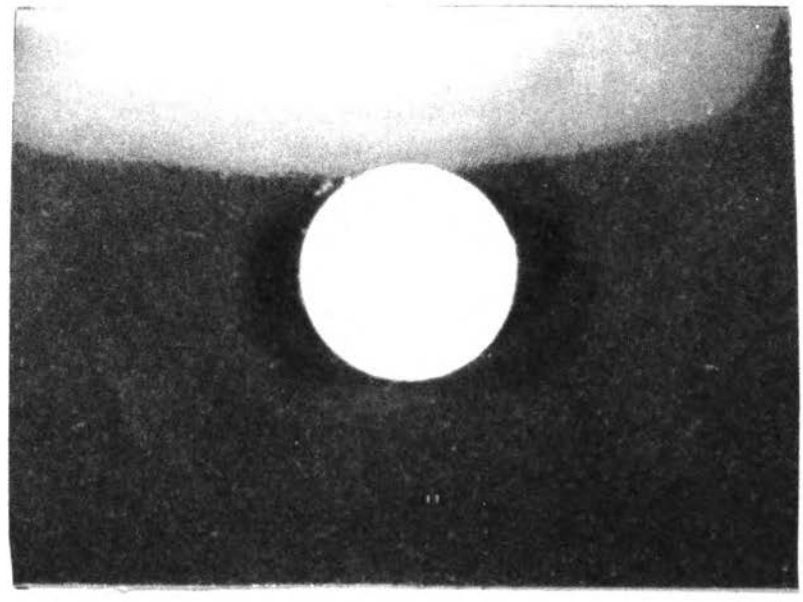


10 Min. 15 Min.



20 Min. 30 Min.

Figure 47 Swelling Characteristic of Tapioca Starch.



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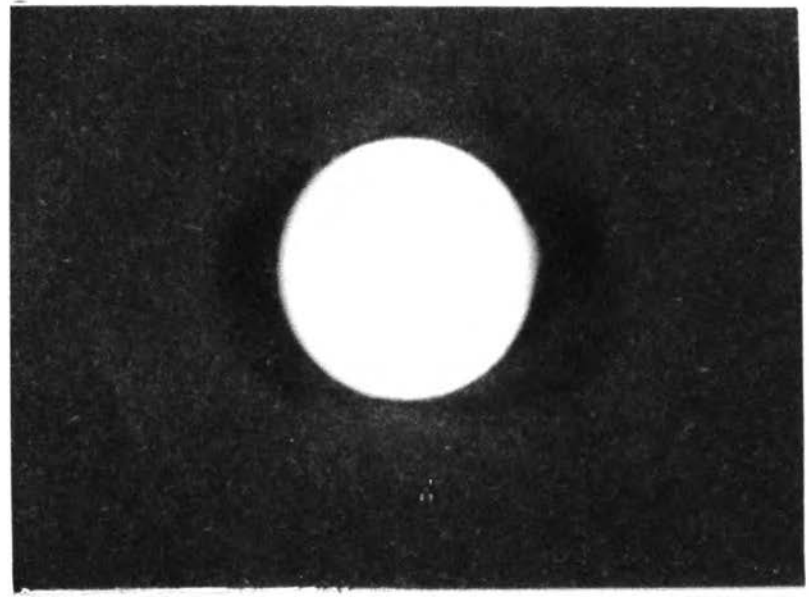

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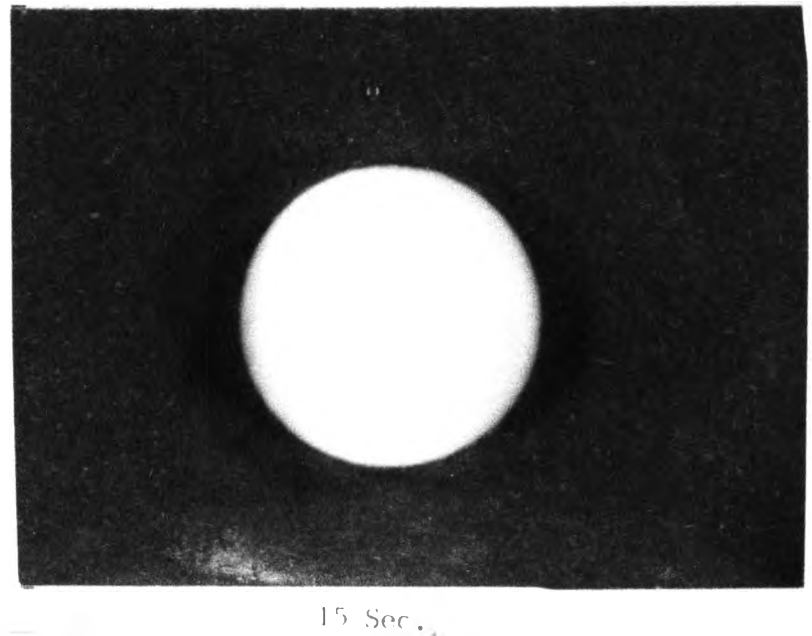

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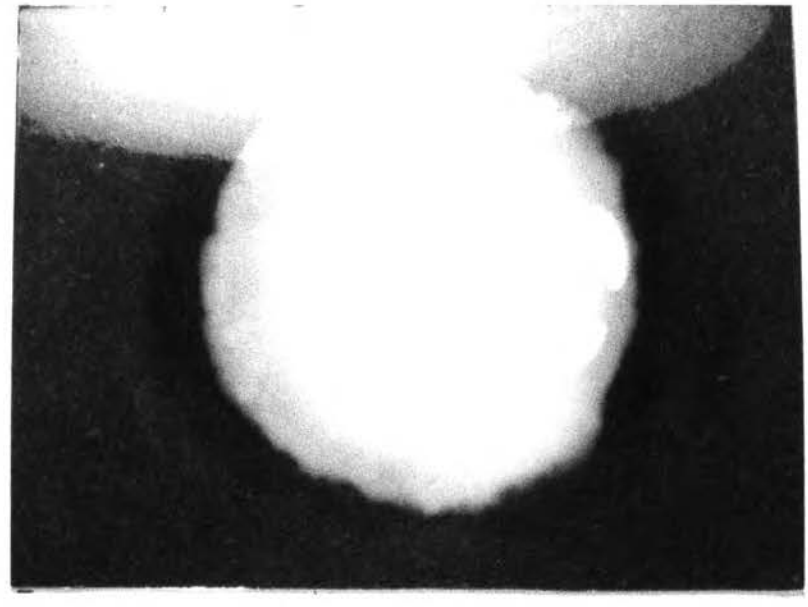
Figure 48-a. Swelling Characteristic of Modified Tapioca Starch



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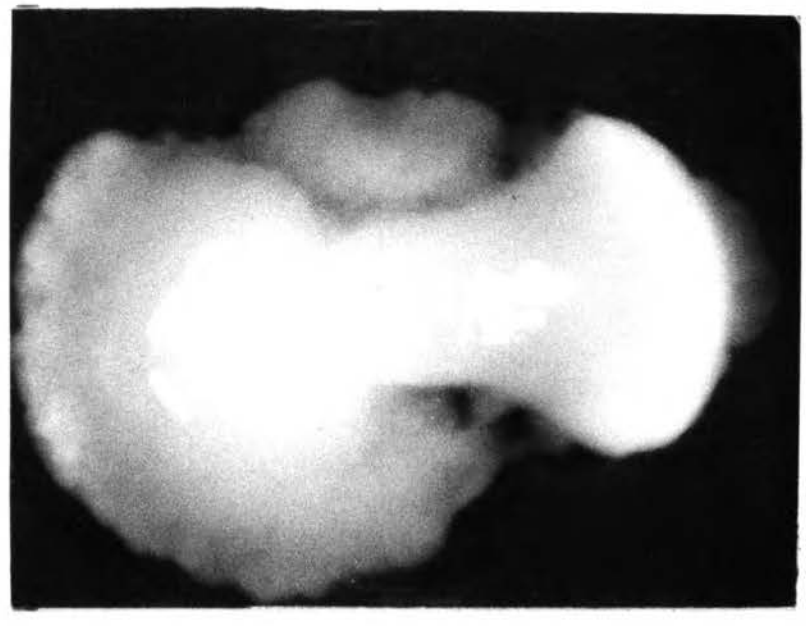
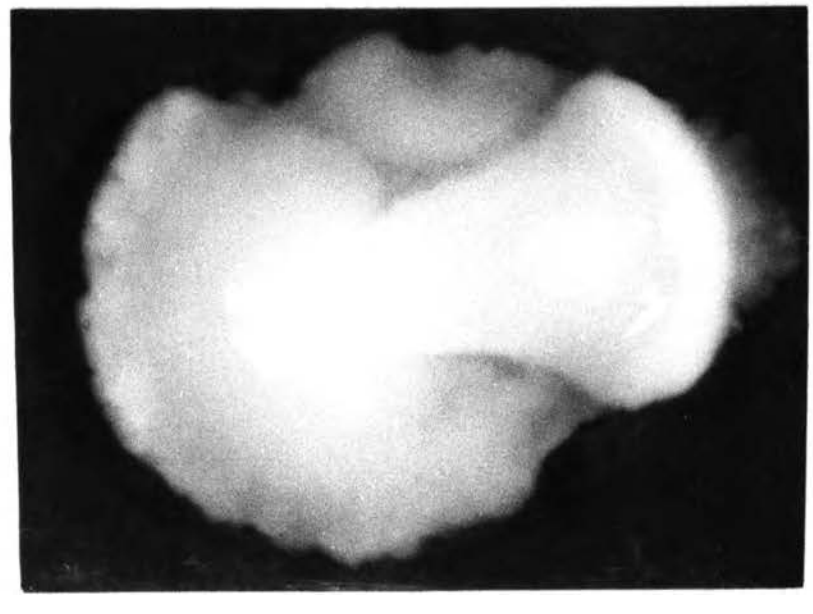


90 Sec.



120 Sec.

Figure 48-b Swelling Characteristic of Modified tapioca Starch.

15 Sec.

45 Sec.

60 Sec.

120 Sec.

Figure 49 Photograph Showed Swelling of Modified Tapioca Starch (Side View).

were a relationship among the swelling capacity, water uptake and disintegration time of dicalcium phosphate tablets containing 4% of these disintegrants. Hence, water uptake and swelling capacity are still useful to consider the disintegrant characteristic of a new disintegrant.

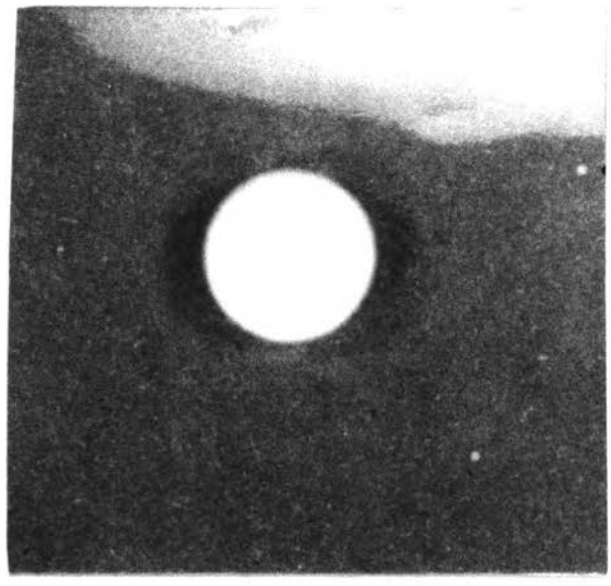
Figure 50-51 and 52-53 showed swelling characteristic of Explotab^{R} and and Primojel^{R} in water at various time intervals. Both Explotab^{R} and Primojel^{R} swelled many times of their own sizes and swelling characteristic were more closely resembled. However, it is clearly demonstrated that MTS exhibited swelling capacity superior over both Explotab^{R} and Primojel^{R}.

4. Sedimentation volume

Although sedimentation volume did not correlate to disintegration time and there was ambiguous, in fact, sedimentation volume are still used to simply explain about swelling volume of disintegrant powder. The sedimentation volume of modified starches was shown in Figure 54. The sedimentation volumes of MTS, Explotab^{R} and Primojel^{R} closely resembled both in water and 0.1N HCl. However, the sedimentation volume of MTS was markedly increased when compared to plain tapioca starch both in water and 0.1N HCl.

5. Hydration capacity

The hydration capacity of modified starches were shown in Figure 55. The hydration capacity were ranked as the following : MTS (28.37 $\pm$ 0.06%) > Primojel^{R} (22.53 $\pm$ 0.25%) > Explotab^{R} (18.34 $\pm$ 0.38%) > tapioca starch (2.57 $\pm$ 0.04%). There were correlated among hydration capacity, bulk swelling and water uptake. Increased water uptake, increased bulk swelling and also increased hydration capacity.



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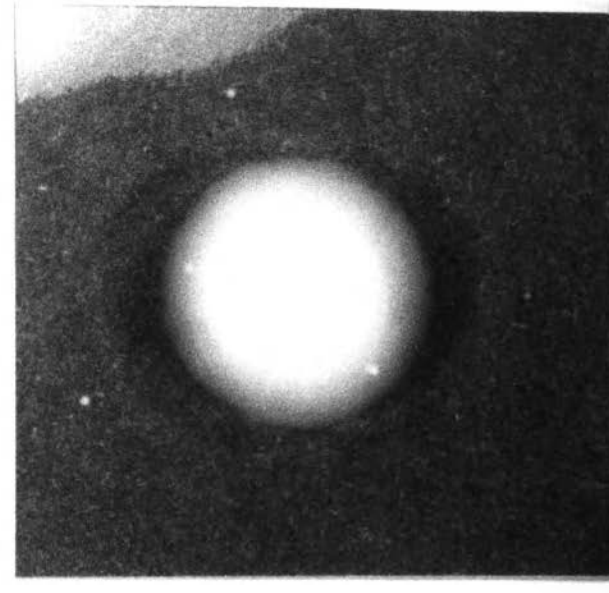

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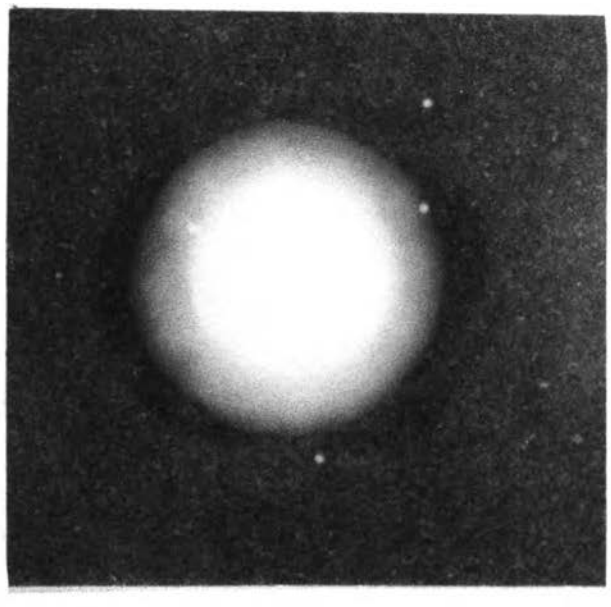

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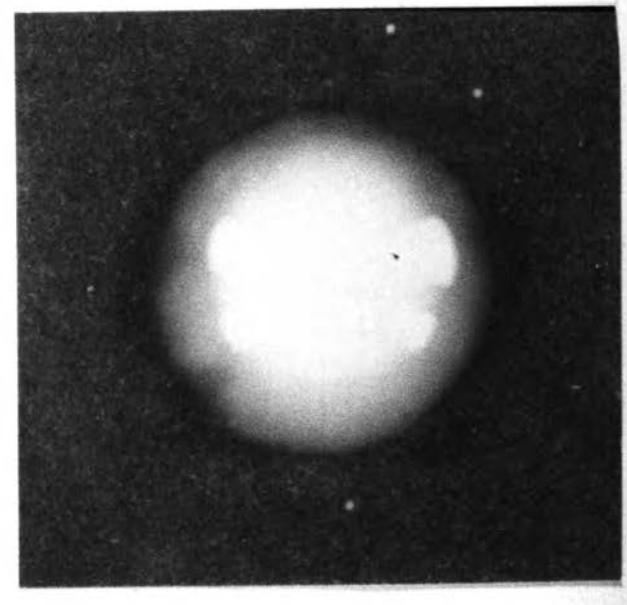

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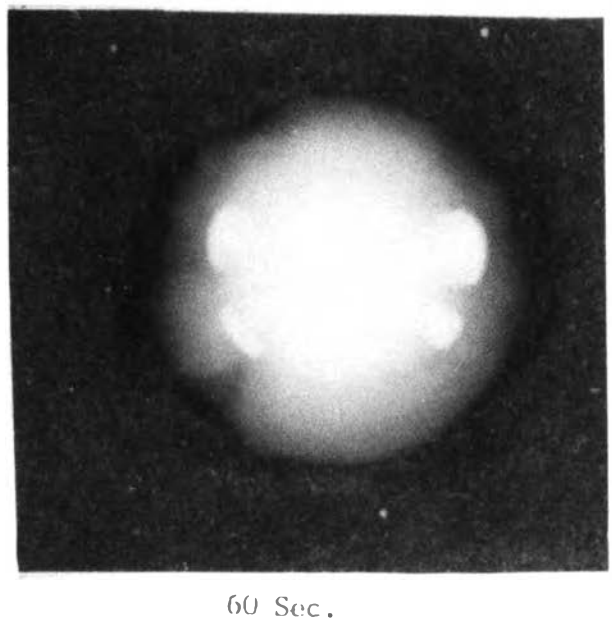

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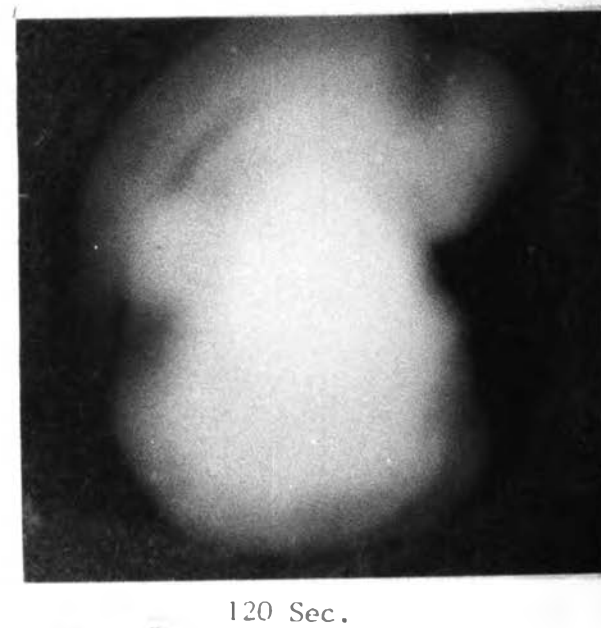
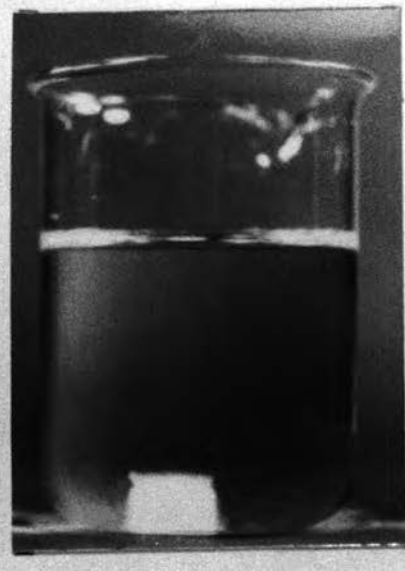


120 Sec.

Figure 50 Swelling Characteristic of Primojel®



15 Sec.

45 Sec.

60 Sec.

120 Sec.

Figure 51 Photograph Showed Swelling of Primojel^{R} (Side View).

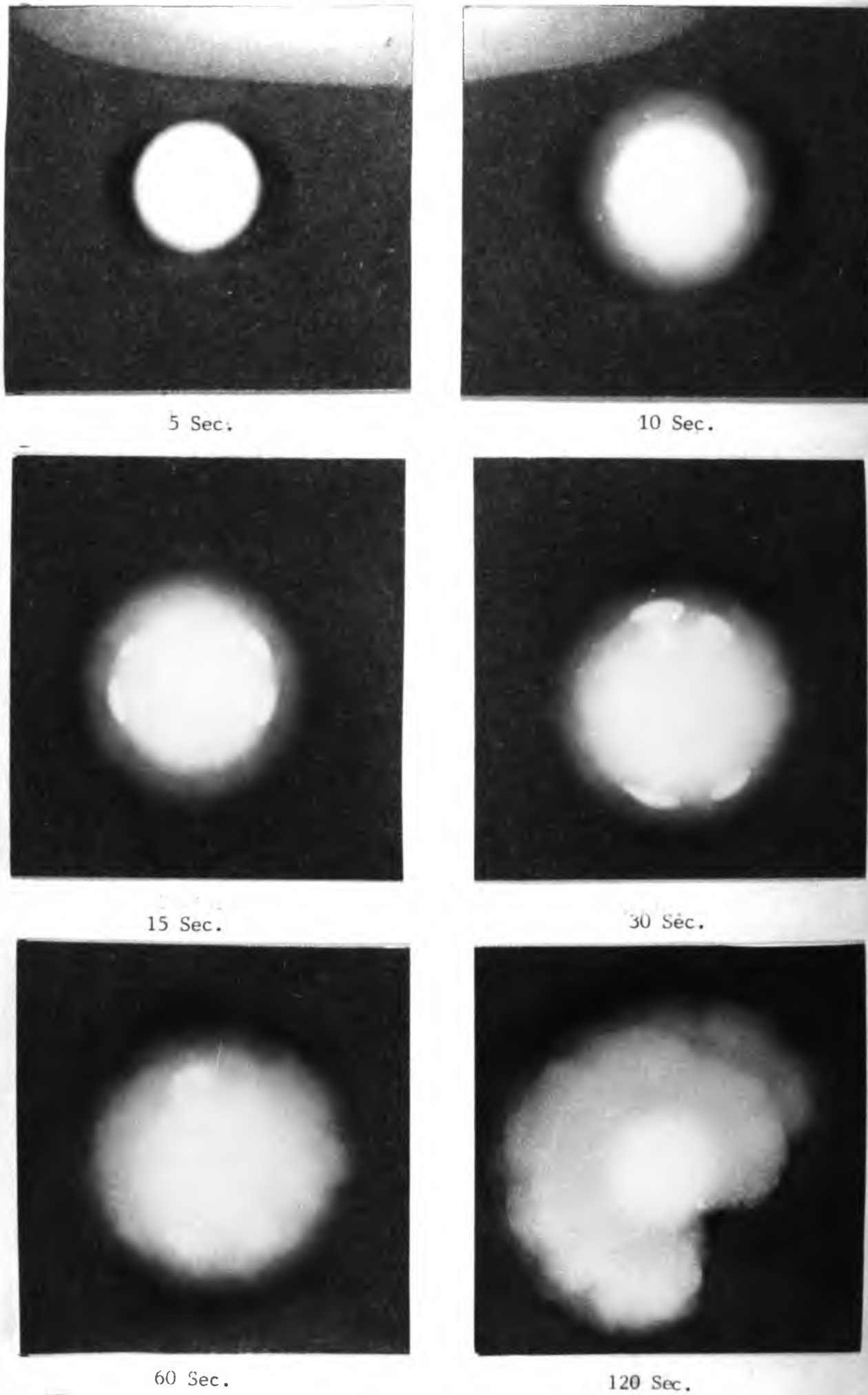
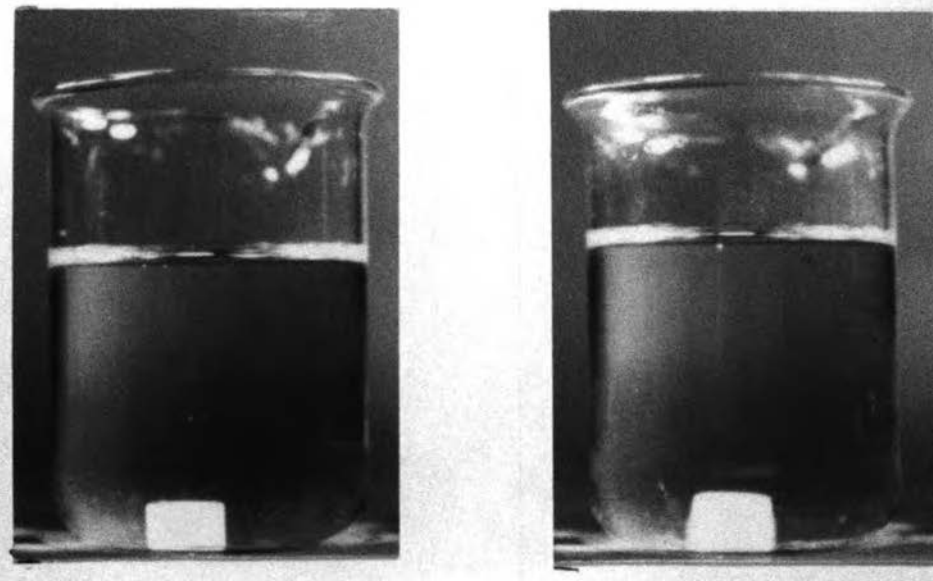
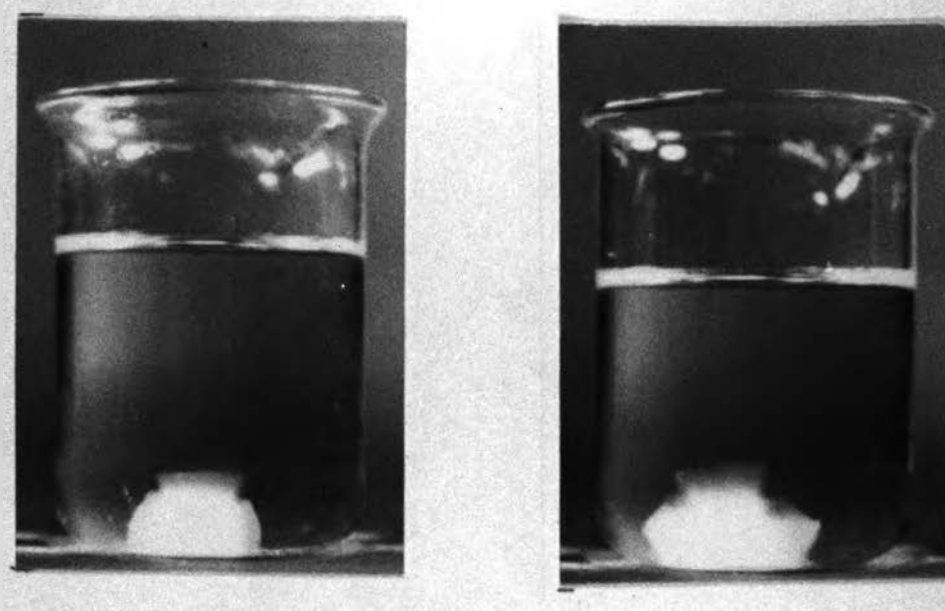


Figure 52 Swelling Characteristic of Explotab.®



15 Sec.

45 Sec.



60 Sec.

120 Sec.

Figure 53 Photograph Showed Swelling of Explotab^{R}(Side View).

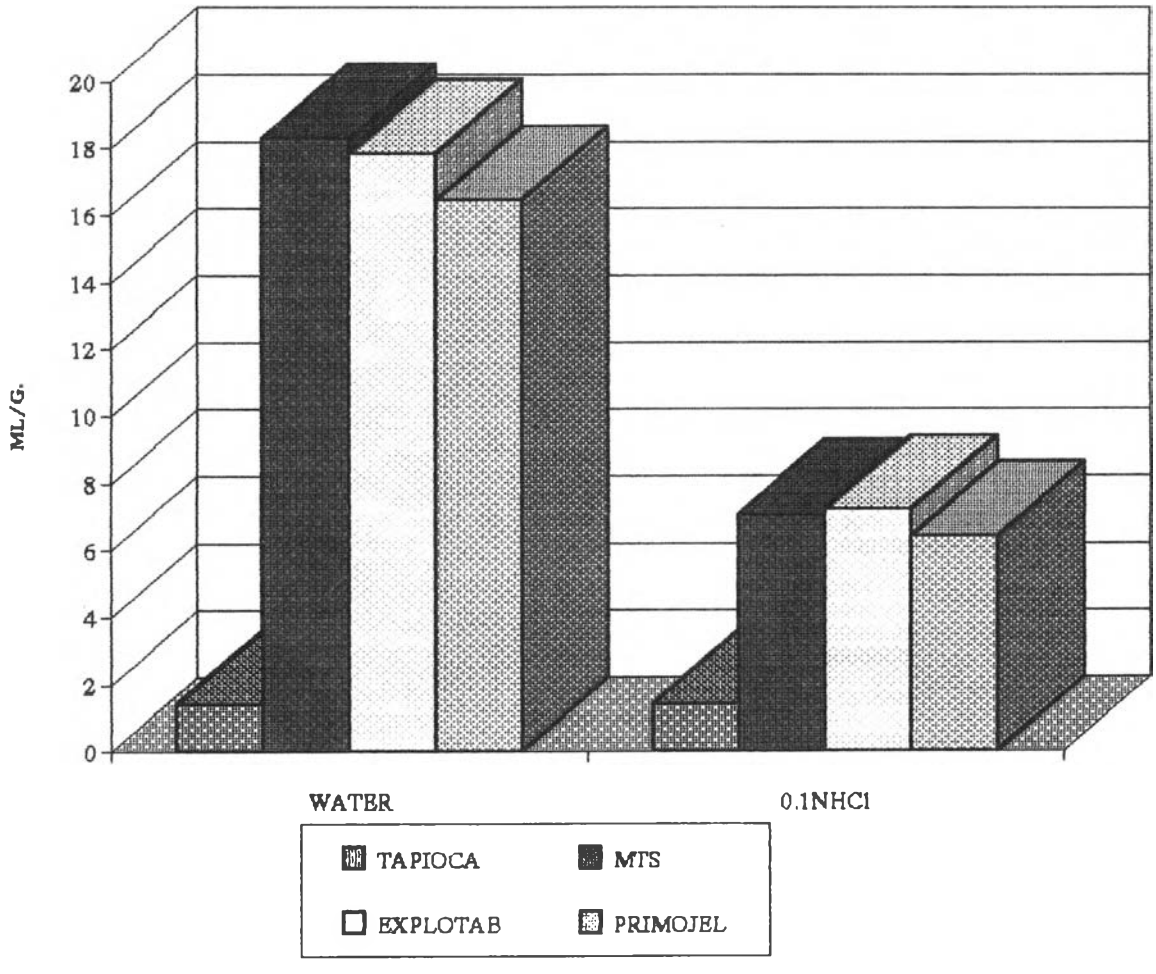


Figure 54 Sedimentation Volumes of Various Modified Starches.

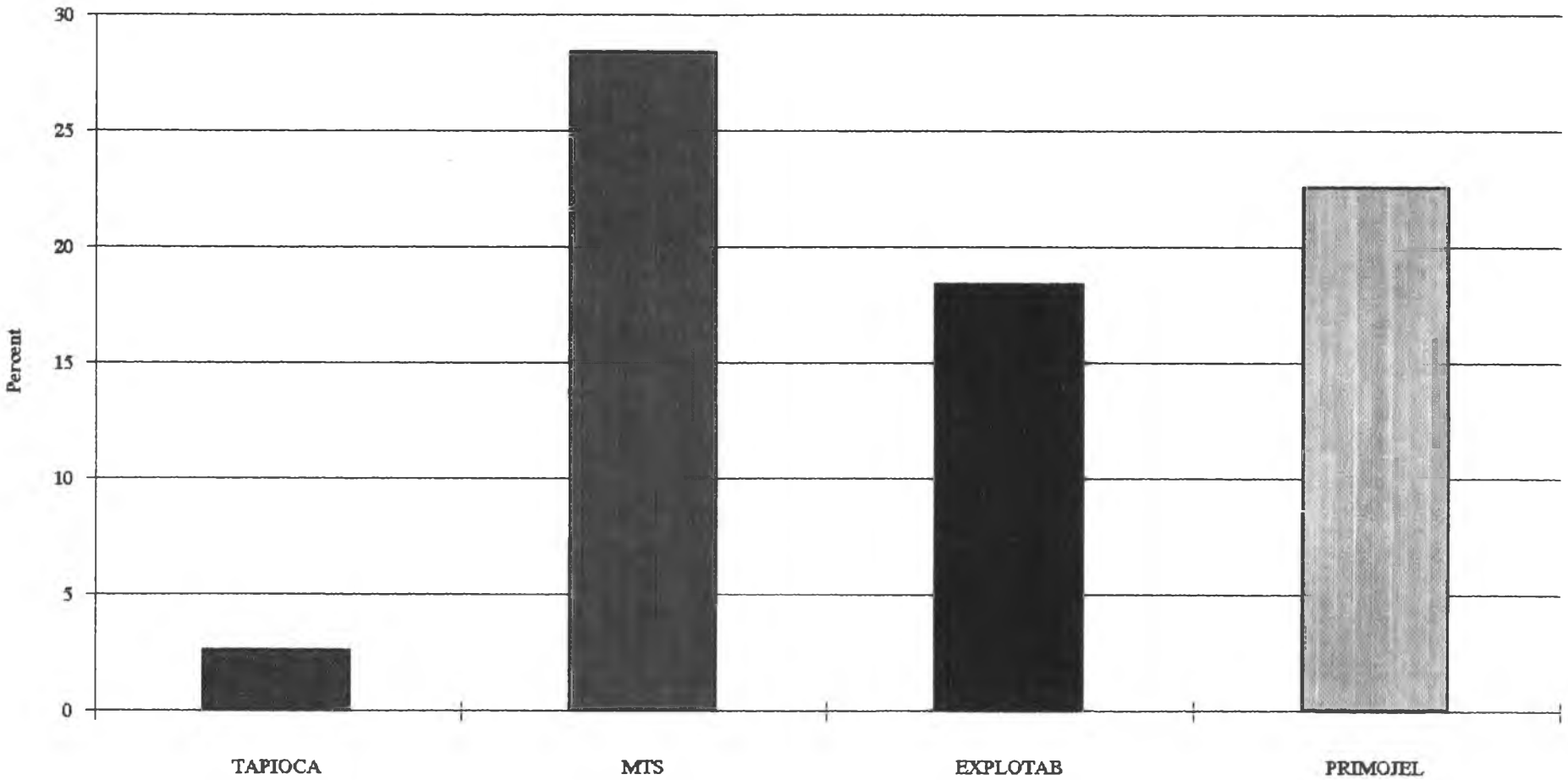


Figure 55 Hydration Capacity of Various Modified Starch.

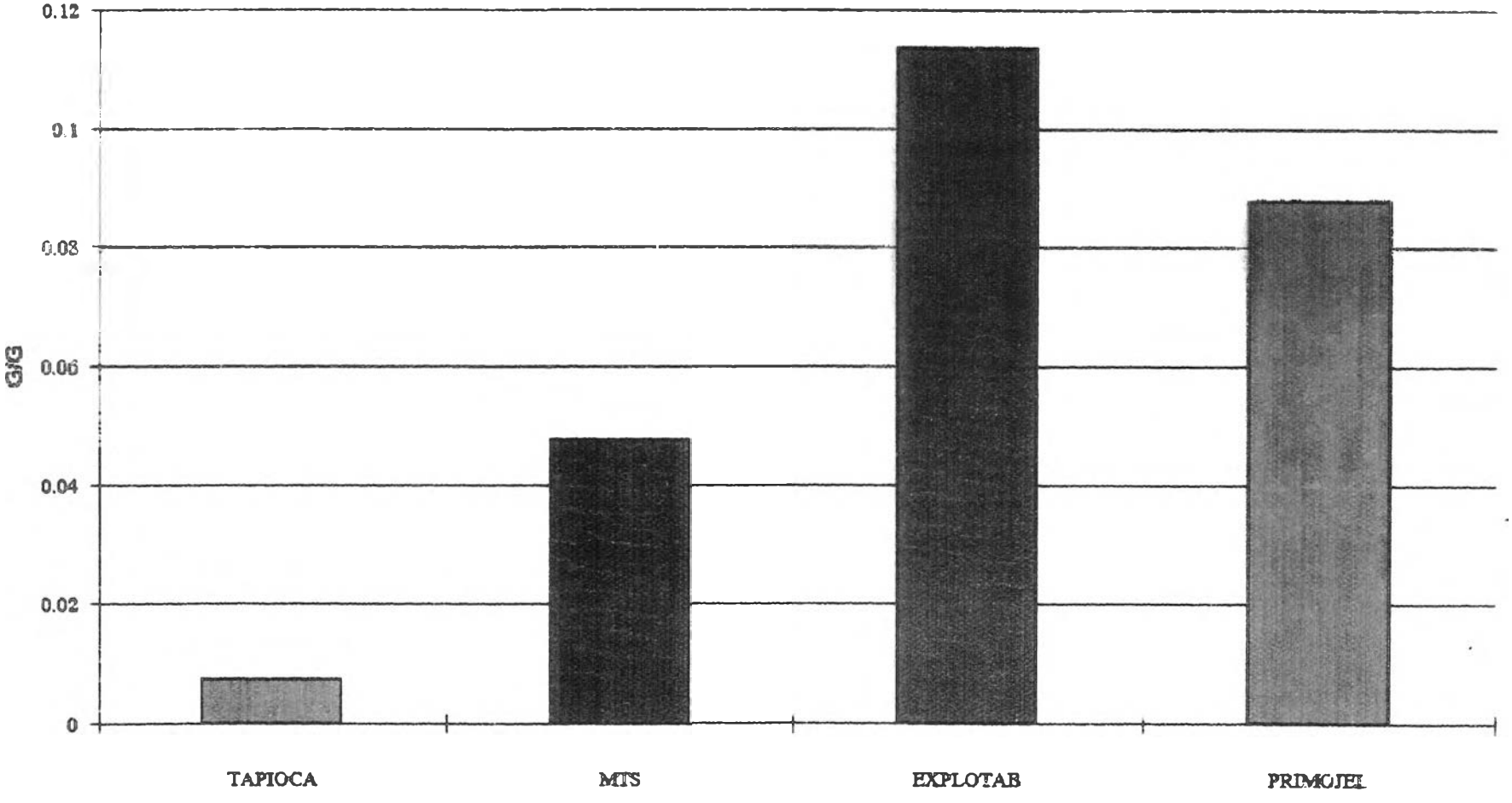


Figure 56 Cold Water Soluble of Various Modified Starch

6. Cold water soluble fraction

From Figure 56, it was found that Explotab^R showed the higher cold water soluble fraction than MTS and Primojel^R. It was due to there were a number of sodium chloride content (byproduct) on the surface of modified starch grain, caused increased the cold water soluble. In the same reason the cold water soluble fraction of Primojel was higher than that of MTS.

7. Viscosity

The viscosity of modified starches were demonstrated in Figure 57. The viscosities of MTS (2.0276 $\pm$ 0.0869 cps.) and Explotab^R (2.0889 $\pm$ 0.1737 cps) more closely resembled and higher than that of Primojel ^{R} (1.6588 $\pm$ 0.0869 cps). The viscosities of modified starches studied were relative low, it was due to all of modified starches were crosslinked to reduce gel formation for the purpose of being a good disintegrant.

8. Sorption isotherm

The sorption isotherm profile of MTS, Explotab^R and Primojel^R were paralleled together, except at the high relative humidity (71.3% RH) the percentage of weight gained of the Explotab^R and Primojel^R were higher than MTS as shown in Figure 58.

9. Bulk density, tapped density and compressibility

The bulk density, tapped density and compressibility were presented in Table 20.

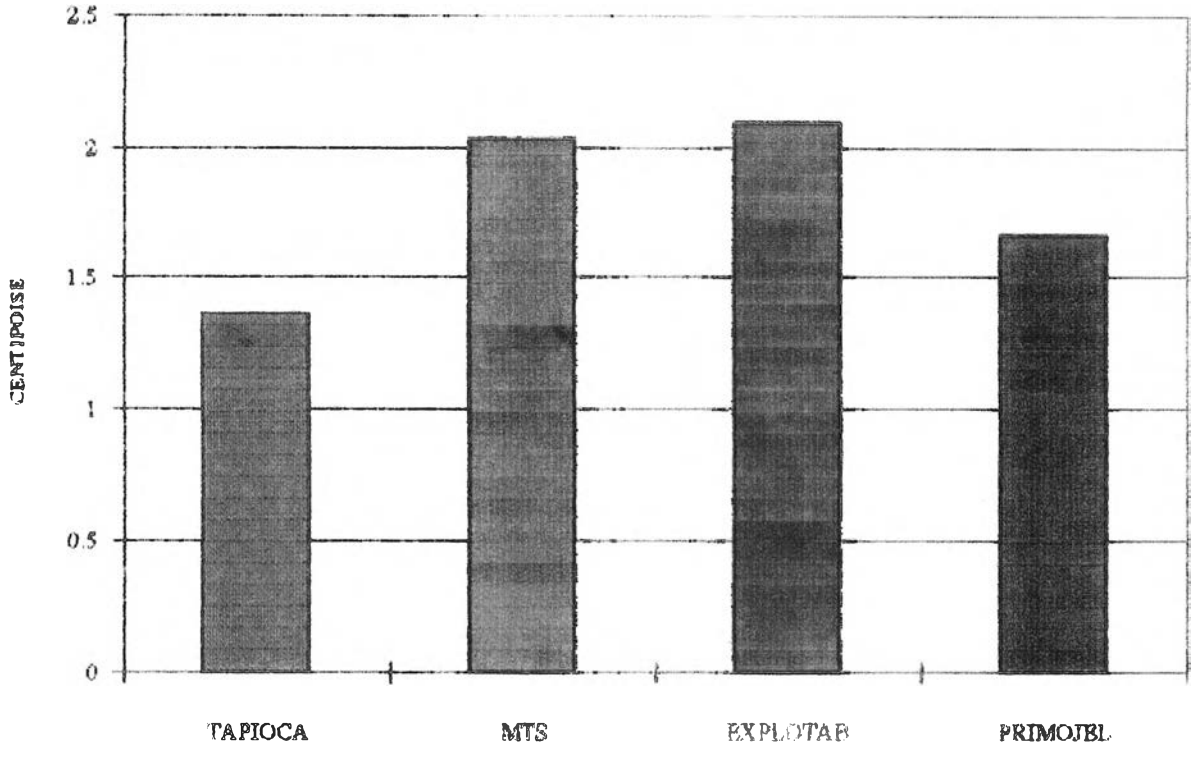


Figure 57 Viscosity of Various Modified Starches.

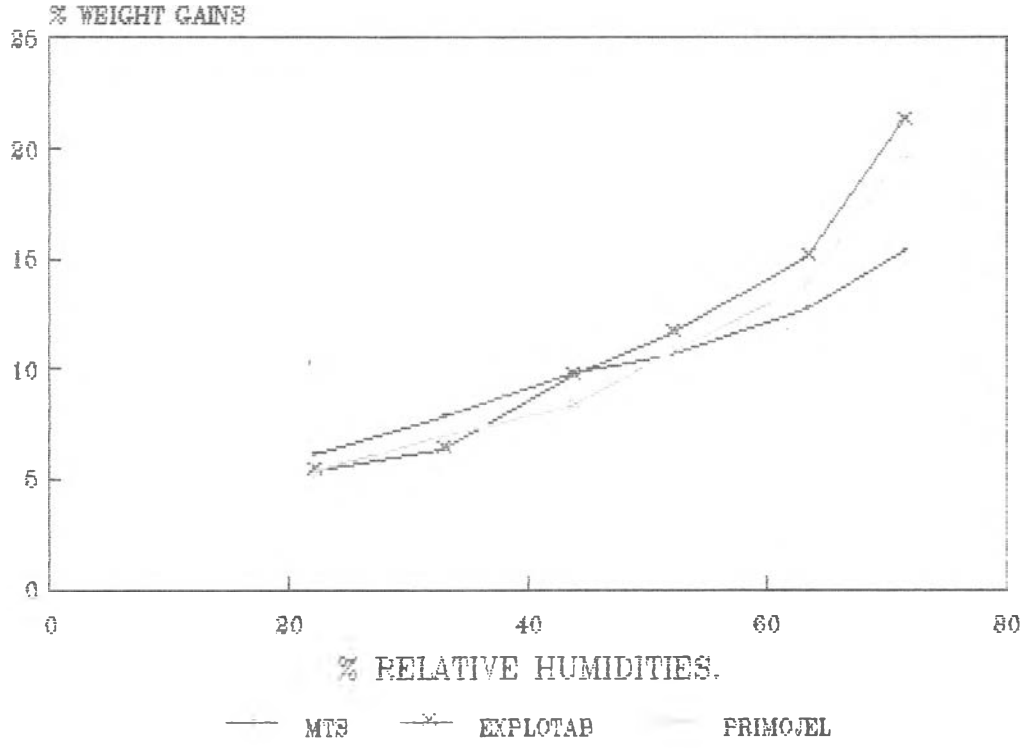


Figure 58 Sorption Isothem of Various Modied Starches.

Table 20. Bulk Density, Tapped Density and Compressibility of Various Disintegrants.

Types	Bulk density (g/ml)	Tapped density (g/ml)	% Compressibility
Tapioca	0.4243 (0.0009)	0.6364 (0.0015)	33.3333 (0.0000)
MTS	0.4500 (0.0000)	0.7220 (0.0085)	37.6688 (0.7325)
Explotab^R	0.6875 (0.0081)	0.8896 (0.0104)	22.7224 (0.0032)
Primojel^R	0.5855 (0.0040)	0.8121 (0.0210)	27.8835 (0.3685)

Standard deviations are in parentheses.

Explotab^R exhibited the highest both bulk density and tapped density but lowest in percent compressibility. The MTS showed the best compressibility characteristics among modified starches studied.

10. Disintegration time study.

10.1 Dicalcium phosphate tablets.

The disintegration times of dicalcium phosphate tablets containing various disintegrant were demonstrated in Figure 59. The tablets containing 4% MTS exhibited the shortest disintegration time (6.50 $\pm$ 0.55 sec.) while those containing 4% Explotab^R and 4% Primojel^R showed the disintegration time to be 24.83 $\pm$ 0.75 sec. and 21.33 $\pm$ 1.03 sec., respectively. MTS was the excellent disintegrant for slightly water soluble tablet system such as dicalcium phosphate. To verify this event the photographic method evaluation was studied and the pictures were shown in Figure 60-62 which exhibited the disintegration characteristics when dicalcium phosphate tablets exposed to the water. It was clearly illustrated MTS showed the best disintegration characteristics among four disintegrants studied : tapioca starch, Explotab^R, Primojel^R and MTS. In addition the tablet containing 4% MTS as disintegrant disintegrated into a more fine discreted

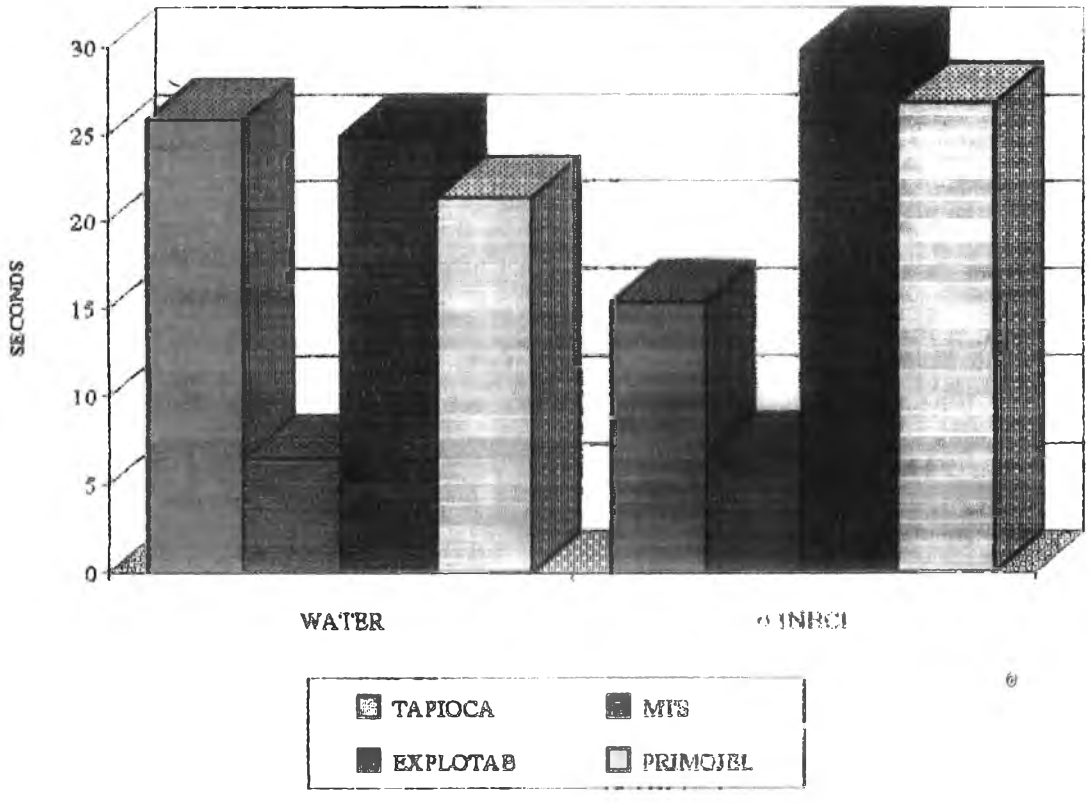


Figure 59 Disintegration Times of Dicalcium Phosphate Tablets Containing 4% Various Disintegrants.

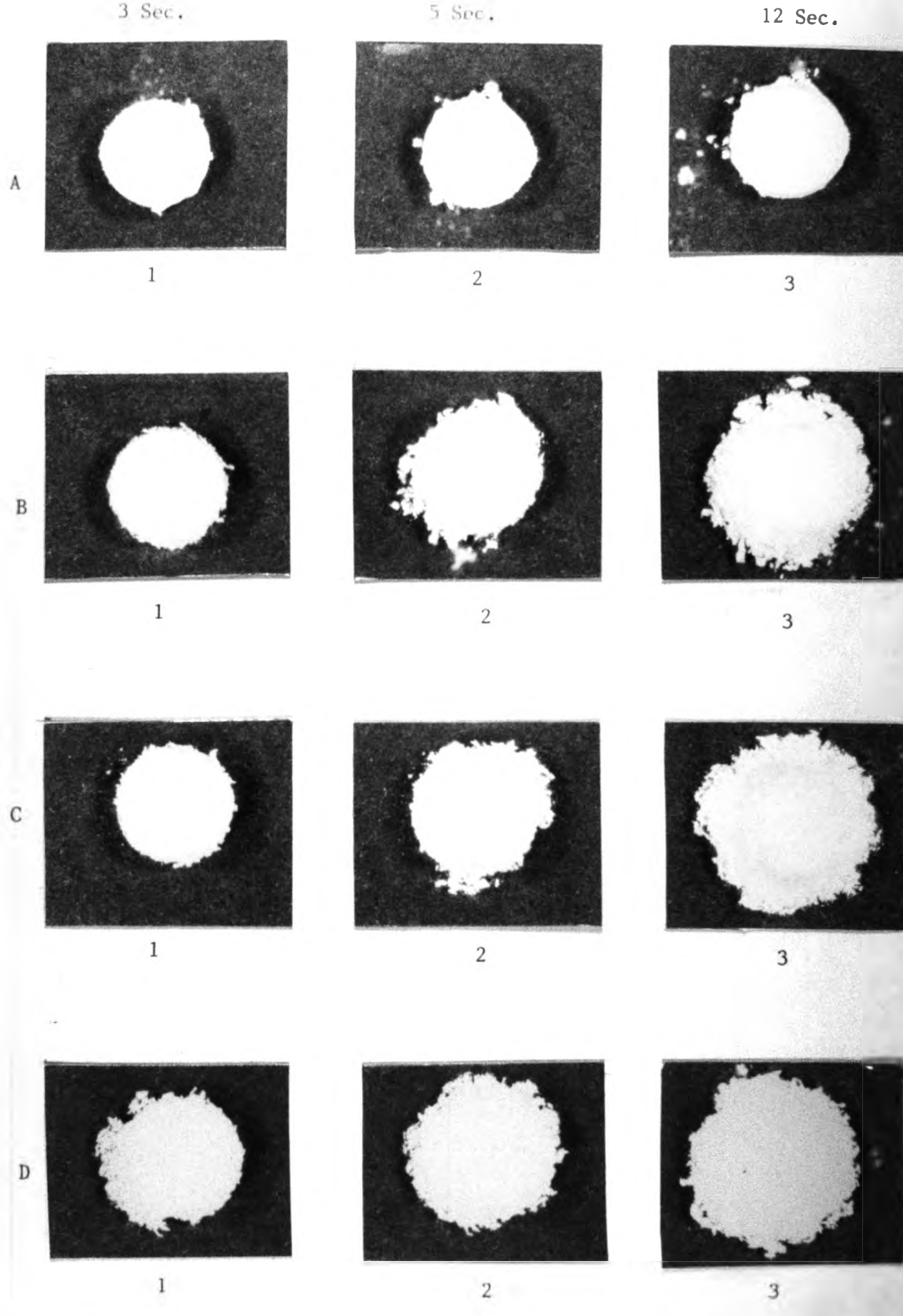
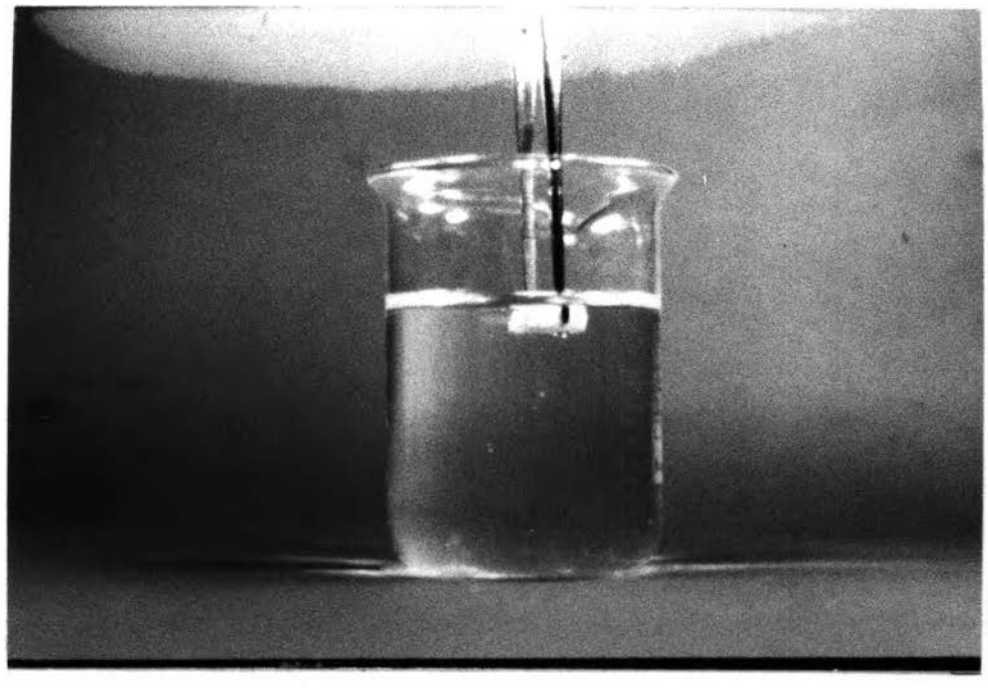
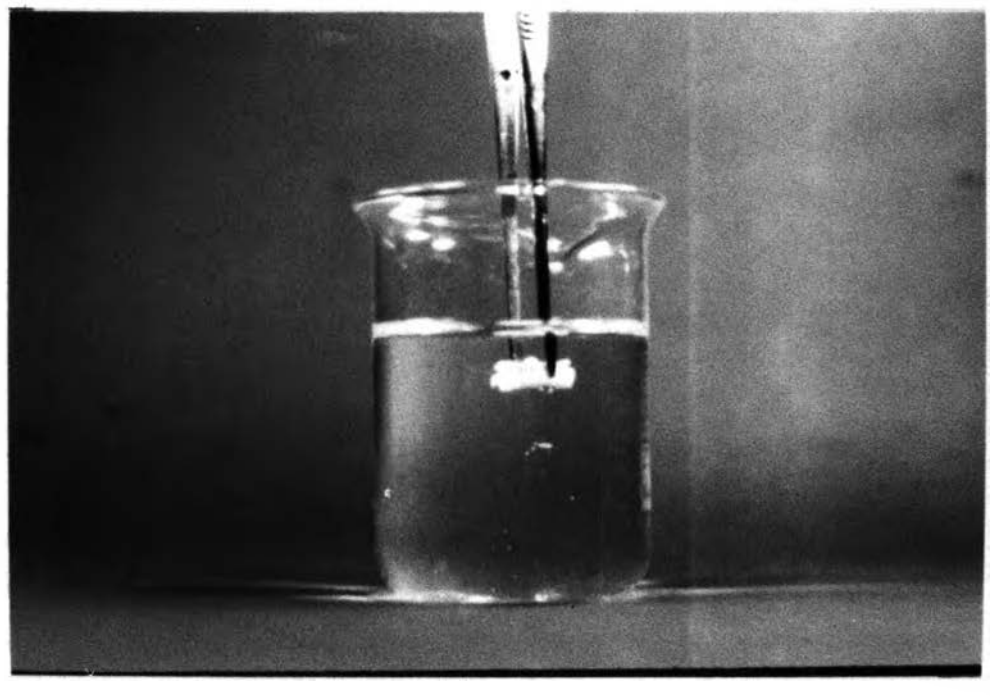


Figure 60 Photograph of disintegrating Characteristics of Dicalcium Phosphate Tablets.



A-1 (2 Sec.)



A-2 (5 Sec.)

Figure 61 Photograph of Disintegration of Dicalcium Phosphate Tablets Using Tapioca Starch as Disintegrant.

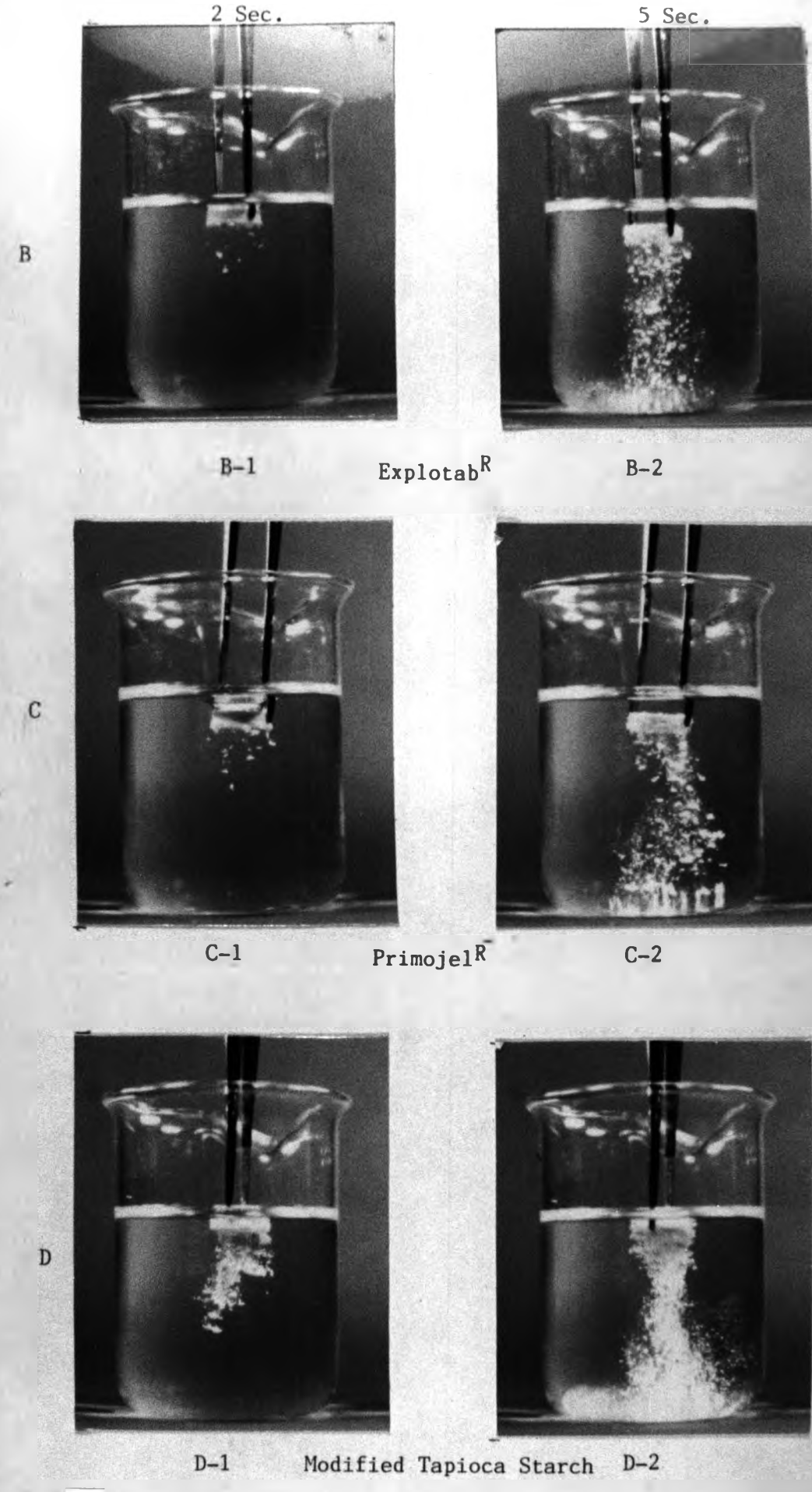


Figure 62 Photograph of Disintegration of Dicalcium Phosphate Tablets Using Different Disintegrants.

particles than tablets containing 4% Explotab[R] and 4% Primojel[R] as disintegrant, this result may cause the drug facilitates to dissove, an increased in dissolution may be occurred. The reason the MTS provided a fine disintegrated particles, it was due to the size of tapioca starch grain was smaller than potato starch grain, therefore the modified tapioca starch grains were smaller with a large surface area and they could be distributed evenly in the tablet matrix. When the tablet exposed to water the rapid water uptake and swelling performed and then the rapid disintegration occurred.

The disintegration times of dicalcium phosphate tablets increased in acid medium (0.1N HCl). It was due to cation from acid medium interfered electrical mutual repulsion of carboxymethyl anions which produced starch derivatives swelling when exposed to water, hence the disintegration was prolonged.

10.2 Lactose tablets

The disintegration times of lactose tablets containing various disintegrant were shown in Figure 63. The disintegration times of the lactose tablets were less affected by the disintegrant. This was due to the soluble nature of lactose which tended to produce tablets dissolved from the outside inward rather than disintegrate rapidly (Kalidindi and Shangraw, 1982).

10.3 Erythromycin stearate tablets

10.3.1 Effect of the extents of MTS disintegrant on disintegration time of erythromycin stearate tablets.

Erythromycin stearate was selected as a model drug of disintegration study due to its hydrophobicity and its difficulty to disintegrate when compressed in tablet forms.

Sodium carboxymethyl starch appeared to be most effective at levels between 4% and 8% (Shangraw, et al., 1984). Therefore, to study the

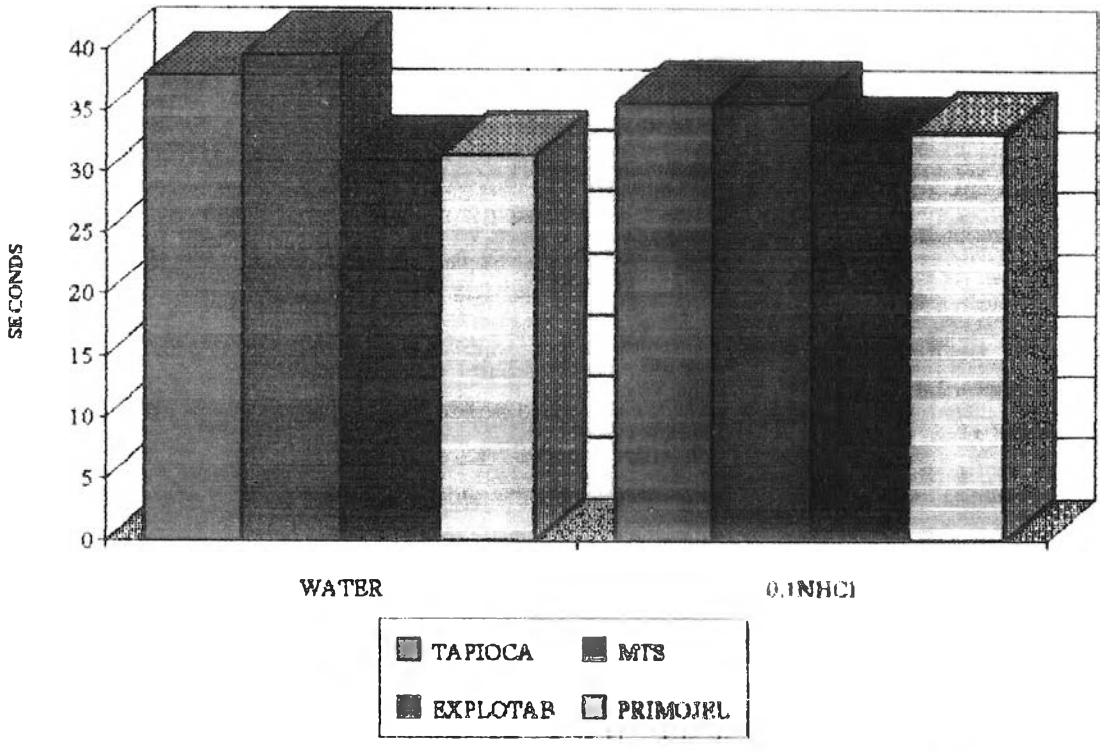


Figure 63 Disintegration Times of Lactose Tablets Containing 4% Various Disintegrant.

effect of the extents of MTS on disintegration times, the erythromycin stearate tablets were prepared by using the MTS as disintegrant concentration of 2,4,6,8 and 10%.

The effect of extent of MTS as disintegrant on disintegration times of erythromycin stearate tablets were shown in Figure 64. It was found that increased concentration of MTS disintegrant, the disintegration times decreased. At the concentration of 8% MTS and 10% MTS, the disintegration times of erythromycin stearate tablets were less than 30 minutes. Hence, to compare the efficiency of MTS as tablet disintegrant to the other ones, the erythromycin stearate tablets containing 8% MTS, 8% Explotab^{R}, 8% Primojel^{R}, 8% Polyplasdone^{R} XL and 8% Ac-Di-Sol^{R} were prepared. Shangraw, et al. (1984) suggested that sodium carboxymethyl starch (Explotab^{R} and Primojel^{R}) appeared to be most effective at levels between 4% and 8%. Levels above 8% generally resulted in increased disintegration times, possibly due to viscosity producing effects.

Figure 65 demonstrated the effect of 8% various disintegrants : MTS, Explotab^{R}, Primojel^{R}, Polyplasdone^{R}XL and Ac-Di-Sol^{R} on disintegration time of erythromycin stearate tablets, at the same level of hardness(15-17 kp). The tablets containing 8% MTS as disintegrant provided the shortest disintegration times. The disintegration times were ranked as the following : MTS (21.72 $\pm$ 0.25 min) < Ac-Di-Sol^{R} (27.38 $\pm$ 0.54 min) < Polyplasdone^{R}XL (34.28 $\pm$ 0.35 min) < Primojel^{R} (42.05 $\pm$ 1.07 min) < Explotab^{R} (48.44 $\pm$ 0.37 min).

10.3.2 Effect of particle size on disintegration times of erythromycin stearate tablets.

Modrzejewski and Wochna (1965) have investigated the swelling power of tablet disintegrant. They concluded that the swelling of the

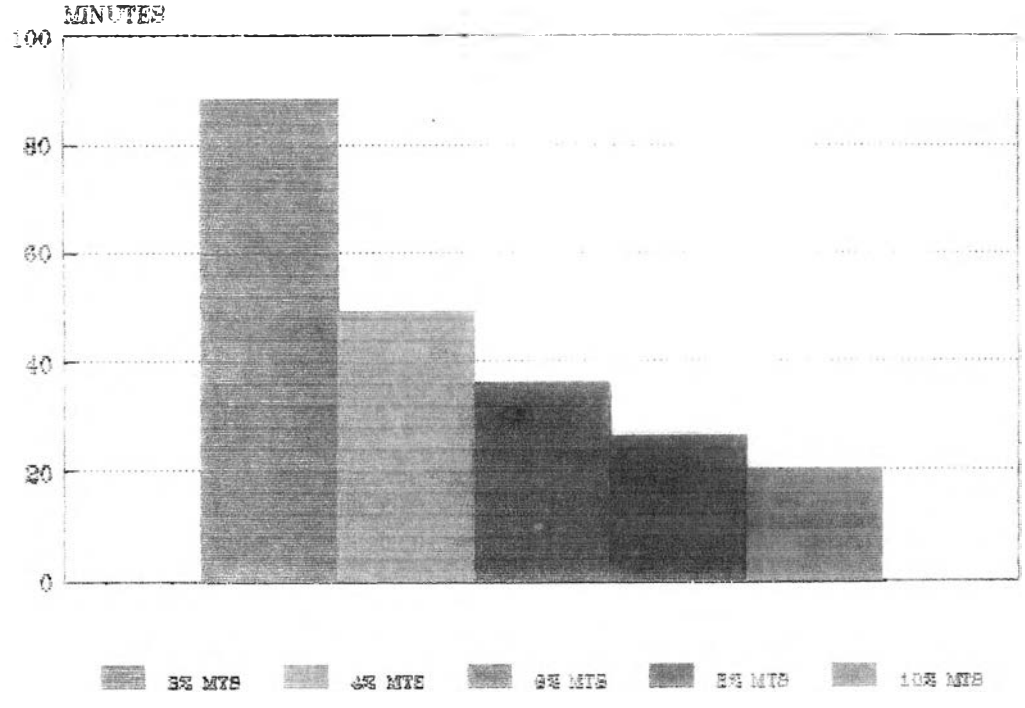


Figure 64 Effect of MTS Concentration on Disintegration Times of Erythromycin Stearate Tablets.

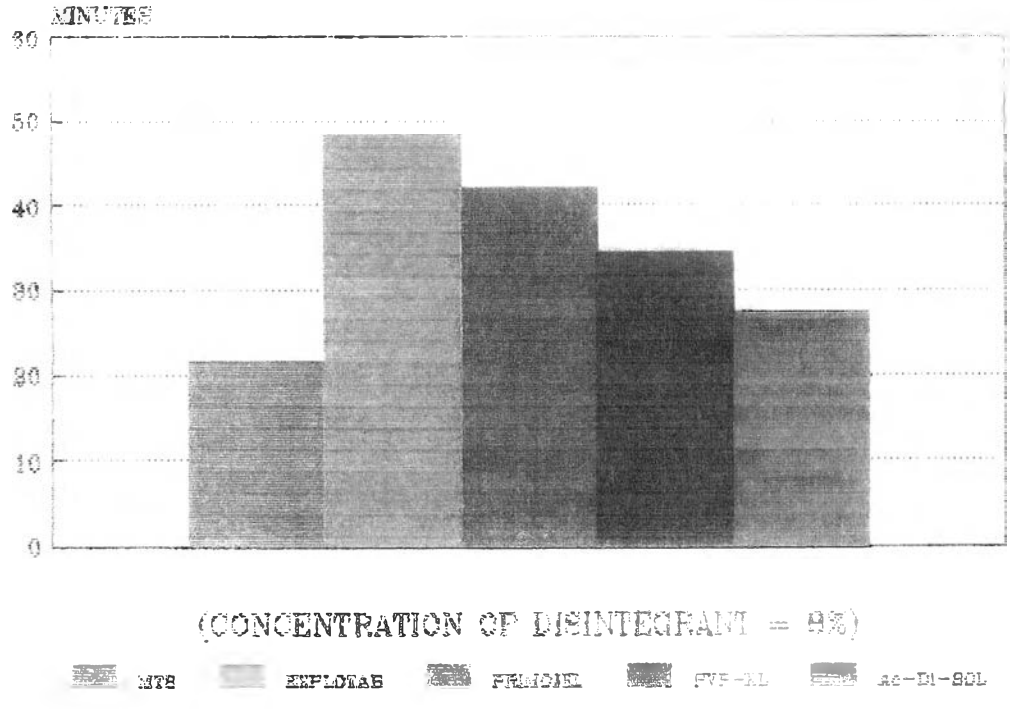


Figure 65 Disintegration Times of Erythromycin Stearate Tablets Using 8 % Various Disintegrants.

smaller grains was stronger, and that of the larger one was weaker. Probably, water penetrated more easily into the smaller grain and pushed apart the carbohydrate chain.

Sakr and Elsabbagh (1976) reported that for guar gum a finer grade of material was a better disintegrant than was a coarse grade. Those findings were especially valid when relatively low levels of guar gum were used.

Studies of the utility of crosslinked polyvinylpyrrolidone as tablet disintegrant by Rudnic et al. (1980). They found that as the particle size of crosslinked polyvinylpyrrolidone was increased, disintegrant activity, dissolution, and flow properties were enhanced.

Paronen, Juslin and Kasnanan (1985) have evaluated xylan and some commercial materials as disintegrant in tablets. They suggested that the swelling of Avicel[R] was rather small and it appeared especially in large particle of Avicel[R].

However, Rudnic et al. (1982) pointed out the rate and extent of intrinsic swelling of sodium starch glycolate were dependent upon particle size. They found the larger particles swelled to a great extent and at a faster rate than did the finer particles. They also found a noticeable correlation between the rate of swelling and the amount of water uptake for the sodium starch glycolate. They postulated that particle size played a important role in overall efficiency of commercial source of sodium starch glycolate.

To verify the effect of particle size of MTS as disintegrant on disintegration characteristic of erythromycin stearate tablets, the tablets containing 8% MTS of various particle sizes (30, 60 and 80 meshes) have been prepared. The result of the effect of particle size on disintegration times was demonstrated in Figure 66. The disintegration times of erythromycin stearate tablets decreased as the particle size of MTS decreased. This can be

attributed that the smaller particle size of disintegrant could be distributed evenly in the tablet matrix with a large surface area, hence when the tablets exposed to water the rapid water uptake and then the rapid disintegration took place. Figure 66, it was found that decreased in particle size, the disintegration times decreased.

Conclusions

Comparative studies of physico-chemical properties of modified tapioca starch and other commercial modified potato starches (Explotab^R and Primojel^R). It was indicated that modified tapioca starch showed the physico-chemical properties better than modified potato starch included rate of water uptake, bulk swelling, hydration capacity, cold water soluble, sodium chloride content and percent compressibility. Furthermore, the sedimentation volume, viscosity and sorption isotherm of modified tapioca starch, Explotab^R and Primojel^R more closely resembled. In addition, modified tapioca starch showed a better disintegrant properties than Explotab^R and primojel^R in dicalcium phosphate tablets. Both the extent and particle size of modified tapioca starch used as tablet disintegrant affected disintegration time of erythromycin stearate tablets. Modified tapioca starch exhibited a disintegrant properties superior over the other commercial modified potato starch, Explotab^R and Primojel^R, in slightly water soluble and hydrophobic tablet systems such as dicalcium phosphate and erythromycin stearate.

In conclusion modified tapioca starch was the excellent disintegrant for the slightly water soluble tablet systems at the concentration of 4-8%.

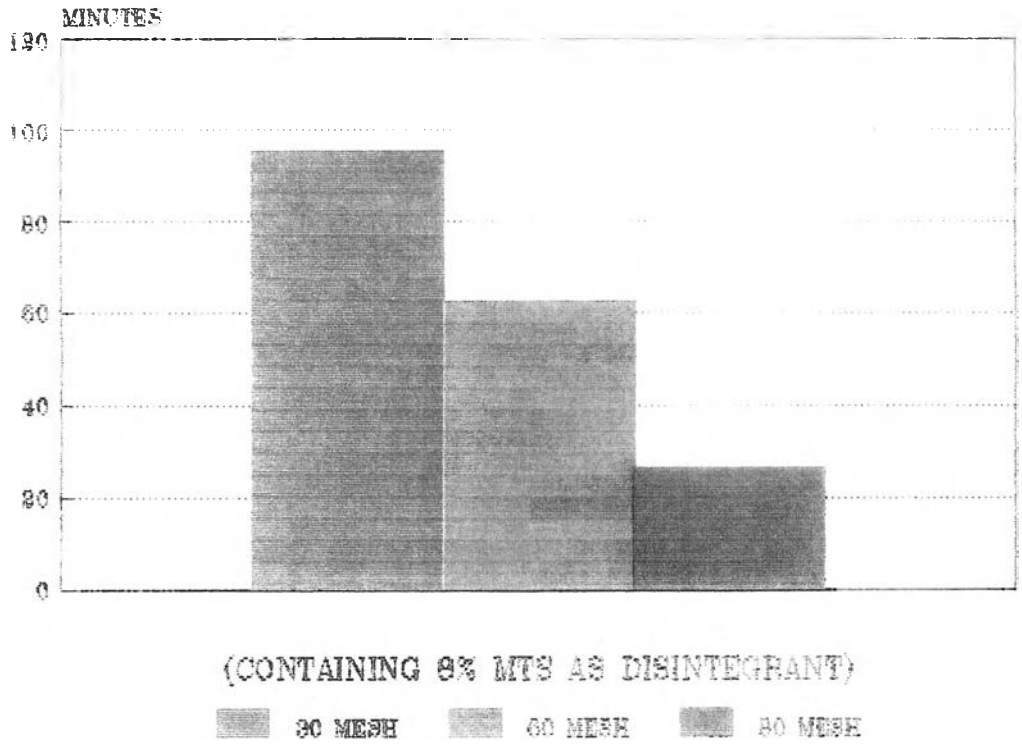


Figure 66 Effect of Particle Sizes on DT of Erythromycin Stearate Tablets Using 8 % MTS as Disintegrant.