# Chapter III

# Results

## Preparation of Modified Rice Starch

Modified rice starch was respectively prepared by deproteinization, crosslinking and spray drying processes. These processes were in accordance with the report by Siriyos Timaroon (1994) as follows.

Deproteinization time of rice starch : 4 hrs

Crosslinking time : 6 hrs

Spray drying condition :

Concentration of dispersion : 50 % W/W

Inlet air temperature : 130 $^{0}$C

Atomizing air pressure : 3.0 bar

Feed rate : 11.5 ml/min

The deproteinization could reduce the protein content of rice starch from 8.75 % to 1.87 %. The crosslinking reaction was processed for 6 hrs to give a degree of crosslinking of 14,560 as depicted in Table 6. Finally, modified rice starch obtained from spray drying process composed of aggregates of rice starch grains in the form of irregular particles.

## Detection of Phosphate and Crosslinking Reaction in Modified Rice Starch

### 1. Percent Phosphate

The percentage of phosphate, degree of substitution and degree of crosslinked in modified rice starch by absorption spectrophotometry are presented in Table 6

Table 6 Phosphate content in modified rice starch

| % Phosphate ($\times 10^{3}$) | Degree of Substitution ($\times 10^{5}$) | Degree of Crosslinking |
|---|---|---|
| 4.02 | 6.86 | 14,560 |

### 2. Differential Scanning Calorimetry

DSC properties of all starch products are compared in Figure 6 and Table 7. The enthalpy change for native rice starch and deproteinized rice starch began at 60.6 $^{0}$C and 62.9 $^{0}$C and gave an endothermic peak at 74.5 $^{0}$C and 75.0 $^{0}$C, respectively. The endotherm area (the enthalpy of the system) of deproteinized rice starch was higher than that of native rice starch. The thermograms of modified rice starch and crosslinked rice starch showed the beginning of enthalpy change at 64.6 $^{0}$C and 65.7 $^{0}$C and endothermic peak at 76.3 $^{0}$C and 77.6 $^{0}$C, respectively. The endotherm area of modified rice starch was less than that of crosslinked rice starch. The endotherm area decreased in the following order: deproteinized rice starch > native rice starch > crosslinked rice starch >modified rice starch.

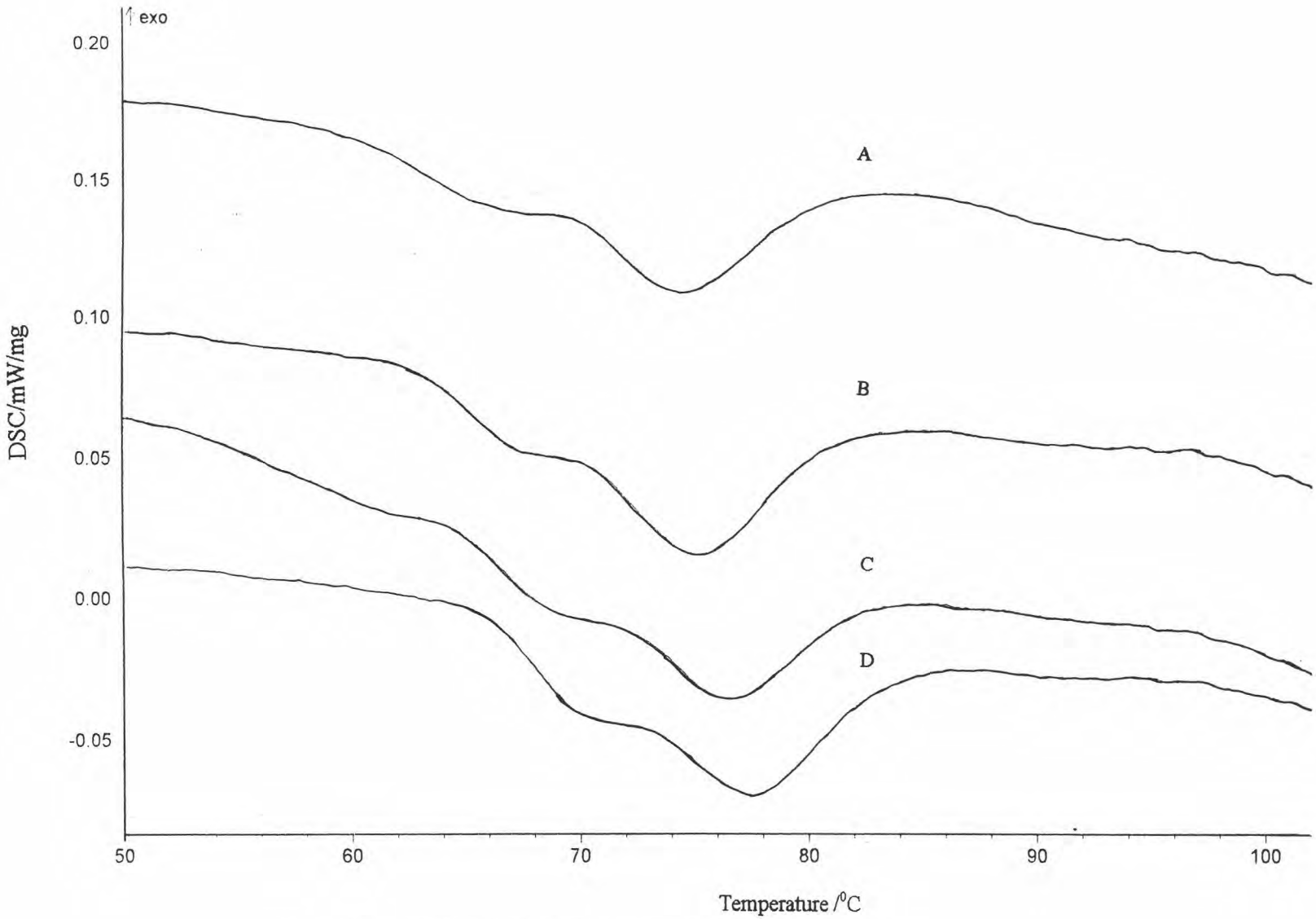



Figure 6 DSC thermogram of various rice starch

A = Native rice starch B = Deproteinized rice starch

C = Modified rice starch D = Crosslinked of deproteinized rice starch

Table 7 Gelatinization characteristics of various starch

| Starch | $T_0$ ($^0$C) | Tp ($^0$C) | ΔH (cal/g) |
|---|---|---|---|
| Natve rice starch | 60.6 | 74.5 | 2.840 |
| Deproteinized rice starch | 62.9 | 75.0 | 3.034 |
| Crosslinked rice starch | 65.7 | 77.6 | 2.747 |
| MDRS | 64.6 | 76.3 | 2.653 |

$T_0$ = Gelatinization temperature

Tp = Peak temperature

ΔH = Enthalpy of system

### 3. Powder X-ray Diffraction

The X-ray diffractograms of native rice starch, deproteinized rice starch, sodium trimetaphosphate, physical mixture of deproteinized rice starch and sodium trimetaphosphate, crosslinked rice starch as well as modified rice starch are presented in Figure 7.

The diffraction pattern of native rice starch was similar to that of deproteinized rice starch. Both native rice starch and deproteinized rice starch gave amorphous and crystalline characters, which was contrast to the pattern of sodium trimetaphosphate which contained crystalline pattern. The peak pattern of physical mixture was actually resulted from the combined peak patterns of deproteinized rice starch and sodium trimetaphosphate. For crosslinked rice starch, the pattern was rather different from that of the physical mixture and sodium trimetaphosphate. The peak pattern of modified rice starch was not different from that of

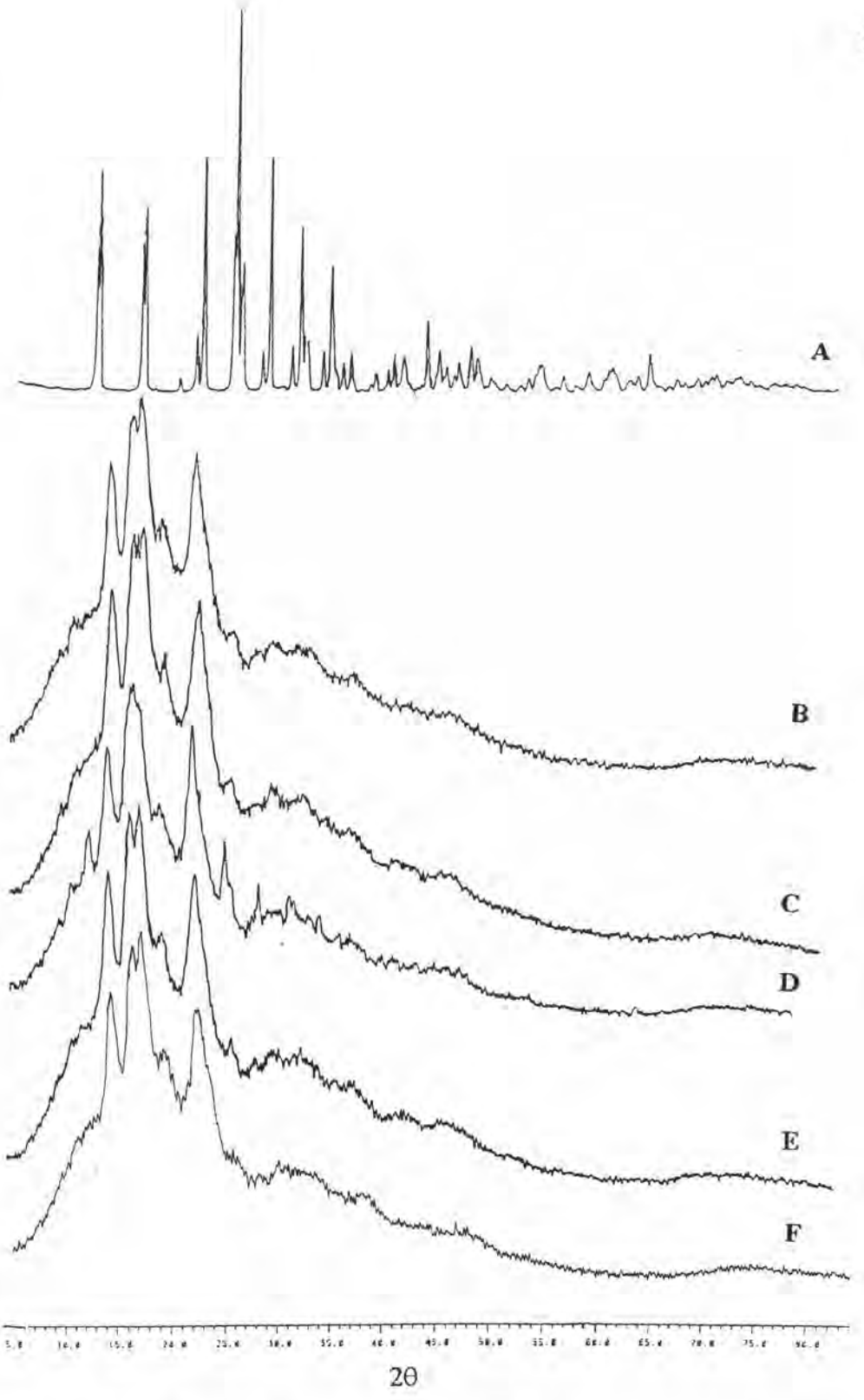



Figure 7 Comparision of X-ray diffractogram

A = Sodium trimetaphosphate
B = Native rice starch
C = Deproteinized rice starch
D = Physical mixture of sodium trimetaphosphate and deproteinized rice starch
E = Crosslinked of deproteinized rice starch
F = Modified rice starch

crosslinked rice starch.

**4. Viscosity**

The viscosity curve of native rice starch is presented in Figure 8. It was about 15 B.U. at room temperature (25 $^{0}$C). It did not change until the temperature increased to 81.9 $^{0}$C. When the temperature reached 83.1 $^{0}$C, the viscosity began to rise gradually to 80 B.U. and then increased immediately to the peak at 960 B.U. at 93.6 $^{0}$C. It decreased gradually to 735 B.U. at 82.7 $^{0}$C of cooling cycle and rose continuously without peak until the end of cooling cycle. At the end of cooling cycle, the viscosity was 1,520 B.U.

When rice starch was deproteinized for 4 hrs, the viscosity curve was similar to that of the native rice starch. The viscosity remain unchanged at 20 B.U. from 25 $^{0}$C to 73.1 $^{0}$C. It increased gradually to 80 B.U. at 76.2 $^{0}$C during heating cycle. It increased steeply to the peak at 980 B.U. at 88.2 $^{0}$C and decreased slowly to 420 B.U. at the end of holding cycle. The viscosity curve began to rise again during the cooling cycle and it reached to 1,780 B.U. at 50 $^{0}$C.

When rice starch was deproteinized and crosslinked, the viscosity curve showed a different curve from previously mentioned. The viscosity remain unchanged at 20 B.U. after heating and holding cycles. It increased slightly to 35 B.U. and was stable at this point until the end of cooling cycle.

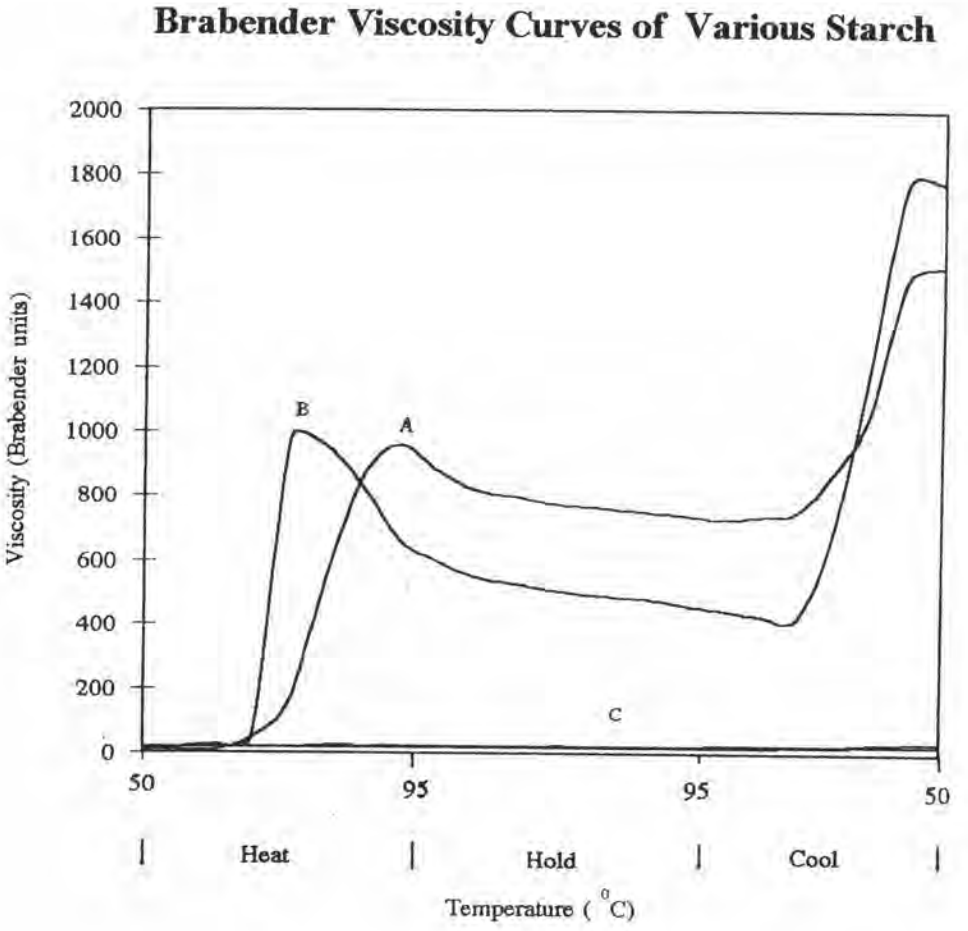



Figure 8 Brabender viscosity curve of various rice starch.

A = Native rice starch

B = Deproteinized rice starch

C = Crosslinked of deproteinized rice starch

## Properties of Modified Rice Starch

Investigation of properties of modified rice starch according to USP XXIII specification was carried out. All of these data were summarized in Table 8. Although modified rice starch dispersed in boiling water was not formed a translucent or whitish jelly, it obtained reddish violet dispersion as conformed to pharmacopoeia. The pH value of the supernatant liquid of modified rice starch was 7.0. Loss on drying was about 4.91 %. In the case of the residue on ignition, the percentage of ash was 0.3775. The tests of iron, oxidizing substance and sulfur were well with in the standard limit. For microbial limit test, modified rice starch met the requirements of the tests for absence of *Salmonella sp.* and *Escherichia coli.*

Table 8 Properties of modified rice starch according to USP XXIII

| Specification | USP Standard Limit | Modified Rice Starch Test |
|---|---|---|
| Identification | | |
| - reddished violet to blue | + | + |
| - translucent, whitish jelly | + | - |
| pH | 4.5-8.0 | 7.0 |
| Loss on drying | 14.0 | 4.914 |
| Residual on ignition | 0.5 | 0.3775 |
| Iron | 0.002 | <0.002 |
| Oxidizing substance | 0.002 | <0.002 |
| Sulfur | 0.008 | <0.008 |
| Microbial limit (*Samonella Species, Escherichia coli)* | conform | conform |

## Evaluation of Physical Properties of Modified Rice Starch Compared with Commercial Diluents

### 1. Powder Morphology

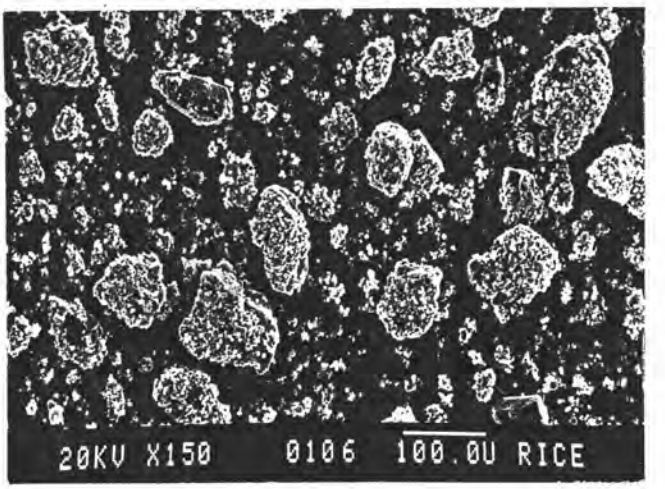
Figure 9 shows the scanning electron photomicrographs of native rice starch powder at different magnifications. It was seen as irregular shape particles with vary sizes at low magnification (X150). Higher magnification (X500 and 3,600) revealed that they were the aggregates of rice starch granules ranging from a few granules to many thousands. When native rice starch was deproteined for 4 hrs before crosslinked for 6 hrs as well as spray-dried at proper condition, modified rice starch obtained were so similar to the product from native rice starch (Figure 10).

Era-Tab$^{R}$ (Figure 11) composed almost entirely of aggregates of rice starch grains in the form of spheres. Starch 1500$^{R}$ (Figure 12) was presented in form of agglomerate but it had a somewhat smooth surface compared to other diluents in this study. The shapes of particles were irregular and the sizes varied widely. Avicel PH 102$^{R}$ (Figure 13) constituted of large agglomerated form and a few short rod fibers. Emcompress$^{R}$ (Figure 14) existed as agglomerates of crystallites.

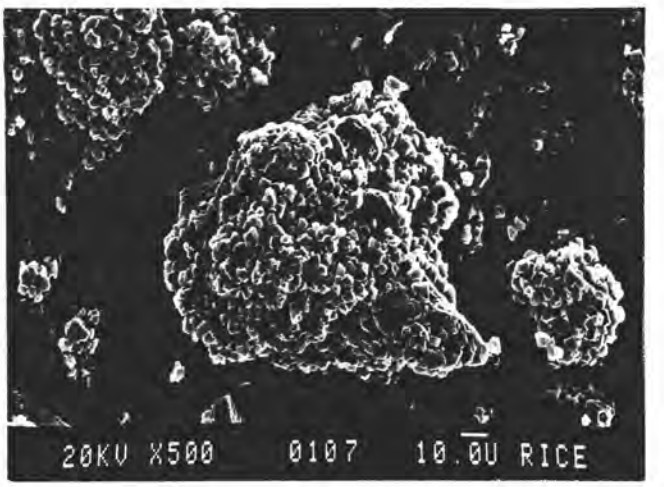
### 2. Particle Size Distribution

The particle size distribution of modified rice starch and commercial diluents are shown in Table 28 (see Appendix II) and depicted in Figure 15. $D_{50}$ of modified rice starch and other diluents are

A




B




C

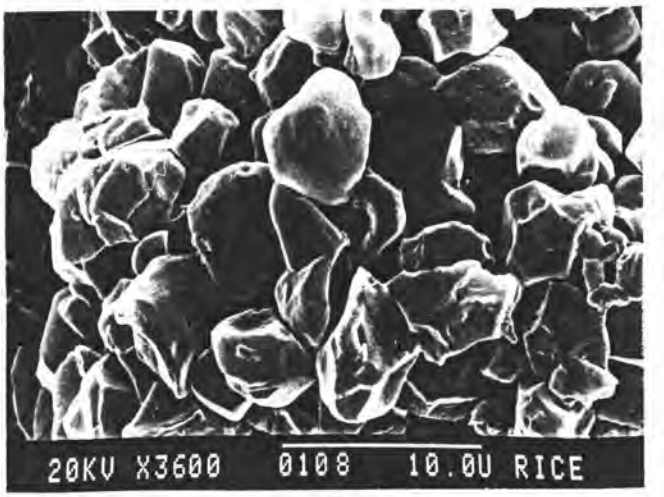
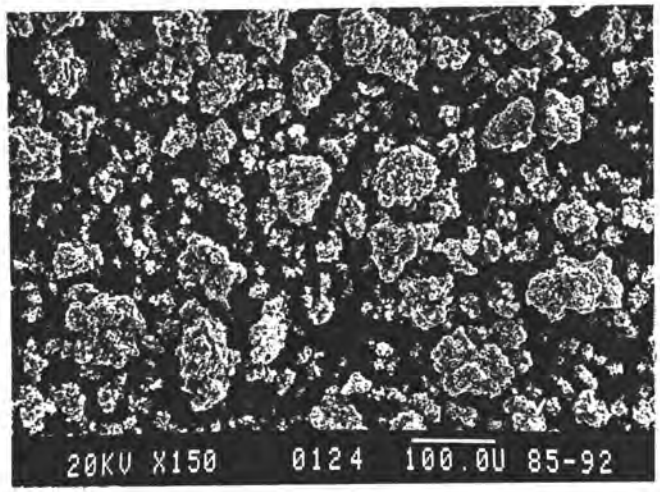
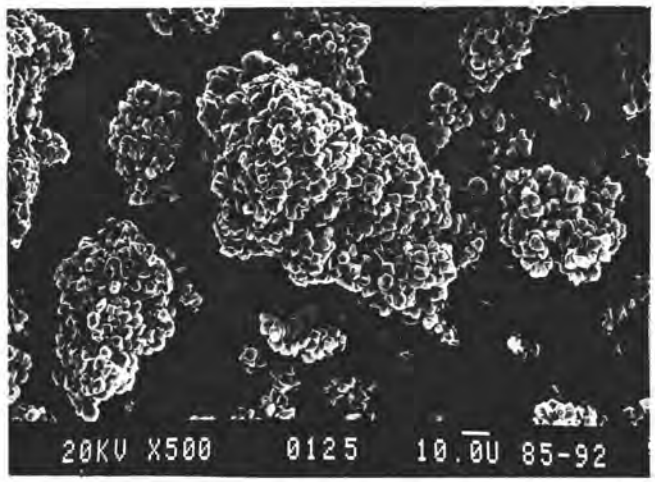



Figure 9 Scanning electron micrographs of native rice starch
( A x 150 , B x 500 , C x 3,600 )

A




B




C

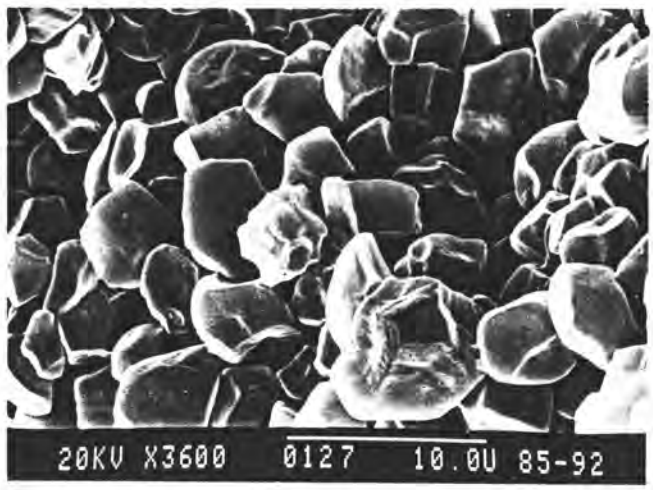
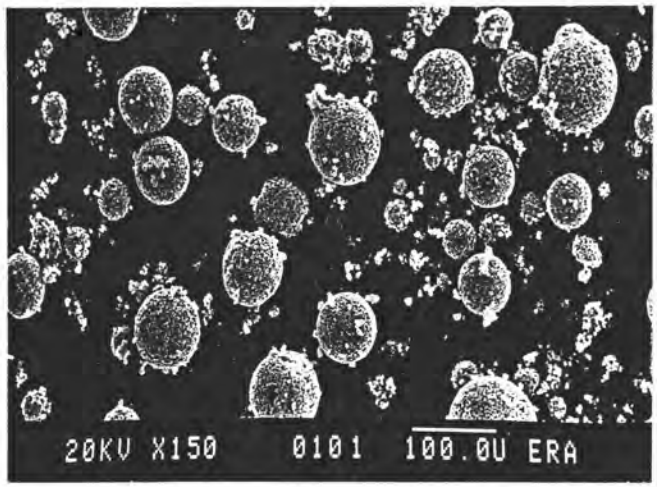
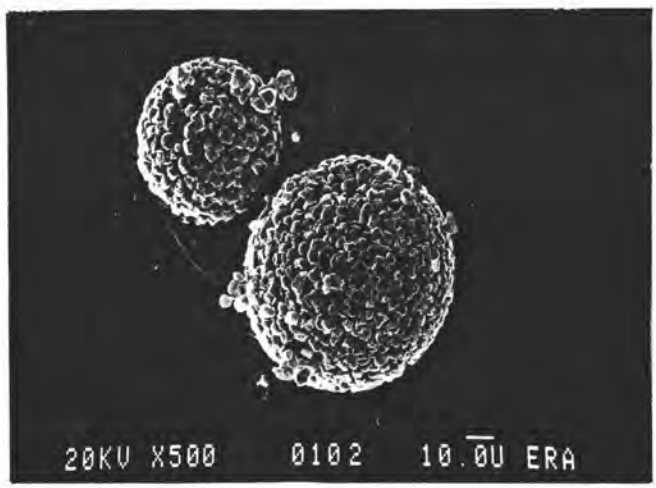



Figure 10 Scanning electron micrographs of modified rice starch
( A x 150 , B x 500 , C x 3,600 )

A




B

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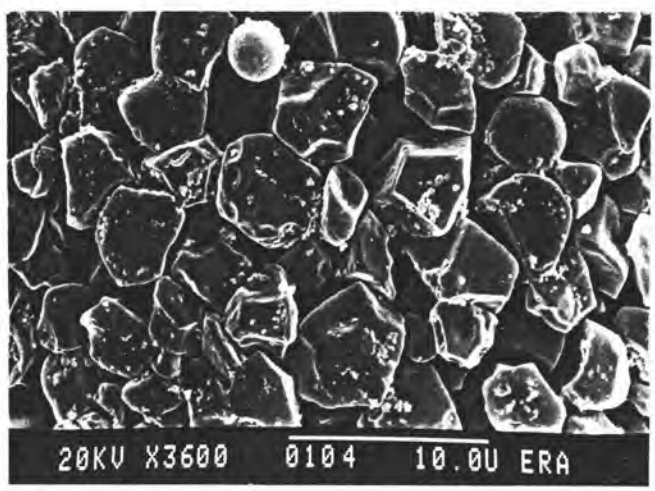
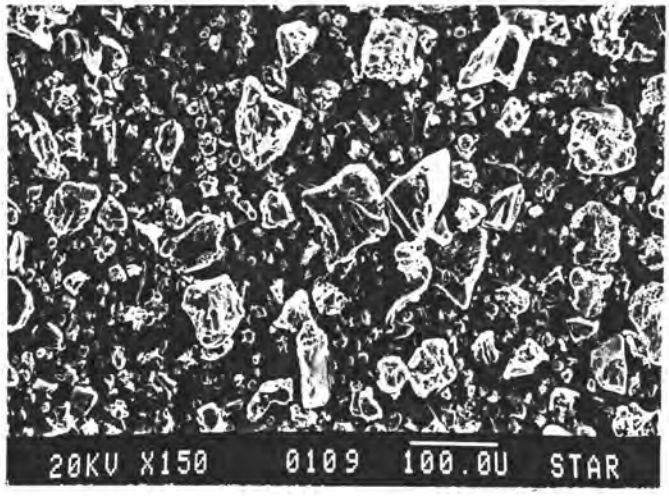


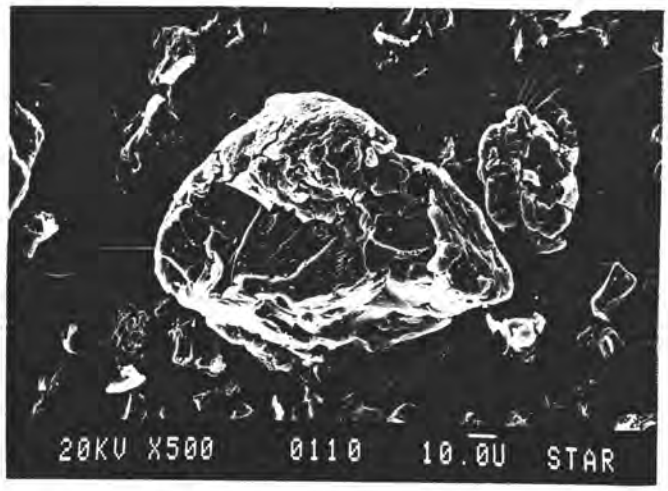

Figure 11 Scanning electron micrographs of Era-Tab$^{R}$

( A x 150 , B x 500 , C x 3,600 )

A




B

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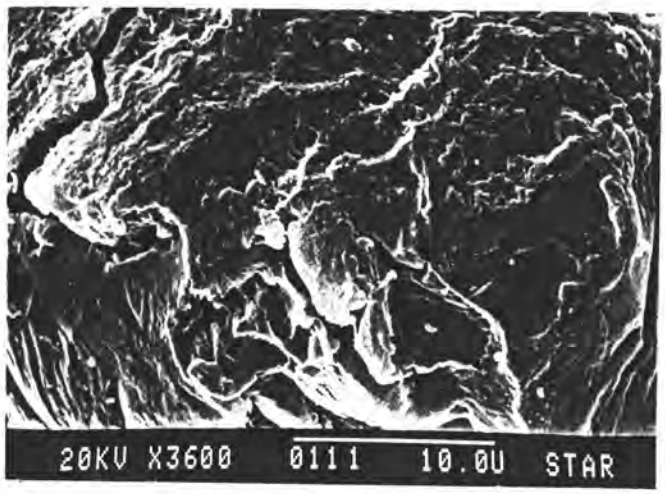
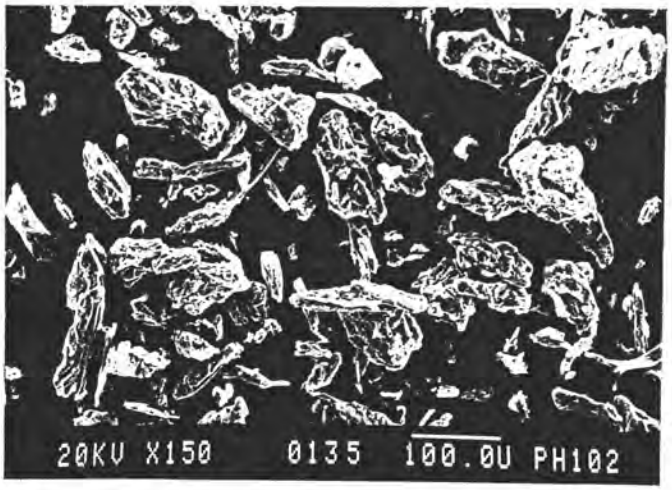


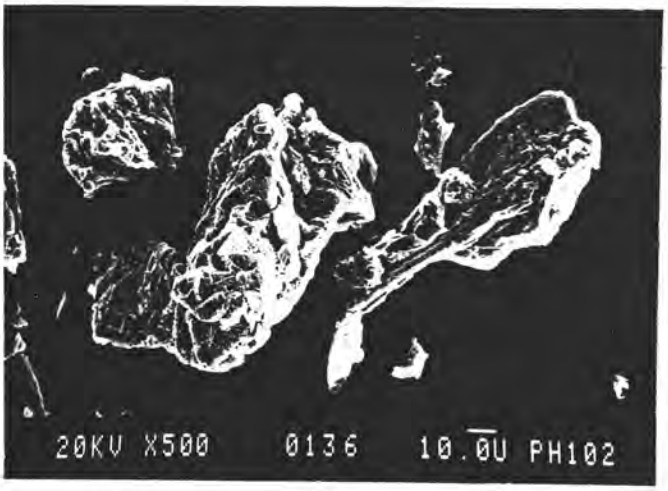

Figure 12 Scanning electron micrographs of Starch 1500$^{R}$

( A x 150 , B x 500 , C x 3,600 )

A




B




C

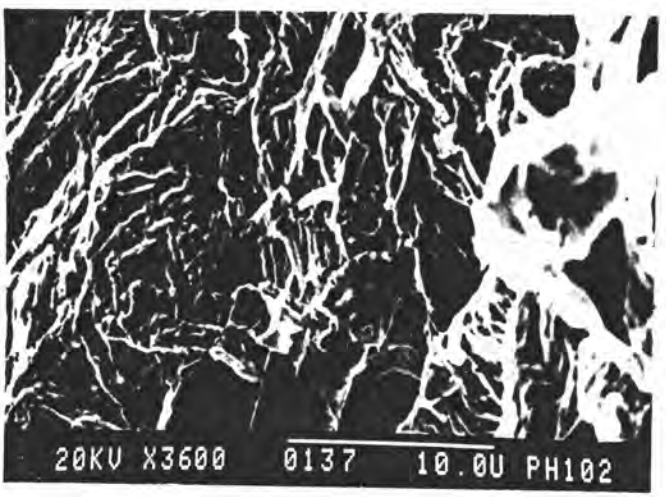
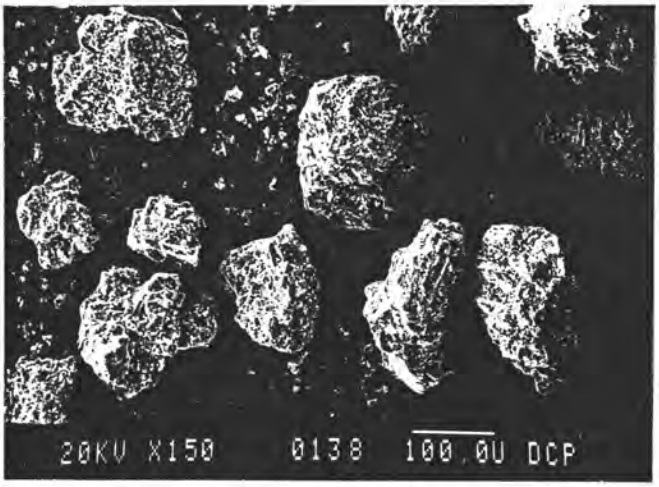


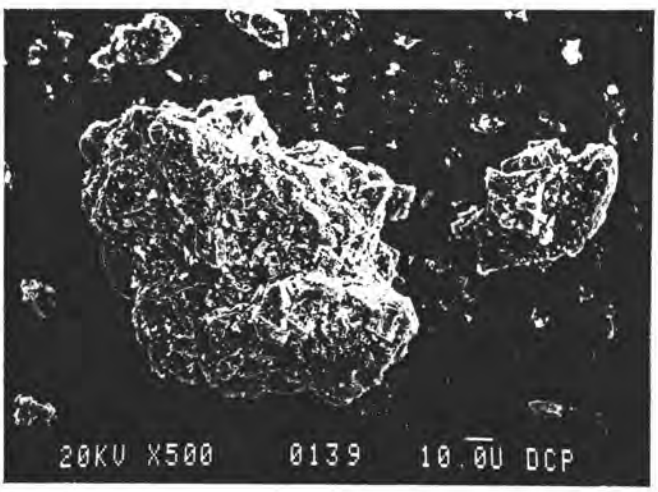

Figure 13 Scanning electron micrographs of Avicel PH 102$^{R}$

( A x 150 , B x 500 , C x 3,600 )

A




B




C


Figure 14 Scanning electron micrographs of Emcompress$^{R}$

( A x 150 , B x 500 , C x 3,600 )

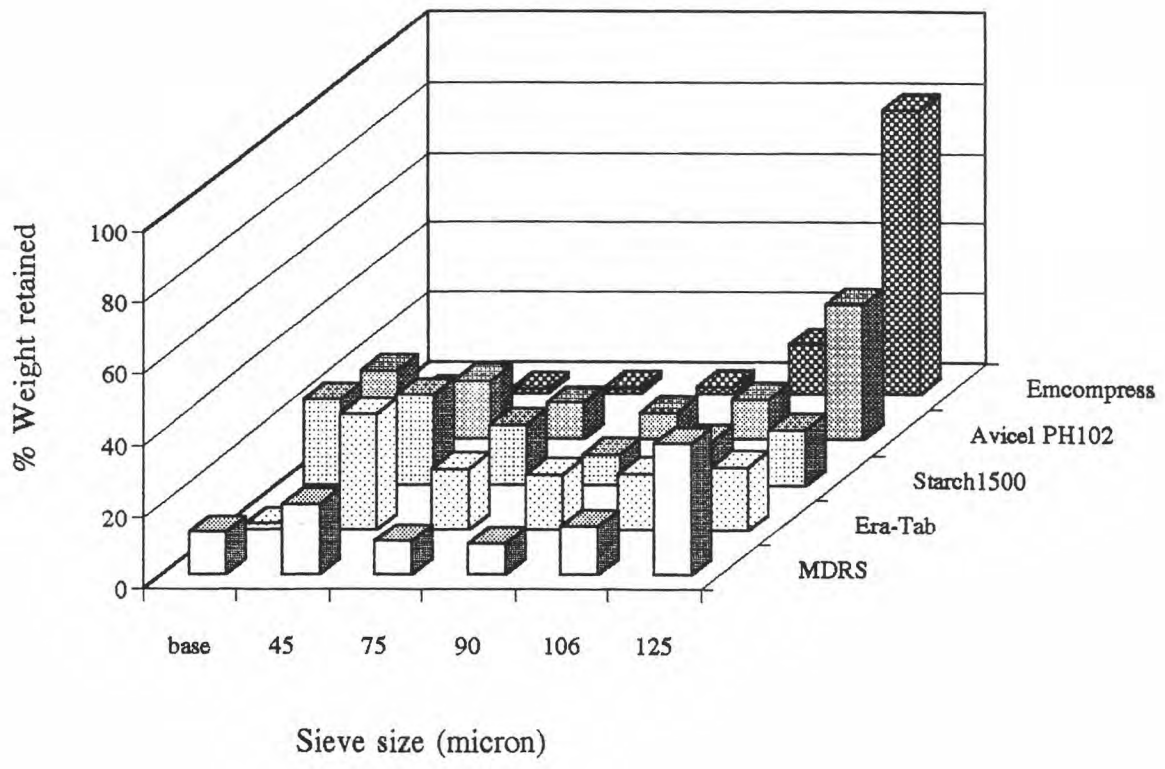



Figure 15 Particle size distribution of MDRS and various diluents

shown in Table 9. Value of cumulative % frequency undersize were transferred into Z value (standard) which presented in Table 29 (see Appendix II) and illustrated versus particle size in Figure 62 (in Appendix II). $D_{50}$ decreased in the following orders: Emcompress$^R$ > Avicel PH 102$^R$ > Modified rice starch > Era-Tab$^R$ > Starch 1500$^R$.

Table 9 Geometric mean diameter of various diluents and MDRS

| Diluents | $D_{50}$* (micron) |
|---|---|
| MDRS | 102.65 |
| Era-Tab | 90.06 |
| Starch 1500 | 73.2 |
| Avicel PH 102 | 105.5 |
| Emcompress | 229.67 |

$D_{50}$* = Geometric mean diameter

**3. Bulk Density, Tapped Density and % Compressibility**

The results of bulk density, tapped density and % compressiblity are shown in Figure 16-18 and in Table 10. Bulk density of these diluents were ranked in the following order: Emcompress$^R$ > Starch 1500$^R$ > Era-Tab$^R$ > Modified rice starch > Avicel PH 102$^R$. Tapped density decreased in the following orders: Emcompress$^R$ > Starch 1500$^R$ > Era-Tab$^R$ > Modified rice starch > Avicel PH 102$^R$. The % compressibility decreased in the following orders: Avicel PH 102$^R$ > Starch 1500$^R$ > Modified rice starch > Era-Tab$^R$ > Emcompress$^R$. The statistical differences ($p < 0.05$) are shown in Table 30-35 (Appendix V).

Table 10 Physical properties of various diluents and MDRS powders

| Diluents | Physical Properties of Powders (±SD) | | | | | |
|---|---|---|---|---|---|---|
| | Moisture Content (%) | Angle of Repose ( degree) | Flow Rate (g/sec) | Bulk Density (g/ml) | Tapped Density (g/ml) | Compressibility (%) |
| MDRS | 9.47 (0.135) | 23.47 (0.897) | 9.31 (0.125) | 0.442 (0.005) | 0.549 (0.011) | 19.49 (1.135) |
| ERA-Tab | 12.15 (0.150) | 22.45 (1.312) | 11.85 (0.811) | 0.498 (0.007) | 0.604 (0.003) | 17.55 (1.059) |
| Starch 1500 | 7.99 (0.480) | 27.95 (0.613) | * | 0.608 (0.009) | 0.782 (0.006) | 22.25 (1.125) |
| Avicel PH 102 | 8.945 (0.575) | 29.82 (0.759) | * | 0.325 (0.003) | 0.444 (0) | 26.8 (0.597) |
| Emcompress | 9.965 (0.975) | 29.57 (1.329) | 16.66 (0.162) | 0.886 (0.007) | 1.046 (0.001) | 15.29 (0.816) |

* = non detectable

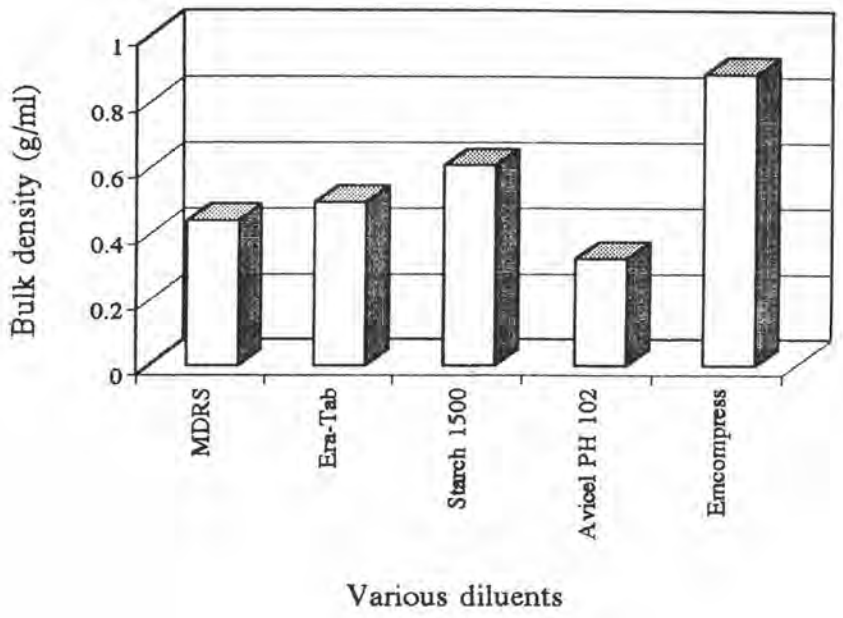



Figure 16 Bulk density of MDRS compared with various diluents

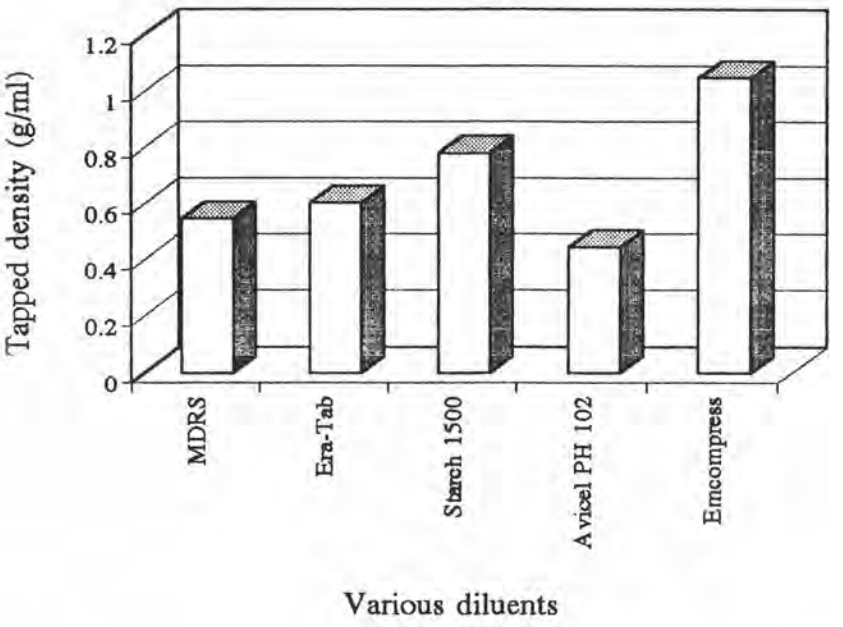



Figure 17 Tapped density of MDRS compared with various diluents

**4. Angle of Repose Determination**

Angle of repose of each diluent is presented in Figure 19 and in Table 10. They were ranked in following orders: Avicel PH 102$^R$ > Emcompress$^R$ > Starch 1500$^R$ > Modified rice starch > Era-Tab$^R$. The statistical differences are presented in Table 36 and 37 (Appendix V). It expressed that no significant differences of angle of repose were observed in the group of diluents: Avicel PH 102$^R$ and Starch 1500$^R$ , Starch 1500$^R$ and Emcompress$^R$ , Avicel PH 102$^R$ and Emcompress$^R$.

**5. Flow Rate**

Flow rate of powders are shown in Figure 20 and in Table 10. They could be ranked as follow: Emcompress$^R$ > Era-Tab$^R$ > Modified rice starch. For Avicel PH 102$^R$ and Starch 1500$^R$, the results of flow rate could not be detectable in this experiment. The statistical differences ($p < 0.05$) are shown in Table 38 and 39 (Appendix V).

**6. Moisture Determination**

Moisture Content of each diluent were calculated as percent moisture content and given in Table 10 and presented in Figure 21. They were ranked as follow: Era-Tab$^R$ > Emcompress$^R$ > Modified rice starch > Avicel PH 102$^R$ > Starch 1500$^R$. The statistical differences are illustrated in Table 40 and 41 (Appendix V). It showed that no significant differences of moisture content were observed in the group of diluents: Avicel PH 102$^R$ and Starch 1500$^R$, Avicel PH 102$^R$ and Era-Tab$^R$, Era-Tab$^R$ and Emcompress$^R$, Avicel PH 102$^R$ and Emcompress$^R$.

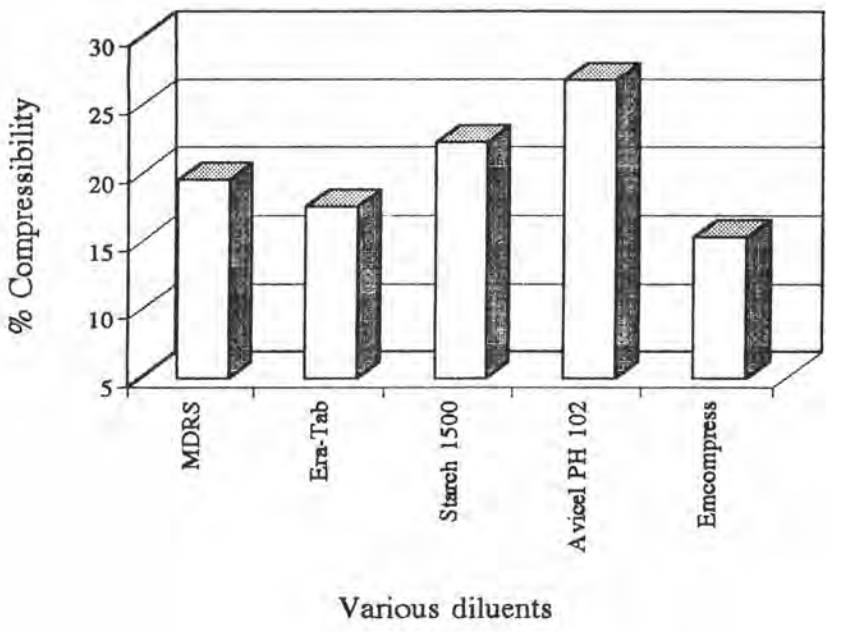



Figure 18 % Compressibility of MDRS compared with various diluents

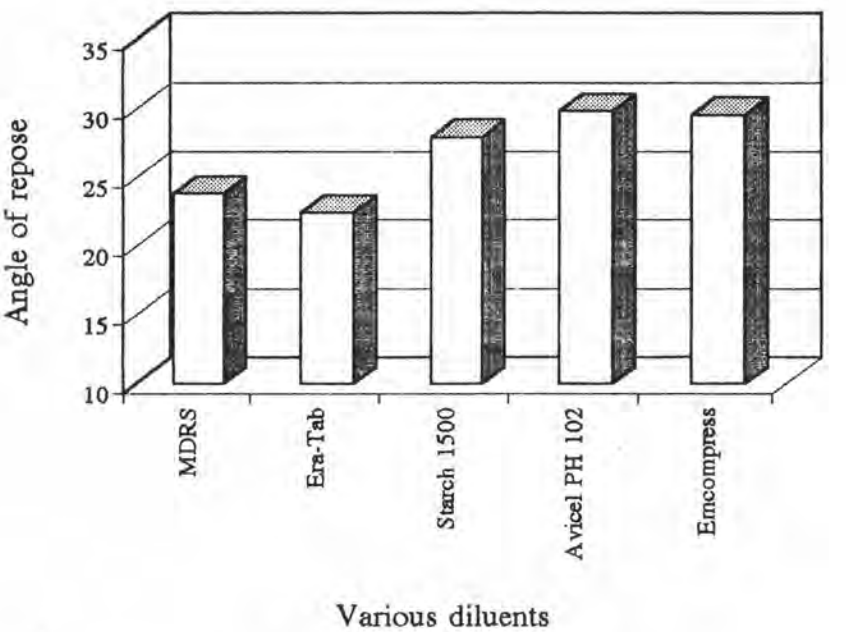



Figure 19 Angle of repose of MDRS compared with various diluents

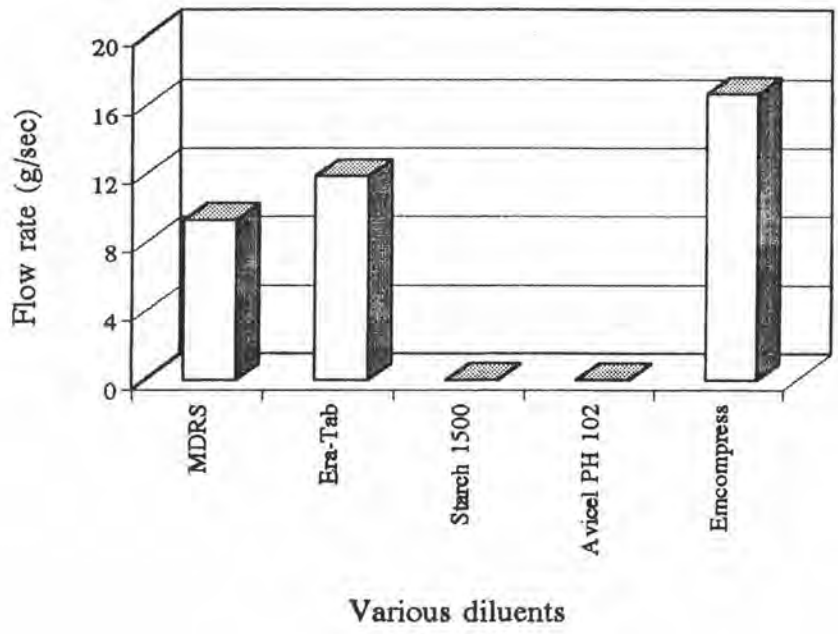



Figure 20 Flow rate of MDRS compared with various diluents

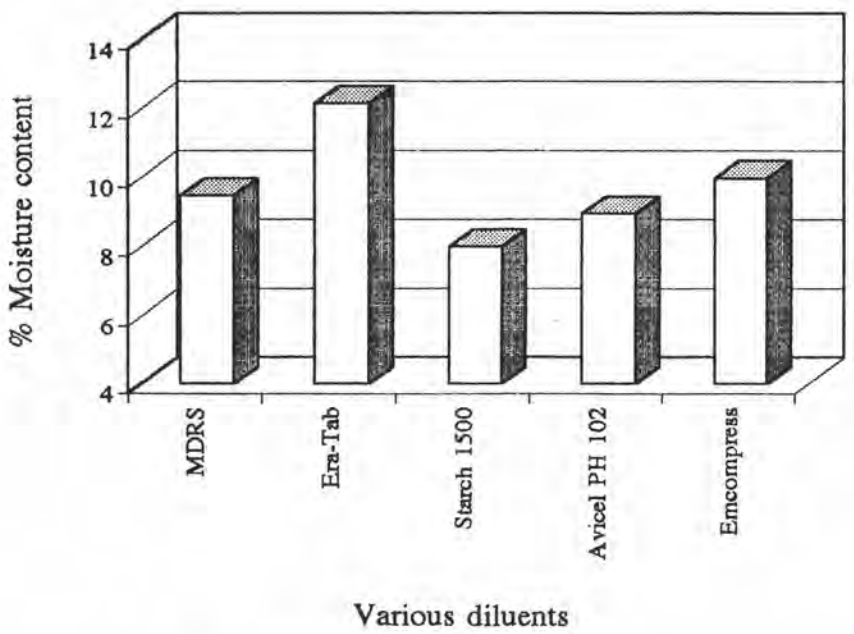



Figure 21 % Moisture content of MDRS compared with various diluents

## Tabletting Characteristics of Modified Rice Starch Compared with Commercial Diluents

The 300 mg tablets were prepared by direct compression using modified rice starch, Era-Tab$^{R}$, Starch 1500$^{R}$ and Avicel PH 102$^{R}$. Emcompress$^{R}$ was not mentioned in this section because its tablets could not be compressed adequately without lubricant. Each diluent was compressed into tablet with compression ranged from 500 upto 2,000 pounds. Avicel PH102$^{R}$ was compressed at compression forces of 500 , 600 , 700 and 800 pounds. It was due to hardness values of tablets were more than 20 kps when increasing compression forces upto 800 and more. Then, all tablets prepared from each diluent were determined for compression force-thickness profiles, compression force-hardness profiles, compression force-friability profiles and compression force-disintegration time profiles.

### 1. Compression Force-Thickness Profiles

Compression force-thickness profiles of each diluent are shown in Table 11 and Figure 22. Generally, It was found that the increase in compression force caused decrease in thickness values.

### 2. Compression Force-Hardness Profiles

Each unlubricated diluent was compacted at different compression forces into tablets and tested on crushing strength. The results presented in Table 11 and Figure 23 clearly revealed that the hardness of tablets increased as compression force increased. At compression force of 500 pounds, the average hardness of modified rice

Table 11 Physical properties of tablets prepared with commercial diluents and MDRS at different compression forces

| Diluents | Compression Force (lbs) | Physical Properties of Tablets | | | |
|---|---|---|---|---|---|
| | | TN. (mm±SD) | HN. (kp±SD) | D.T. (min±SD) | Fria. (%) |
| MDRS | 500 | 4.290 (0.083) | 4.740 (0.578) | 2:230 (0.153) | 2.036 |
| | 1000 | 3.561 (0.102) | 11.090 (1.407) | 2:320 (0.225) | 0.085 |
| | 1500 | 3.263 (0.037) | 18.811 (1.052) | 2.420 (0.057) | 0.057 |
| | 2000 | 3.129 (0.056) | >20.00 | 2:510 (0.132) | 0.049 |
| Era-Tab | 500 | 3.730 (0.022) | 2.850 (0.350) | 0:532 (0.099) | 1.638 |
| | 1000 | 3.213 (0.032) | 9.370 (0.310) | 1:355 (0.149) | 0.372 |
| | 1500 | 2.978 (0.021) | 14.760 (0.697) | 1:370 (0.417) | 0.067 |
| | 2000 | 2.905 (0.028) | 17.130 (1.224) | 2:140 (0.272) | 0.051 |

Wt. = Weight TN. = Thickness

HN. = Hardness D.T. = Disintegration time

Table 11 (cont.) Physical properties of tablets prepared with commercial diluents and MDRS at different compression forces

| Diluents | Compression Force (lbs) | Physical Properties of Tablets | | | |
|---|---|---|---|---|---|
| | | TN. (mm±SD) | HN. (kp±SD) | D.T. (min±SD) | Fria. (%) |
| Starch 1500 | 500 | 3.654 (0.023) | 2.26 (0.417) | 13:251 (0.785) | 2.954 |
| | 1000 | 3.242 (0.011) | 6.937 (0.295) | 15:281 (0.987) | 1.591 |
| | 1500 | 3.085 (0.042) | 10.812 (0.586) | 19:250 (0.857) | 1.104 |
| | 2000 | 3.017 (0.065) | 12.960 (0.941) | 22:451 (0.564) | 0.957 |
| Avicel PH 102 | 500 | 3.621 (0.028) | 12.00 (3.43) | 1:501 (0.976) | 0.876 |
| | 600 | 3.476 (0.027) | 14.133 (0.249) | 2:480 (0.978) | 0.775 |
| | 700 | 3.352 (0.012) | 16.371 (0.449) | 3.591 (1.059) | 0.598 |
| | 800 | 3.281 (0.063) | 17.500 (1.153) | 5:292 (1.002) | 0.587 |

Wt. = Weight TN. = Thickness

HN. = Hardness D.T. = Disintegration time

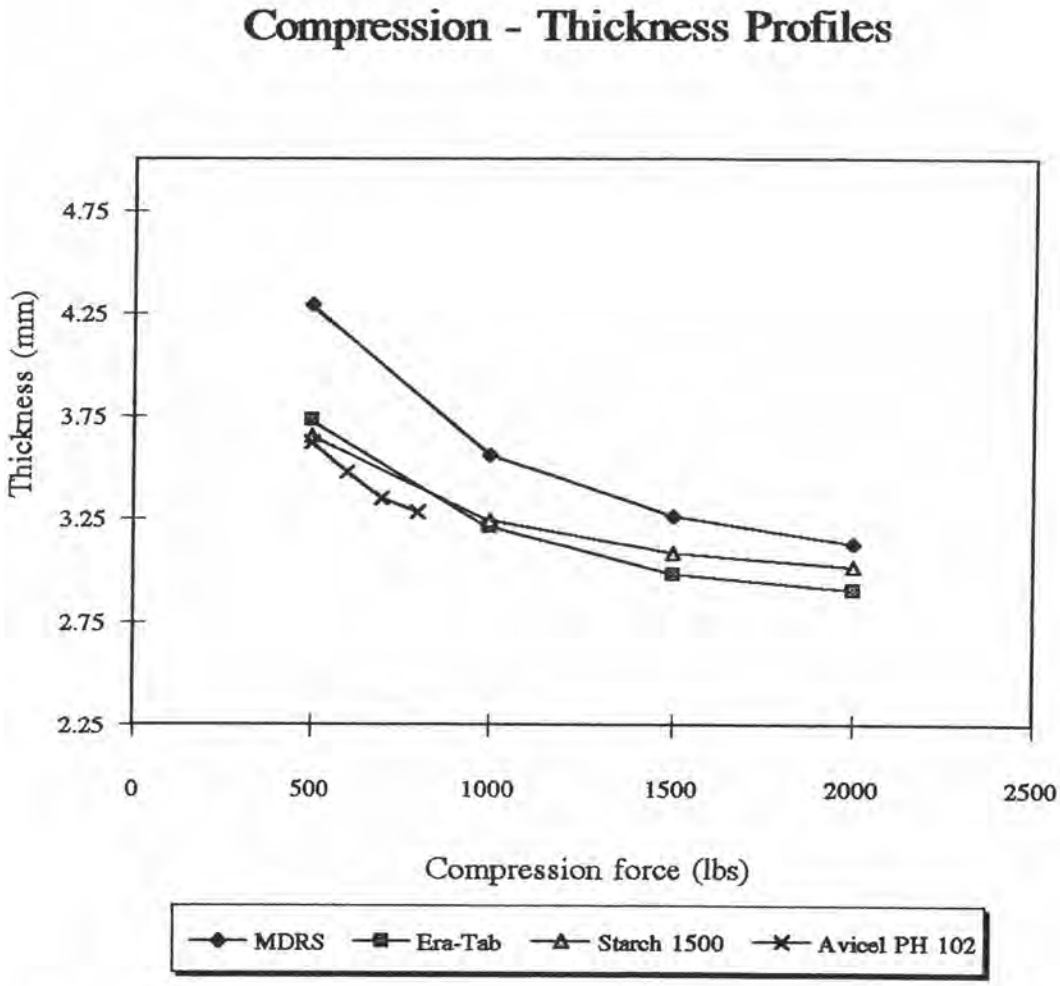



Figure 22 Comparison the compression force-thickness profiles of various diluents and MDRS

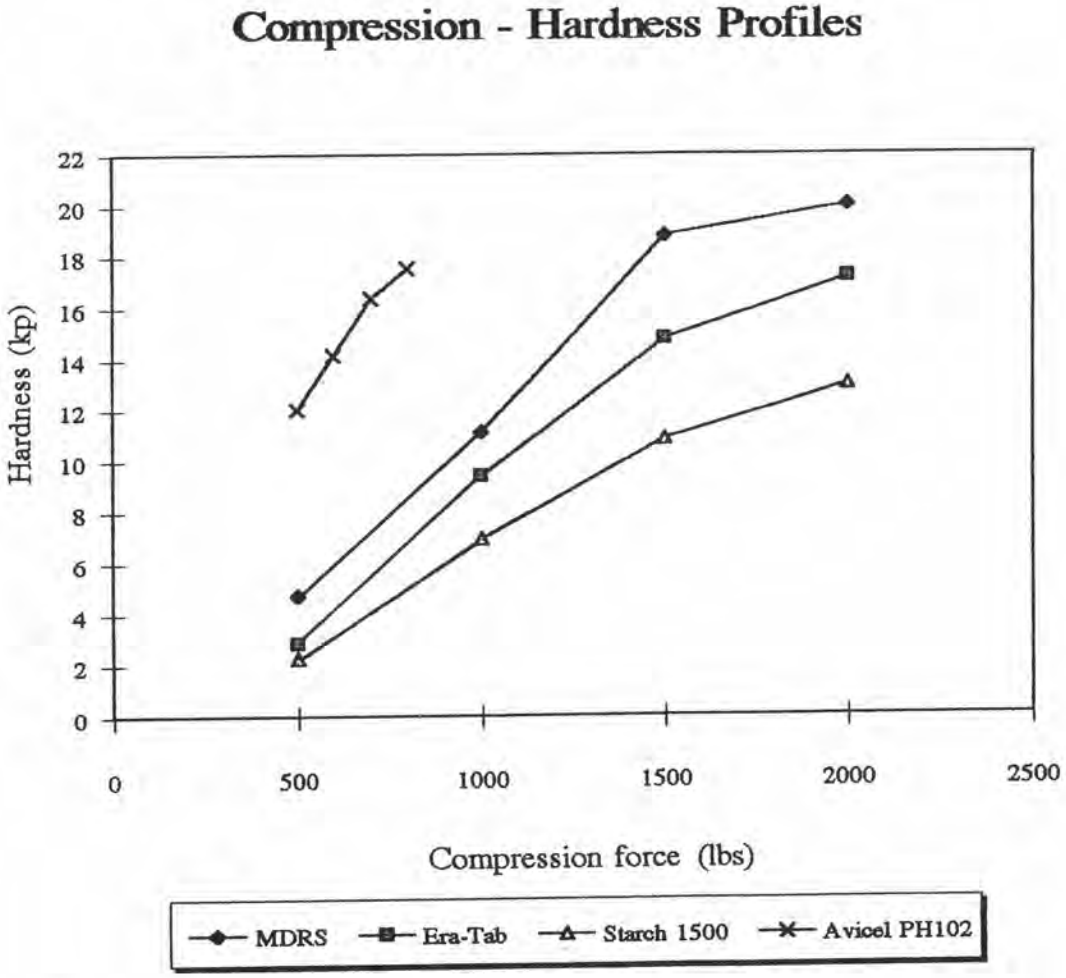



Figure 23 Comparison the compression force-hardness profiles of various diluents and MDRS

starch, Era-Tab$^R$, Starch 1500$^R$ and Avicel PH 102$^R$ were 4.74, 2.85, 2.26 and 12.00 kps, respectively. It was seen that the average hardness of Avicel PH 102$^R$ was extremely higher than other diluents at allcompression forces in this study. Modified rice starch and Era-Tab$^R$ were highly compressible. The tablet hardness were ordered as follow: modified rice starch > Era-Tab$^R$ > Starch 1500$^R$. At compression force of 2,000 pounds, the hardness of modified rice starch was more than 20 kps while hardness of Era-Tab$^R$ and Starch 1500$^R$ were 17.13 kps and 12.96 kps, respectively.

**3. Compression Force-Friability profiles**

Principally, friability of tablets decrease with increasing compression force for all diluents as illustrate in Table 11 and Figure 24. At 500 pounds, the ranks of friability decreased as follow: Starch 1500$^R$ > Modified rice starch > Era-Tab$^R$ > Avicel PH 102$^R$. These data showed that friability of each diluent was more than 1 % except Avicel PH 102$^R$. At 1,000 pounds, friablity of modified rice starch and Era-Tab$^R$ were less than 1 % but it of starch 1500$^R$ was more than 1%. From the compression force 1,500 upto 2000 pounds, friability of each diluent was less than 1 %. Friability of modified rice starch tablets at 1,000 pounds upto 2,000 pounds was less than that of Era-Tab$^R$ and Starch 1500$^R$. Friability of modified and Era-Tab$^R$ tablets compressed at 1,000, 1,500 and 2,000 pounds were not significantly different.

**4. Compression Force-Disintegration Time Profiles**

Compression force-disintegration time profiles of modified rice starch and commercial diluents are illustrated in Table 11 and Figure 25.

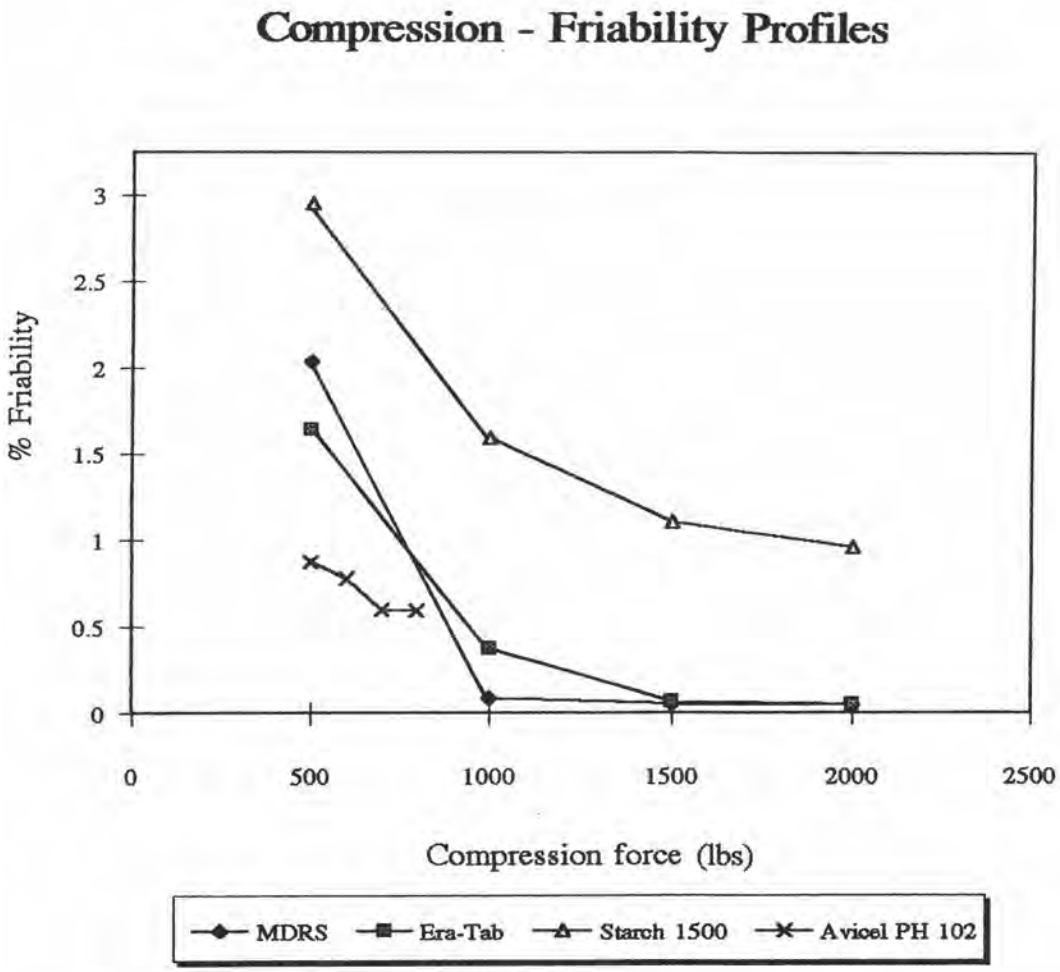



Figure 24 Comparison the compression force-friability profiles of various diluents and MDRS

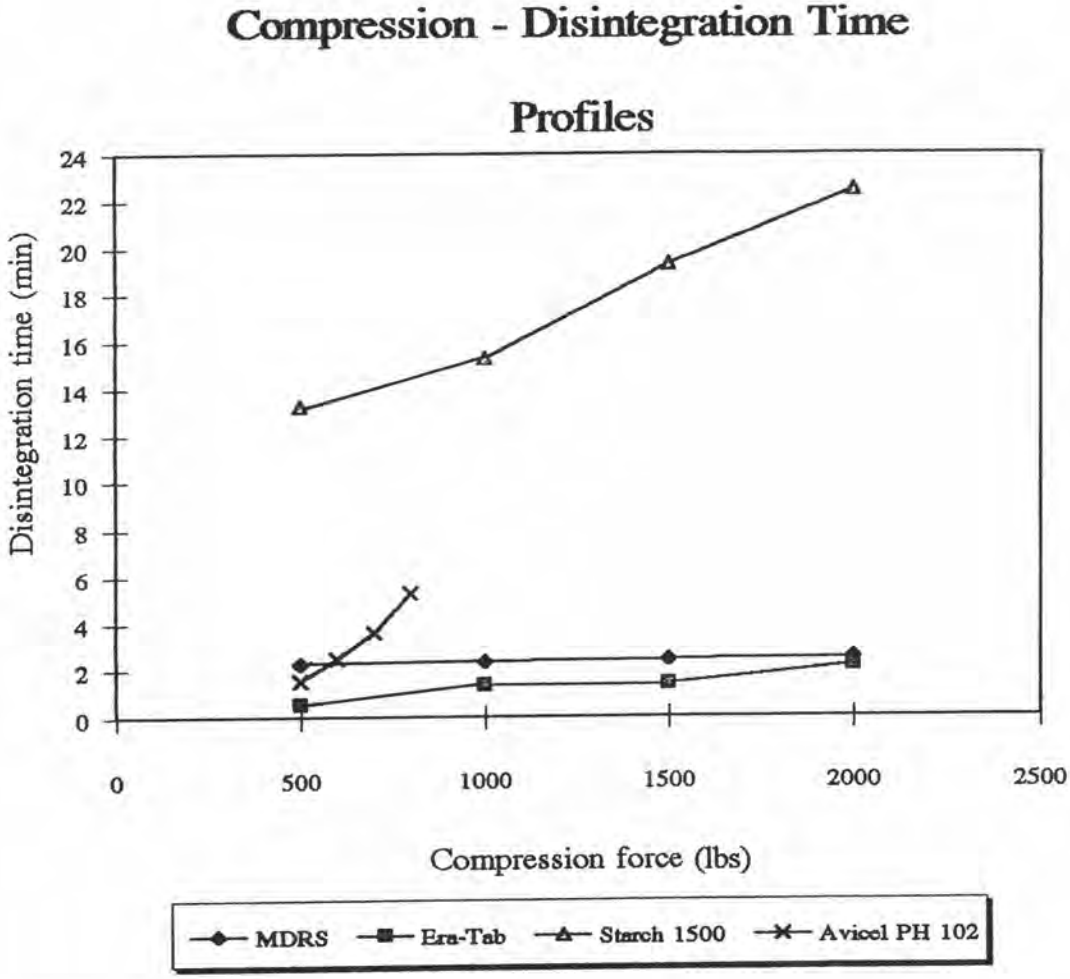



Figure 25 Comparison the compression force-disintegration time profiles of various diluents and MDRS

The disintegration time of tablet containing each diluent increased with the increased compression force. Disintegration time of Starch 1500$^R$ tablets was considerably longer than any other diluents. Its disintegration time increased very rapidly when increasing compression force. At the same compression force (500 pounds), the orders of decrease were: Starch 1500$^R$ > Modified rice starch > Avicel PH 102$^R$ > Era-Tab$^R$. Disintegration time of modified rice starch was almost constant at any compression forces in this study.

## Comparative Dilution Potential Ability of Modified Rice Starch and Commercial Diluents

Dilution potential data of each diluent with ascorbic acid at four compression forces are given in Tables 12-16 and Figures 26-30. Comparative dilution potential of various diluents at different compression forces are illustrated in Figures 31-34. For all diluents except Emcompress$^R$, thickness of tablets slightly decreased with increasing amount of ascorbic acid at all compression forces. Generally, thickness values also decreased when compression force increased. It was obviously seen that the increase in percentage of ascorbic acid caused decrease in hardness value at all compression forces.

At compression force of 2,000 pounds, hardness values of tablets containing modified rice starch were more than 20 kps at the level of ascorbic acid of 10 %. For Era-Tab$^R$ and Starch 1500$^R$, hardness values were below 20 kps at all compression forces and every amount of ascorbic acid. At the compression force of 500 pounds, tablets of modified rice starch and Era-tab$^R$ were zero when increasing percentage

Table 12 Dilution potential of MDRS with ascorbic acid

| Percent Ascorbic Acid | Physical Properties of Tablets (±SD) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | 1000 lbs | | 1500 lbs | | 2000 lbs | |
| | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) |
| 0 | 4.791 (0.071) | 4.137 (0.234) | 4.056 (0.027) | 11.290 (1.3126) | 3.737 (.033) | 20.00 (1.061) | 3.637 (0.015) | >20.00 |
| 10 | 4.531 (0.387) | 3.075 (0.512) | 4.031 (0.036) | 9.750 (0.865) | 3.653 (0.039) | 16.900 (0.886) | 3.530 (0.046) | >20.00 |
| 20 | 4.614 (0.078) | 2.360 (0.413) | 3.925 (0.031) | 8.880 (1.2015) | 3.572 (0.015) | 14.920 (0.678) | 3.429 (0.032) | 18.670 (0.703) |
| 30 | 4.418 (0.046) | 2.200 (0.916) | 3.846 (0.029) | 7.130 (0.467) | 3.531 (0.026) | 12.220 (0.734) | 3.387 (0.024) | 15.780 (0.929) |
| 40 | 4.278 (0.0327) | 0 | 3.724 (0.044) | 5.150 (0.425) | 3.423 (0.027) | 9.620 (1.062) | 3.299 (0.021) | 13.080 (0.930) |
| 50 | 4.086 (0.028) | 0 | 3.598 (0.036) | 4.380 (0.384) | 3.364 (0.027) | 7.140 (0.458) | 3.218 (0.019) | 9.1680 (0.496) |

TN. = Thickness (mm)

HN. = Hardness (kp)

Table 13 Dilution potential of Era-Tab with ascorbic acid

| Percent Ascorbic Acid | Physical Properties of Tablets (±SD) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | 1000 lbs | | 1500 lbs | | 2000 lbs | |
| | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) |
| 0 | 4.312 (0.019) | 3.110 (0.453) | 3.703 (0.019) | 11.180 (0.275) | 3.489 (0.042) | 17.120 (0.689) | 3.384 (0.034) | >20.00 |
| 10 | 4.225 (0.026) | 2.650 (0.734) | 3.675 (0.038) | 9.010 (0.359) | 3.403 (0.035) | 13.940 (0.720) | 3.308 (0.029) | 18.100 (0.817) |
| 20 | 4.129 (0.031) | 2.270 (0.405) | 3.572 (0.028) | 8.260 (0.484) | 3.349 (0.018) | 13.290 (0.763) | 3.267 (0.027) | 16.600 (0.909) |
| 30 | 4.025 (0.035) | 2.100 (0.305) | 3.499 (0.055) | 6.720 (0.433) | 3.313 (0.025) | 9.350 (0.634) | 3.214 (0.047) | 13.860 (1.219) |
| 40 | 3.935 (0.020) | 0 | 3.469 (0.029) | 5.05 (0.327) | 3.256 (0.023) | 8.550 (0.023) | 3.164 (0.019) | 11.380 (0.468) |
| 50 | 3.827 (0.018) | 0 | 3.443 (0.015) | 2.930 (0.224) | 3.239 (0.022) | 5.391 (0.436) | 3.128 (0.024) | 7.430 (0.361) |

TN. = Thickness (mm)

HN. = Hardness (kp)

Table 14 Dilution potential of Starch1500 with ascorbic acid

| Percent Ascorbic Acid | Physical Properties of Tablets (±SD) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | 1000 lbs | | 1500 lbs | | 2000 lbs | |
| | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) |
| 0 | 4.197 (0.051) | 1.015 (0.950) | 3.729 (0.024) | 5.937 (0.264) | 3.471 (0.041) | 9.375 (0.356) | 3.368 (0.024) | 11.780 (0.453) |
| 10 | 4.098 (0.041) | 0 | 3.594 (0.031) | 4.930 (0.290) | 3.394 (0.020) | 7.580 (0.545) | 3.309 (0.024) | 8.800 (0.689) |
| 20 | 4.058 (0.036) | 0 | 3.571 (0.021) | 3.720 (0.374) | 3.369 (0.041) | 6.080 (0.309) | 3.276 (0.329) | 8.100 (0.508) |
| 30 | 4.031 (0.024) | 0 | 3.555 (0.022) | 2.930 (0.483) | 3.362 (0.028) | 4.610 (0.336) | 3.279 (0.022) | 6.200 (0.449) |
| 40 | 3.976 (0.0236) | 0 | 3.519 (0.017) | 1.377 (0.752) | 3.306 (0.020) | 3.367 (0.194) | 3.224 (0.0239) | 4.650 (0.397) |
| 50 | 3.885 (0.015) | 0 | 3.4.95 (0.013) | 0 | 3.289 (0.009) | 2.380 (0.172) | 3.222 (0.074) | 3.680 (0.074) |

TN. = Thickness (mm)

HN. = Hardness (kp)

Table 15 Dilution potential of Avicel PH 102 with ascorbic acid

| Percent Ascorbic Acid | Physical Properties of Tablets (±SD) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | 600 lbs | | 700 lbs | | 800 lbs | |
| | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) |
| 0 | 4.041 (0.023) | 15.550 (0.346) | 3.896 (0.017) | 18.400 (0.338) | 3.751 (0.018) | >20.00 | 3.665 (0.037) | >20.00 |
| 10 | 4.021 (0.021) | 12.100 (0.150) | 3.835 (0.044) | 14.562 (0.569) | 3.709 (0.022) | 16.550 (0.554) | 3.652 (0.024) | 18.171 (0.328) |
| 20 | 4.008 (0.021) | 8.925 (0.248) | 3.856 (0.022) | 10.737 (0.342) | 3.717 (0.026) | 12.110 (0.336) | 3.635 (0.026) | 13.800 (0.229) |
| 30 | 3.967 (0.026) | 6.912 (0.183) | 3.818 (0.025) | 8.500 (0.239) | 3.684 (0.013) | 9.587 (0.266) | 3.619 (0.023) | 10.950 (0.320) |
| 40 | 3.918 (0.020) | 4.650 (0.202) | 3.766 (0.018) | 5.750 (0.141) | 3.677 (0.031) | 7.011 (0.566) | 3.596 (0.036) | 7.862 (0.132) |
| 50 | 3.848 (0.027) | 3.225 (0.0192) | 3.742 (0.027) | 3.912 (0.271) | 3.620 (0.036) | 4.437 (0.259) | 3.541 (0.036) | 5.250 (0.150) |

TN. = Thickness (mm)

HN. = Hardness (kp)

Table 16 Dilution potential of Emcompress with ascorbic acid

| Percent Ascorbic Acid | Physical Properties of Tablets (±SD) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | 1000 lbs | | 1500 lbs | | 2000 lbs | |
| | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) | TN. (mm) | HN. (kp) |
| 0 | * | * | 2.543 (0.015) | 0.510 (0.320) | 2.447 (0.024) | 2.383 (0.254) | 2.372 (0.012) | 3.217 (0.186) |
| 10 | * | * | 2.607 (0.028) | 0.400 (0.700) | 2.501 (0.021) | 1.780 (0.467) | 2.437 (0.012) | 2.550 (0.214) |
| 20 | * | * | 2.665 (0.011) | 0.275 (0.476) | 2.538 (0.009) | 0.986 (0.481) | 2.493 (0.016) | 1.900 (0.271) |
| 30 | * | * | * | * | * | * | * | * |
| 40 | * | * | * | * | * | * | * | * |
| 50 | * | * | * | * | * | * | * | * |

TN. = Thickness (mm)

HN. = Hardness (kp)

* = Can't be compressed

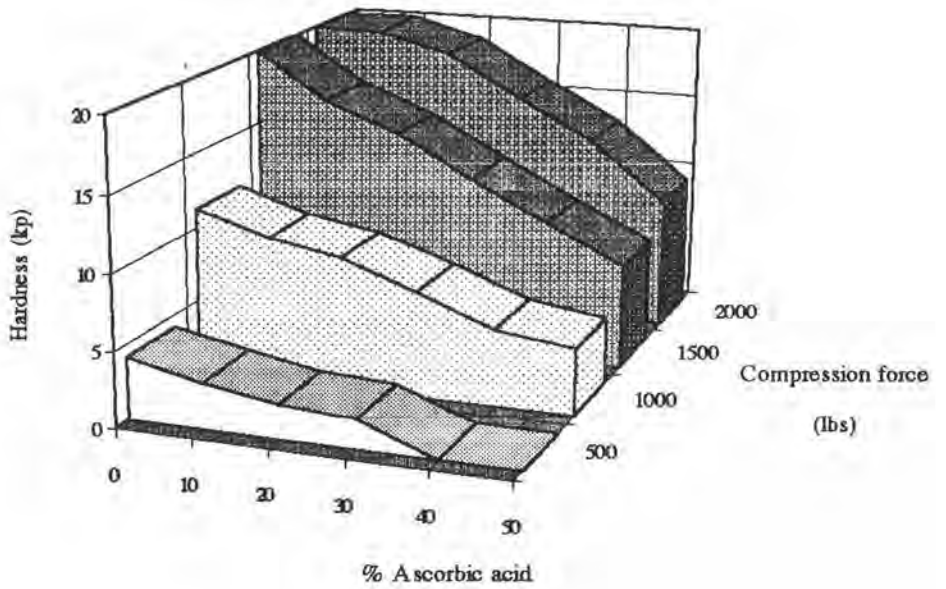



Figure 26 Dilution potential of MDRS with ascorbic acid compressed at 500, 1,000, 1,500 and 2,000 lbs

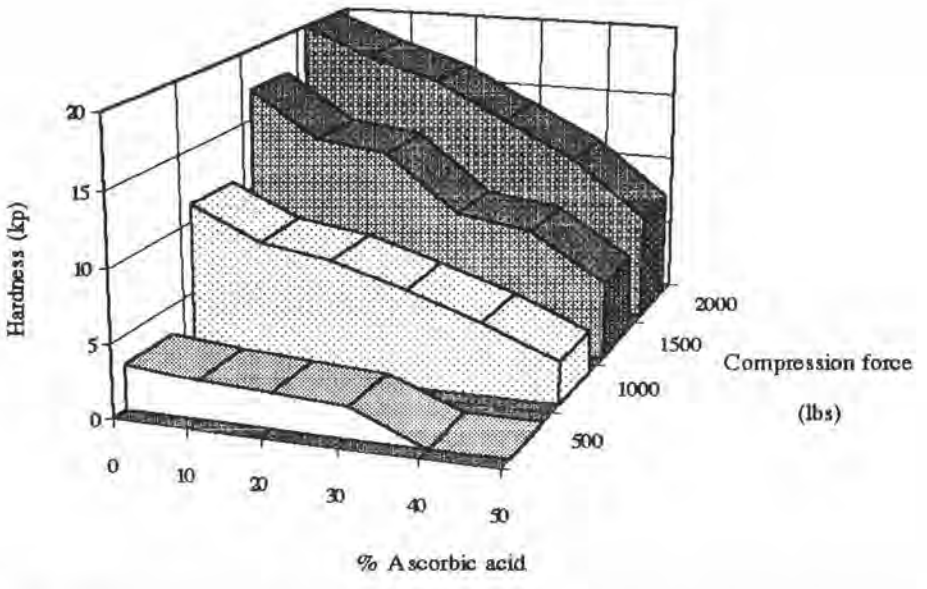



Figure 27 Dilution potential of Era-Tab$^{R}$ with ascorbic acid compressed at 500, 1,000, 1,500 and 2,000 lbs

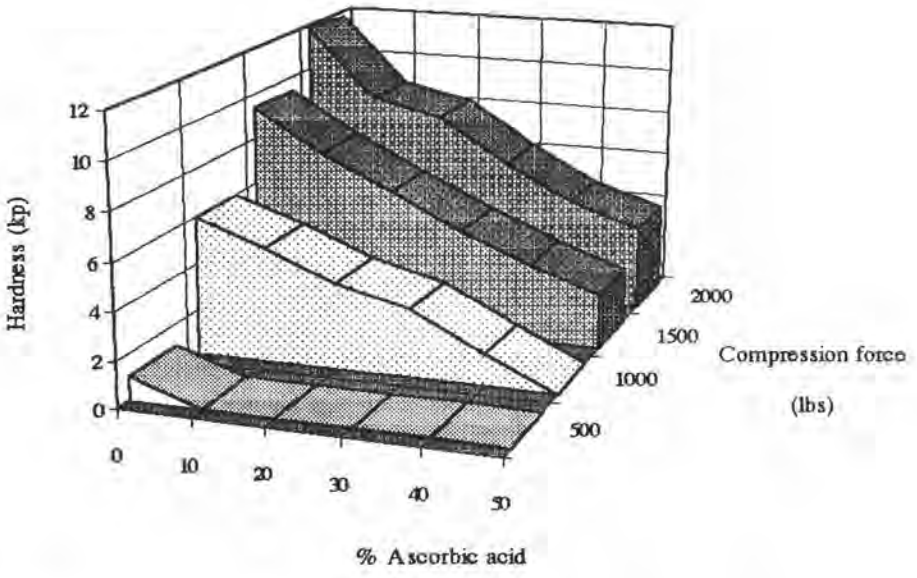



Figure 28 Dilution potential of Starch 1500$^{R}$ with ascorbic acid compressed at 500,1,000, 1,500 and 2,000 lbs

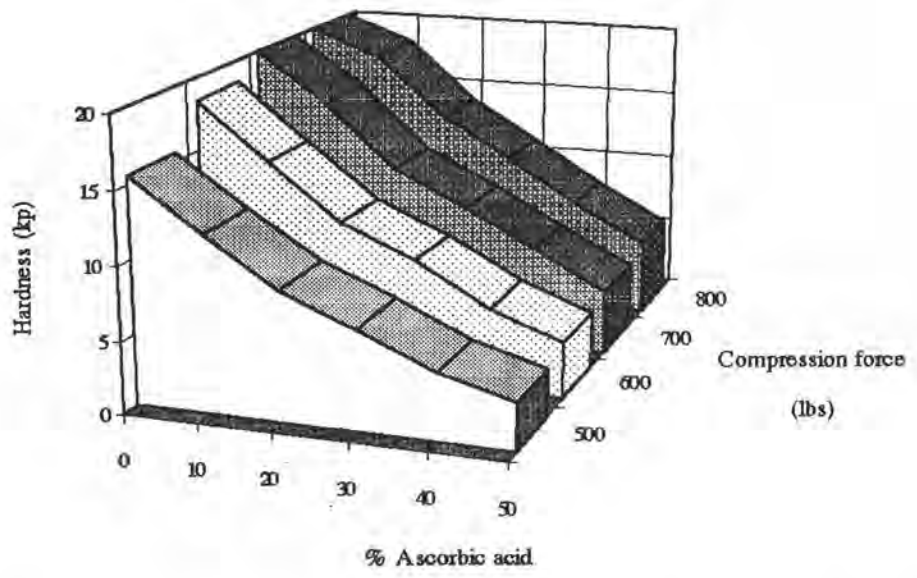



Figure 29 Dilution potential of Avicel PH 102$^{R}$ with ascorbic acid compressed at 500, 600, 700 and 800 lbs

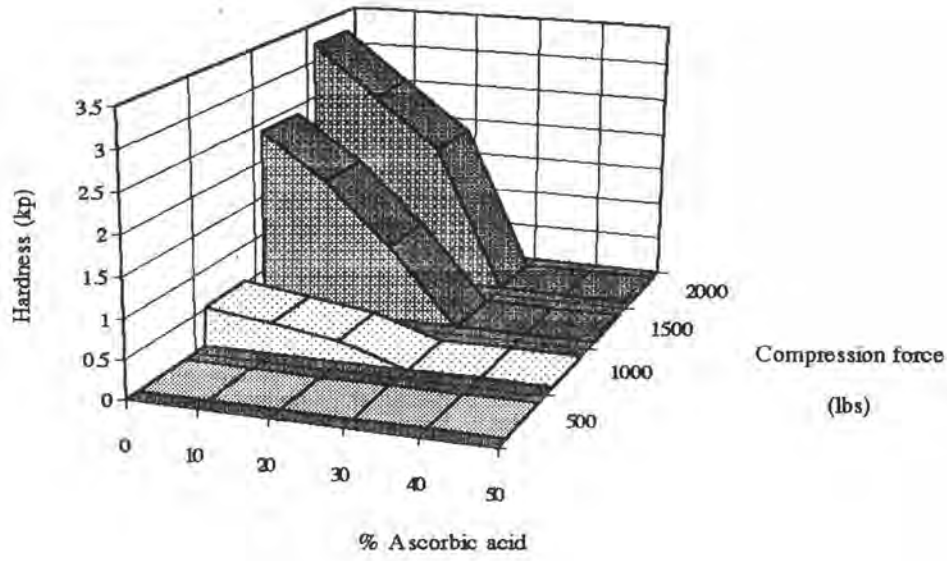



Figure 30 Dilution potential of Emcompress$^{R}$ with ascorbic acid compressed at 500,1,000, 1,500 and 2,000 lbs

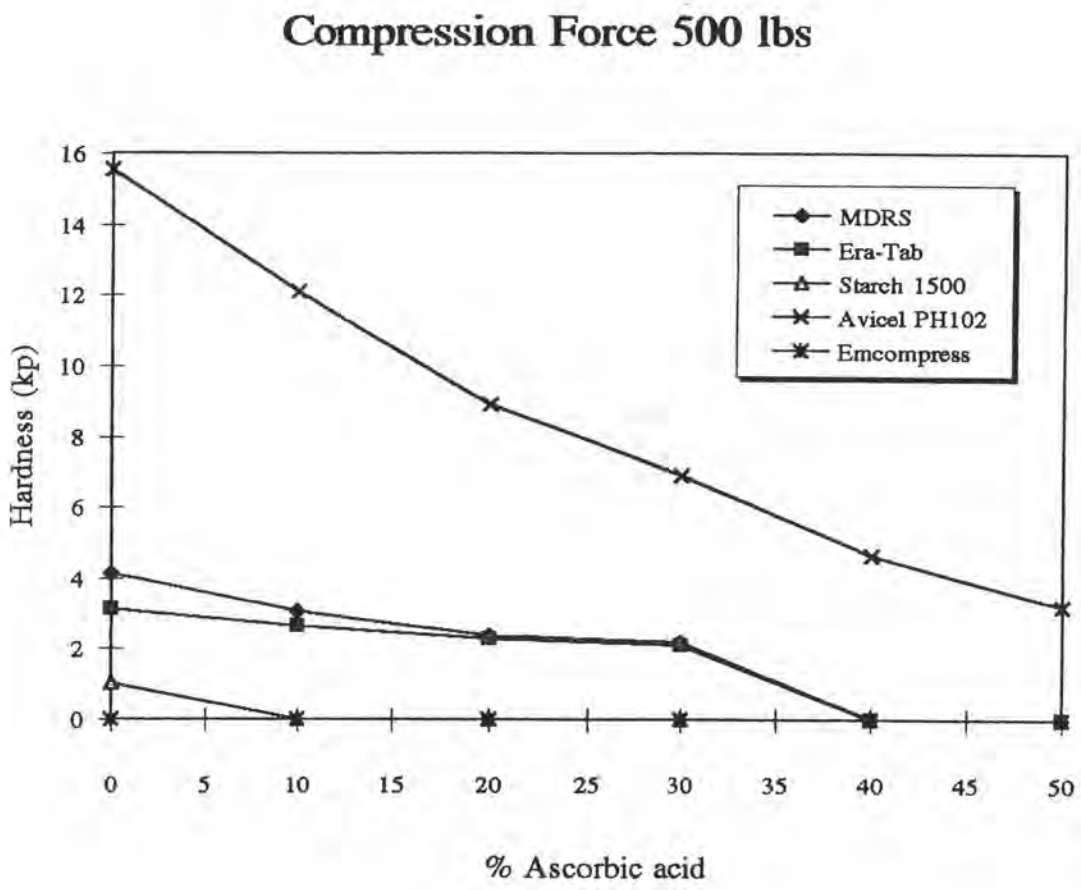



Figure 31 Comparative evaluation of dilution potential of various diluents and MDRS with ascorbic acid compressed at 500 lbs

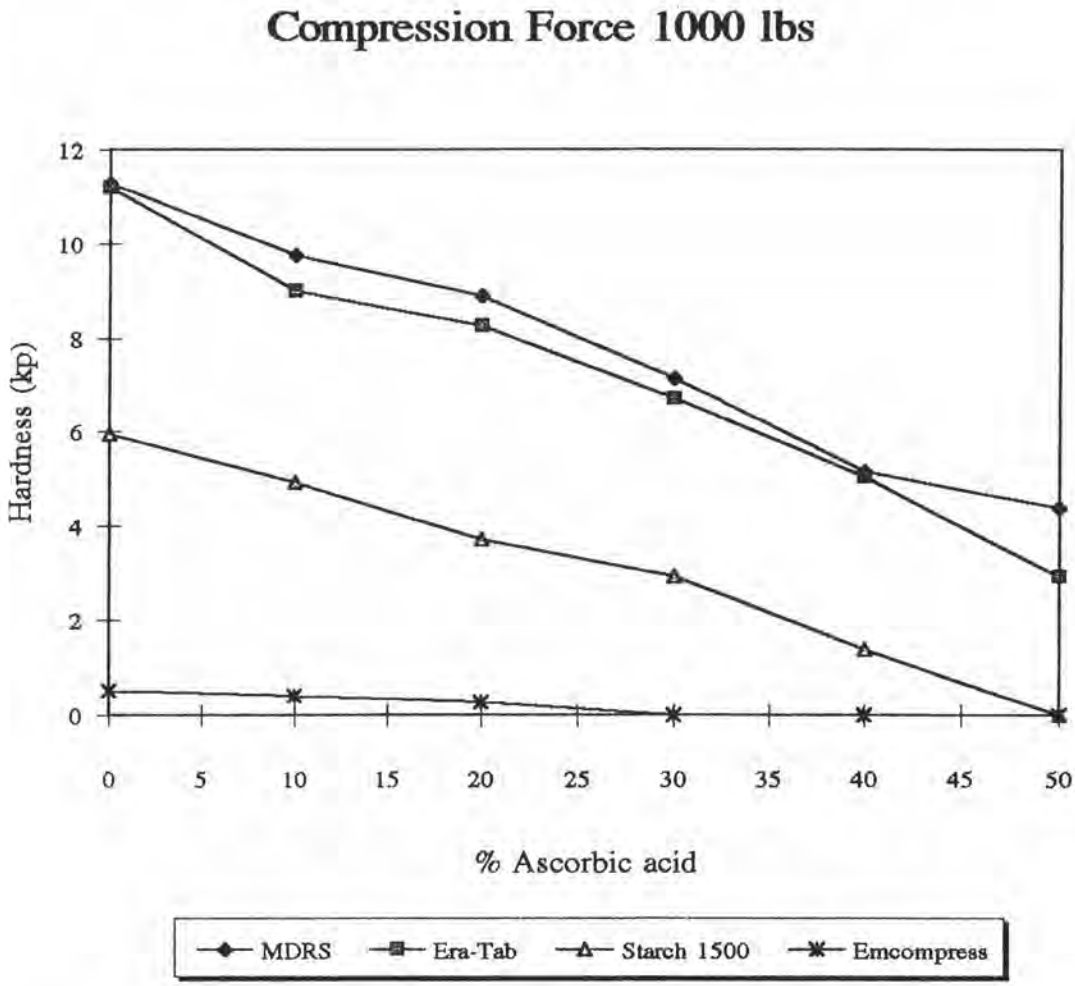



Figure 32 Comparative evaluation of dilution potential of various diluents and MDRS with ascorbic acid compressed at 1,000 lbs

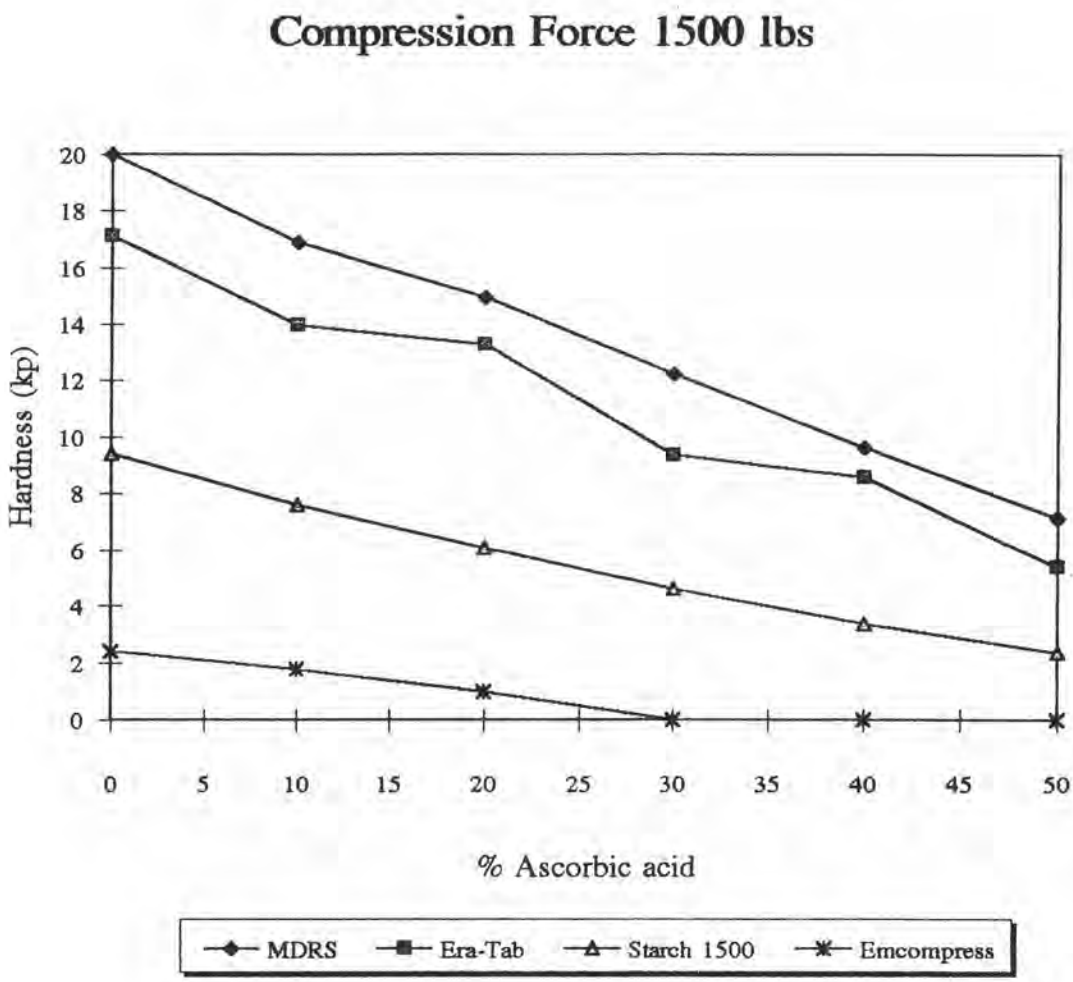



Figure 33 Comparative evaluation of dilution potential of various diluents and MDRS with ascorbic acid compressed at 1,500 lbs

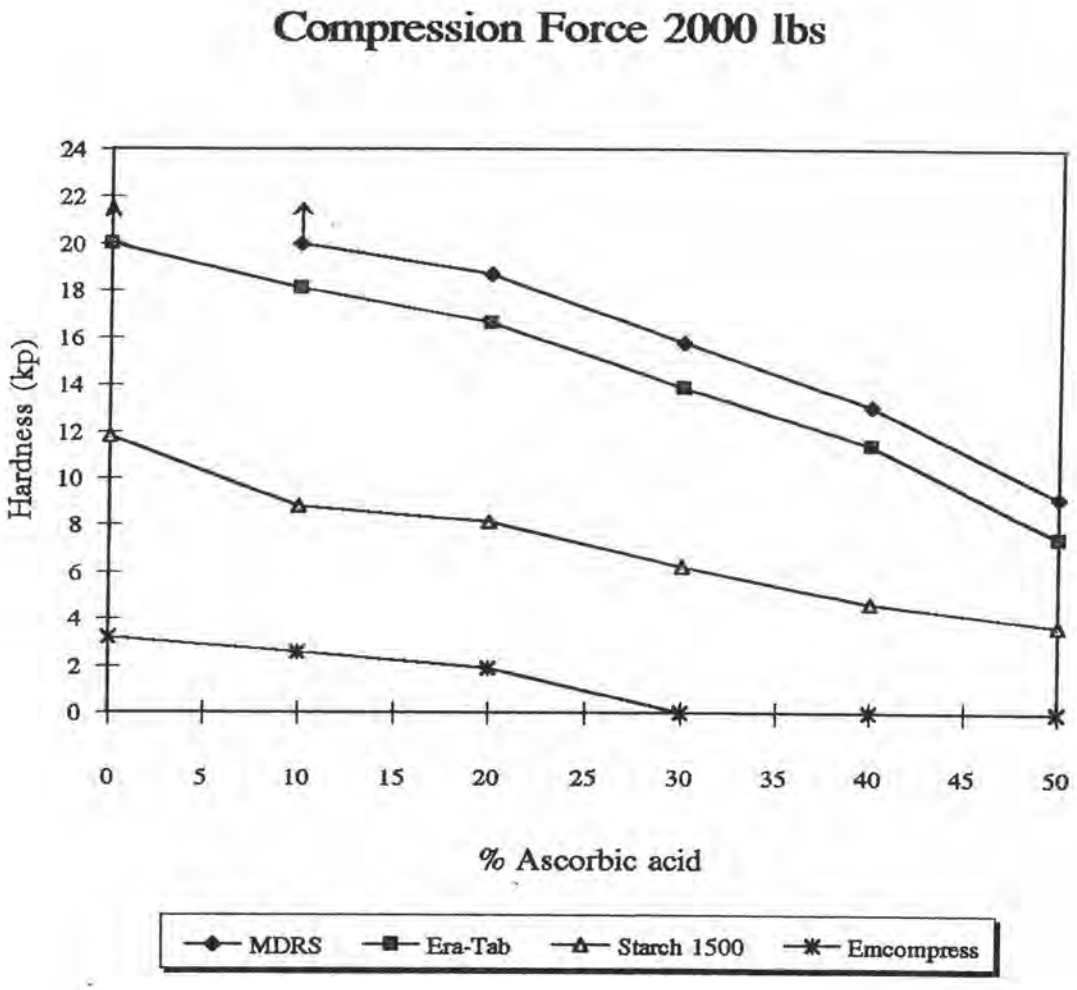



Figure 34 Comparative evaluation of dilution potential of various diluents and MDRS with ascorbic acid compressed at 2,000 lbs (The arrow signs indicate that the hardness of tablets were more than 20 kps.)

of ascorbic acid upto 40 and more. For Starch 1500$^R$, tablet hardness were zero when increasing percentage of ascorbic acid upto 10 and more. In case of Emcompress$^R$, their tablets could not be compressed into tablet at 500 pounds even if at 0 % of ascorbic acid. At compression forces of 1,000, 1,500 and 2,000 pounds, Emcompress could not be compressed into tablet when increasing percentage of ascorbic acid upto 30 and more. For Avicel PH 102$^R$, their tablets could be compressed at all compression forces and hardness values were below 20 kps at every level of ascorbic acid. Comparative evaluation of the dilution potential of each diluent with ascorbic acid at four compression forces are presented in Figure 31-34. At 500 pounds, Avicel PH 102$^R$ explicited higher hardness values than any other diluent at all percentage of ascorbic acid employed. The hardness of tablets of modified rice starch and Era-Tab$^R$ were in vicinity while Starch 1500$^R$ tablets possessed the less strength. The order of decrease were: Avicel PH 102$^R$ > Modified rice starch ≈ Era-Tab$^R$ > Starch 1500$^R$ > Emcompress$^R$. In the cases of modified rice starch, Era-Tab$^R$, Starch 1500$^R$ and Emcompress$^R$, modified rice starch explicited higher hardness values than these diluents at 500-2,000 pounds. It might be concluded that the ability of various diluents to improve compressibility of ascorbic acid could be ranked in the following orders: Avicel PH 102$^R$ > Modified rice starch > Era-Tab$^R$ > Starch 1500$^R$ > Emcompress$^R$.

## Effect of Lubricant on Tabletting Characteristics

Magnesium stearate is the most widely used pharmaceutical lubricant; for this reason, it was selected to investigate the effect of lubricant on some physical properties of tablet. Tablet containing diluent

only and diluent lubricated with magnesium stearate were prepared at different compression forces. For Emcompress$^{R}$, tablets could not be compressed adequately with lubricant concentration below 0.75 %. From this observation, it could appear that lower concentration of magnesium stearate was insufficient to lubricate the granules of Emcompress$^{R}$ to facilitate compression and ejection.

**Hardness**

The effect of lubricant concentration on the hardness and disintegration time of tablets prepared from various diluents at four compression forces are reported in Table 17-21 and Figure 35-43. It was generally known that the hardness of tablets increased with compression force. In ordinary, the hardness of tablets decreased with increased lubricant concentration, besides that of Emcompress$^{R}$. Emcompress$^{R}$ tablets were rather unchanged in accordance with lubricant concentration.

For modified rice starch, Era-Tab$^{R}$, Starch 1500$^{R}$ and Avicel PH 102$^{R}$, the addition of lubricant resulted in the decrease of tablets hardness of each diluent. At compression force of 500 pounds, Emcompress$^{R}$ could not be compressed to tablet at any lubricant concentration. Although the increase of compression force from 1,000 to 2,000 pounds were applied, the hardness of Emcompress$^{R}$ tablets were not acceptable.

In the case of starch-based fillers, the hardness of Starch 1500$^{R}$ tablets compressed at 1,000 pounds or higher was acceptable except the compression force of 500 pounds. The reduction of the hardness of modified rice starch and Era-Tab$^{R}$ were distinctly; however, the hardness of the tablets compressed at 500 to 2,000 pounds were higher than 4 kps,

Table 17 Effect of magnesium stearate on physical properties of MDRS tablets at diferrent compression forces

| % $MgST$ | Physical Properties of Tablets (±SD) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | | 1000 lbs | | | 1500 lbs | | | 2000 lbs | | |
| | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) |
| 0 | 4.635 (0.356) | 6.450 (0.876) | 1:590 (0.289) | 4.032 (0.035) | 16.471 (0.749) | 2:090 (0.351) | 3.801 (0.049) | >20.00 | 2:190 (0.184) | 3.645 (0.097) | >20.00 | 2:240 (0.584) |
| 0.25 | 4.718 (0.4362) | 5.362 (0.824) | 2:490 (0.100) | 4.086 (0.057) | 14.70 (1.121) | 2:480 (0.279) | 3.786 (0.031) | >20.00 | 3:089 (0.011) | 3.628 (0.028) | >20.00 | 3:230 (0.148) |
| 0.50 | 4.851 (0.031) | 5.275 (0.435) | 3:071 (0.346) | 4.098 (0.019) | 13.550 (0.622) | 3:110 (0.517) | 3.783 (0.018) | 20.00 (0.811) | 3:190 (0.118) | 3.587 (0.031) | >20.00 | 3:510 (0.253) |
| 0.75 | 4.531 (0.387) | 4.430 (0.573) | 3:200 (0.397) | 4.056 (0.027) | 12.014 (0.867) | 3:140 (0.205) | 3.737 (0.034) | 20.00 (1.061) | 3:380 (0.386) | 3.637 (0.015) | >20.00 | 4:210 (0.344) |
| 1.00 | 4.843 (0.058) | 4.137 (0.234) | 3:530 (0.411) | 4.092 (0.031) | 11.290 (1.313) | 3:150 (0.326) | 3.750 (0.030) | 20.00 (0.739) | 4:187 (0.305) | 3.625 (0.023) | >20.00 | 4:340 (0.437) |

TN. = Thickness (mm)

HN. = Hardness (kp)

D.T. = Disintegration Time (min:sec)

Table 18 Effect of magnesium stearate on physical properties of Era-Tab tablets at different compression forces

| % MgST | Physical Properties of Tablets (±SD) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | | 1000 lbs | | | 1500 lbs | | | 2000 lbs | | |
| | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) |
| 0 | 4.326 (0.038) | 5.904 (0.324) | 1:010 (0.082) | 3.721 (0.037) | 15.387 (0.857) | 1:450 (0.845) | 3.503 (0.025) | >20.00 | 2:010 (0.118) | 3.408 (0.023) | >20.00 | 2:340 (0.187) |
| 0.25 | 4.268 (0.033) | 5.272 (0.335) | 1:030 (0.033) | 3.681 (0.021) | 14.387 (0.309) | 1:520 (0.122) | 3.492 (0.014) | 20.00 (1.046) | 2:05 (0.3442) | 3.401 (0.017) | >20.00 | 2:400 (0.132) |
| 0.50 | 4.311 (0.027) | 4.387 (0.385) | 1:048 (0.203) | 3.724 (0.022) | 12.075 (0.211) | 2:170 (0.181) | 3.609 (0.116) | 18.267 (0.343) | 2:190 (0.333) | 3.396 (0.014) | >20.00 | 2:450 (0.203) |
| 0.75 | 4.312 (0.019) | 4.000 (0.300) | 1:094 (0.235) | 3.703 (0.019) | 11.180 (0.275) | 2:191 (0.111) | 3.489 (0.042) | 17.120 (0.689) | 2:29 (0.028) | 3.384 (0.034) | 20.00 (0.628) | 3:010 (0.107) |
| 1.00 | 4.289 (0.031) | 3.110 (0.453) | 1:150 (0.166) | 3.668 (0.025) | 11.087 (0.431) | 2:273 (0.161) | 3.478 (0.025) | 16.057 (0.792) | 2:41 (0.166) | 3.379 (0.024) | 20.00 (0.934) | 3:110 (0.185) |

TN. = Thickness (mm)

HN. = Hardness (kp)

D.T. = Disintegration Time (min:sec)

Table 19 Effect of magnesium stearate on physical properties of Starch1500 tablets at different compression forces

| % MgST | Physical Properties of Tablets (±SD) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | | 1000 lbs | | | 1500 lbs | | | 2000 lbs | | |
| | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) |
| 0 | 4.171 (0.025) | 3.950 (0.050) | 10:150 (1.437) | 3.687 (0.027) | 10.050 (0.150) | 14:216 (0.924) | 3.567 (0.038) | 12.100 (0.648) | 16:461 (0.831) | 3.423 (0.032) | 15.733 (0.205) | 18:540 (0.977) |
| 0.25 | 4.207 (0.028) | 2.450 (0.287) | 11:110 (1.047) | 3.716 (0.030) | 7.114 (0.422) | 16:163 (0.295) | 3.544 (0.024) | 10.567 (0.368) | 18:229 (0.467) | 3.441 (0.039) | 13.260 (0.811) | 20:049 (1.324) |
| 0.50 | 4.195 (0.025) | 1.620 (0.293) | 11:439 (1.103) | 3.704 (0.041) | 6.867 (0.471) | 16:229 (0.131) | 3.539 (0.041) | 9.460 (0.332) | 18:380 (0.258) | 3.477 (0.034) | 11.780 (0.453) | 23:190 (0.643) |
| 0.75 | 4.197 (0.051) | 1.015 (0.950) | 11:440 (0.551) | 3.729 (0.024) | 5.937 (0.264) | 16:580 (0.677) | 3.471 (0.040) | 9.375 (0.356) | 18:498 (0.499) | 3.368 (0.024) | 11.200 (0.238) | 23:461 (0.733) |
| 1.00 | 3.207 (0.035) | 0.433 (0.637) | 11:510 (0.150) | 3.734 (0.037) | 5.300 (0.081) | 17:108 (0.020) | 3.516 (0.027) | 8.550 (0.222) | 19:150 (0.012) | 3.463 (0.034) | 9.730 (0.824) | 25:299 (1.784) |

TN. = Thickness (mm)

HN. = Hardness (kp)

D.T. = Disintegration Time (min:sec)

Table 20 Effect of magnesium stearate on physical properties of Avicel PH102 tablets at diferrent compression forces

| % MgST | Physical Properties of Tablets (+SD) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | | 600 lbs | | | 700 lbs | | | 800 lbs | | |
| | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) |
| 0 | 4.097 (0.043) | 16.050 (0.350) | 1:186 (0.034) | 3.945 (0.016) | 19.100 (0.089) | 1:216 (0.078) | 3.839 (0.032) | >20.00 | 3:126 (0.088) | 3.735 (0.022) | >20.00 | 4:406 (0.303) |
| 0.25 | 4.171 (0.022) | 15.550 (0.346) | 4:051 (0.597) | 3.970 (0.025) | 18.400 (0.338) | 5:582 (0.041) | 3.837 (0.019) | >20.00 (0.644) | 8:819 (0.885) | 3.727 (0.028) | >20.00 | 21:19 (0.608) |
| 0.50 | 4.143 (0.034) | 14.733 (0.188) | 4:436 (0.675) | 3.941 (0.031) | 17.730 (0.339) | 7:134 (0.144) | 3.802 (0.020) | >20.00 | 11:494 (2.014) | 3.691 (0.024) | >20.00 | 17:199 (2.691) |
| 0.75 | 4.042 (0.023) | 14.567 (0.197) | 4:548 (1.154) | 3.896 (0.017) | 17.500 (0.167) | 6:230 (1.120) | 3.751 (0.018) | >20.00 | 13:431 (2.806) | 3.665 (0.037) | >20.00 | 22:497 (3.667) |
| 1.00 | 4.116 (0.027) | 14.100 (0.163) | 6:287 (0.643) | 3.938 (0.025) | 16.850 (0.214) | 10:034 (0.269) | 3.800 (0.022) | 19.117 (0.273) | 16:090 (0.829) | 3.725 (0.017) | >20.00 | 23:592 (1.141) |

TN. = Thickness (mm)

HN. = Hardness (kp)

D.T. = Disintegration Time (min:sec)

Table 21 Effect of magnesium stearate on physical properties of Emcompress tablets at different compression forces

| % MgST | Physical Properties of Tablets (+SD) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 500 lbs | | | 1000 lbs | | | 1500 lbs | | | 2000 lbs | | |
| | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) | TN. (mm) | HN. (kp) | D.T. (min:sec) |
| 0.75 | * | * | ** | 2.543 (0.015) | 0.510 (0.320) | ** | 2.447 (0.024) | 1.780 (0.466) | ** | 2.372 (0.012) | 3.217 (0.186) | ** |
| 1.00 | * | * | ** | 2.529 (0.025) | 0.733 (0.789) | ** | 2.445 (0.014) | 2.550 (0.330) | ** | 2.387 (0.015) | 2.933 (0.667) | ** |
| 1.25 | * | * | ** | 2.529 (0.017) | 0.950 (0.723) | ** | 2.435 (0.013) | 2.033 (0.256) | ** | 2.363 (0.017) | 3.00 (0.252) | ** |

TN. = Thickness (mm)

HN. = Hardness (kp)

D.T. = Disintegration Time (min:sec)

* = Can't be compressed

** = > 1 hr.

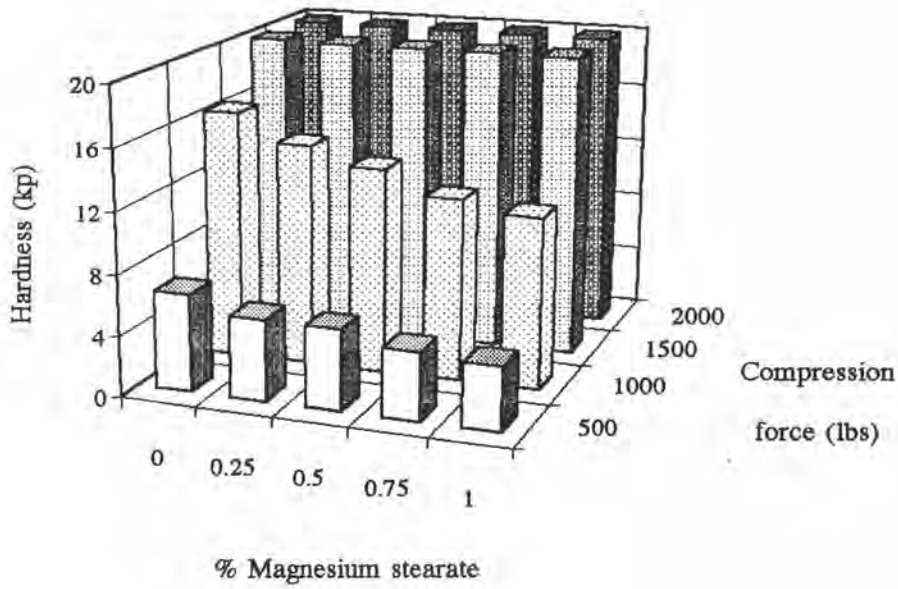



Figure 35 Effect of magnesium stearate on hardness of MDRS tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

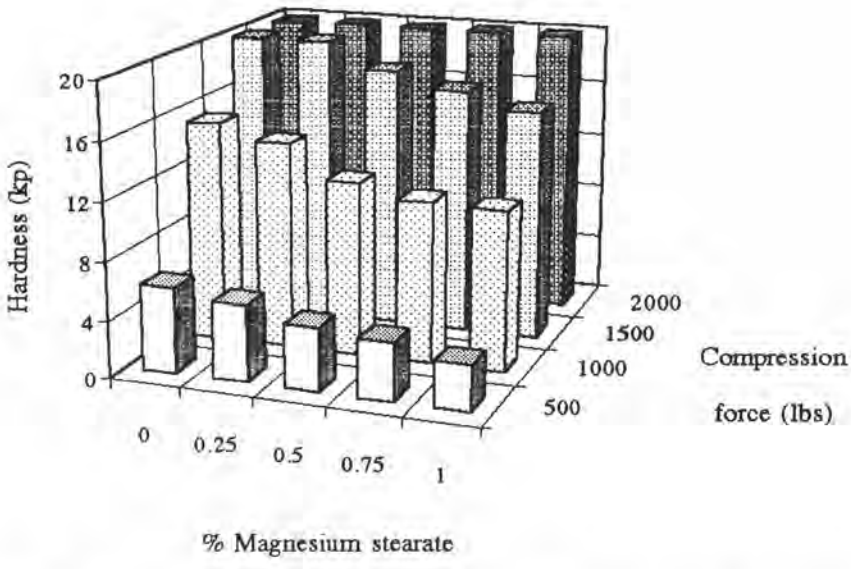



Figure 36 Effect of magnesium stearate on hardness of Era-Tab$^{R}$ tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

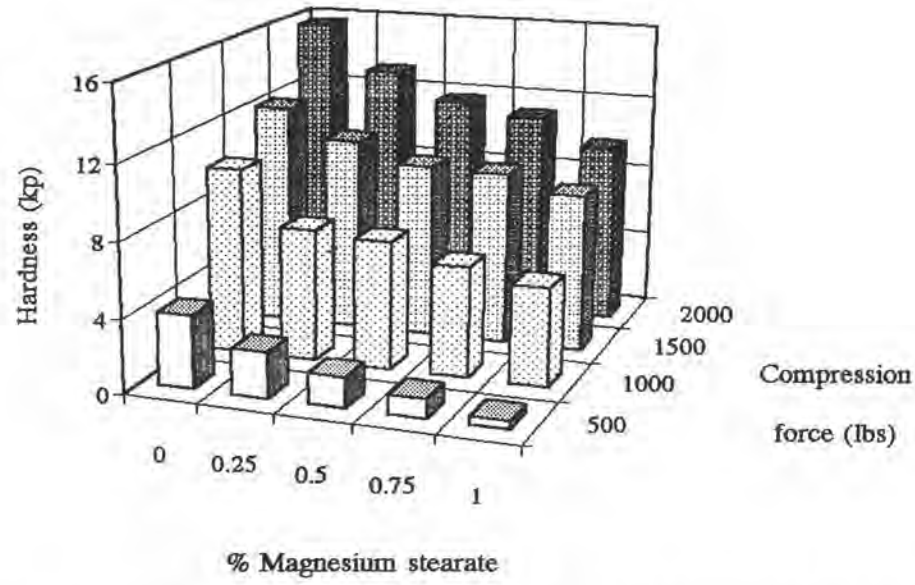



Figure 37 Effect of magnesium stearate on hardness of Starch 1500[R] tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

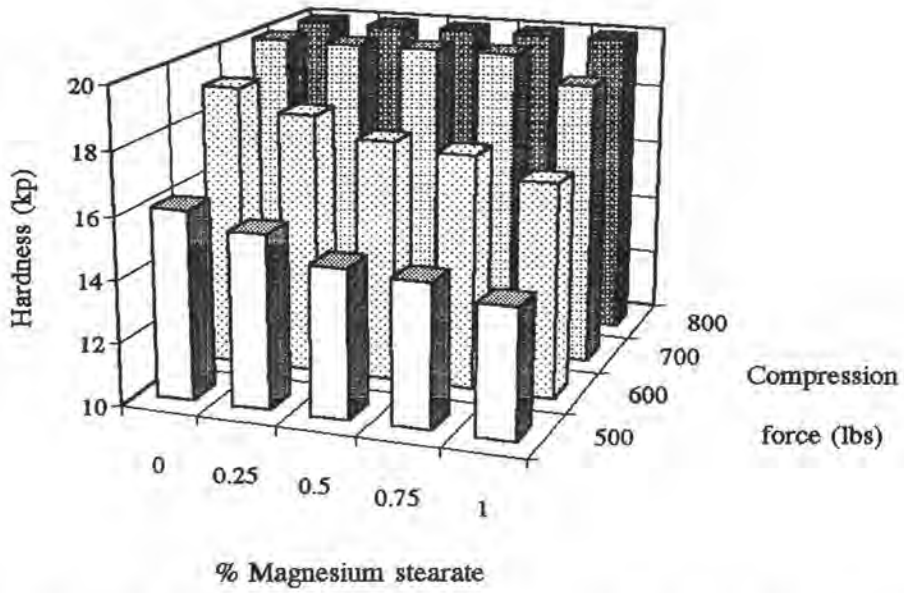



Figure 38 Effect of magnesium stearate on hardness of Avicel PH 102[R] tablets compressed at 500, 600, 700 and 800 lbs

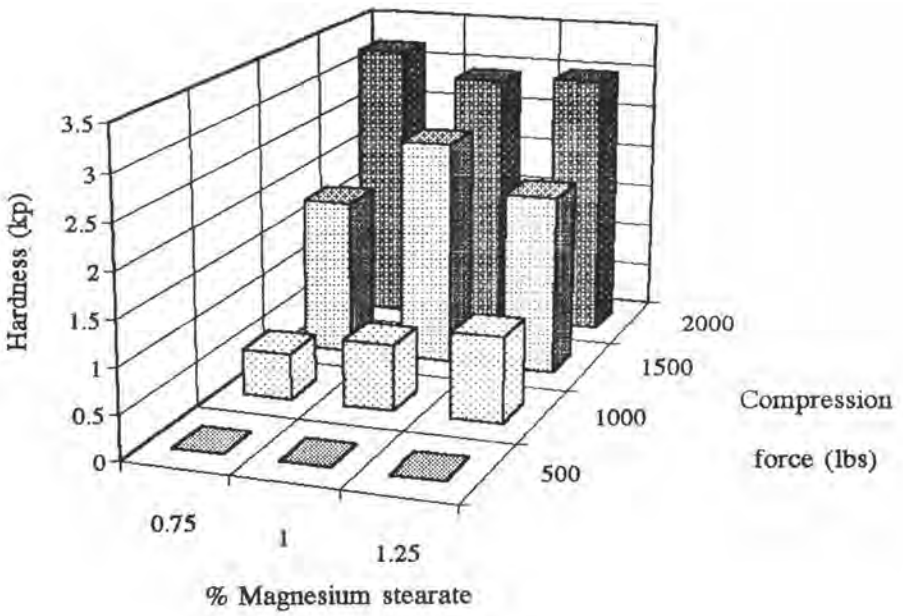



Figure 39 Effect of magnesium stearate on hardness of Emcompress[R] tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

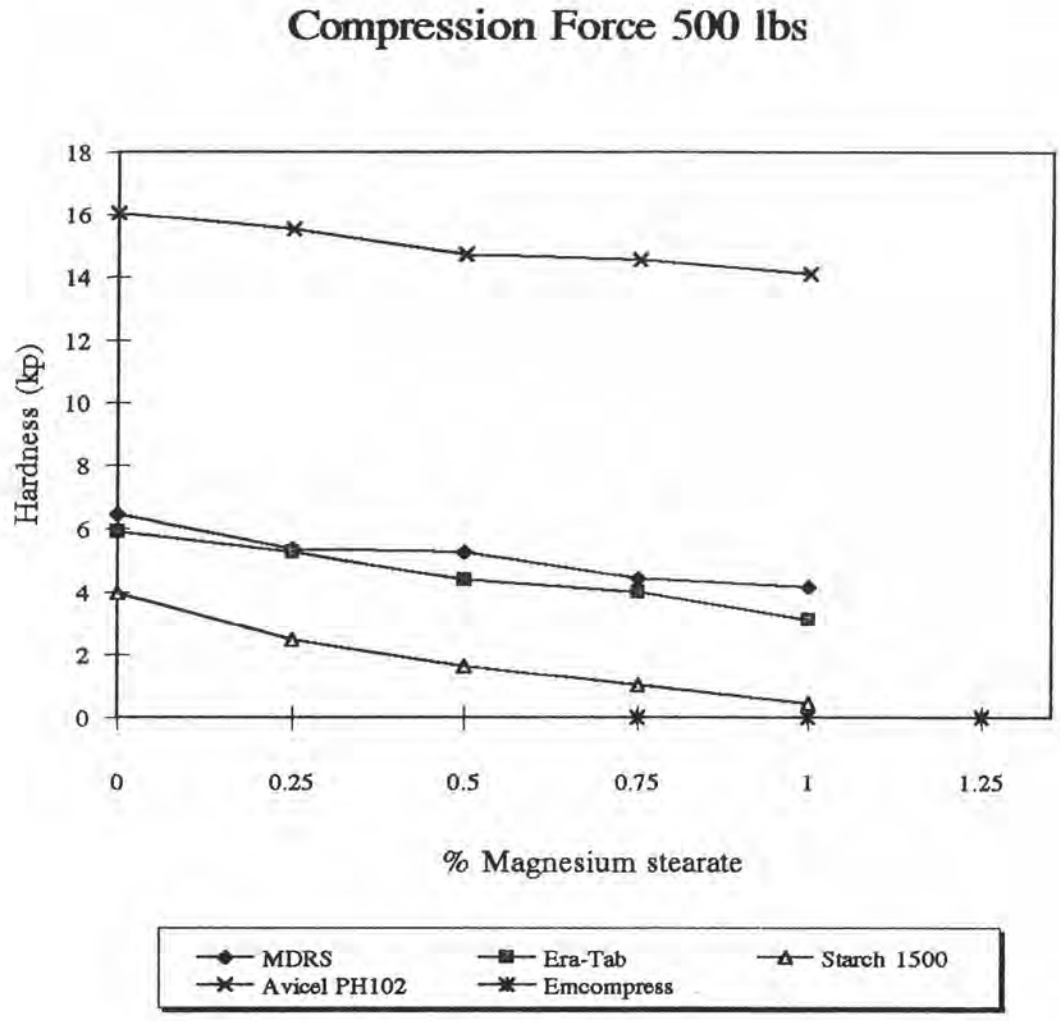



Figure 40 Comparative evaluation of magnesium stearate on hardness of various diluents and MDRS compressed at 500 lbs

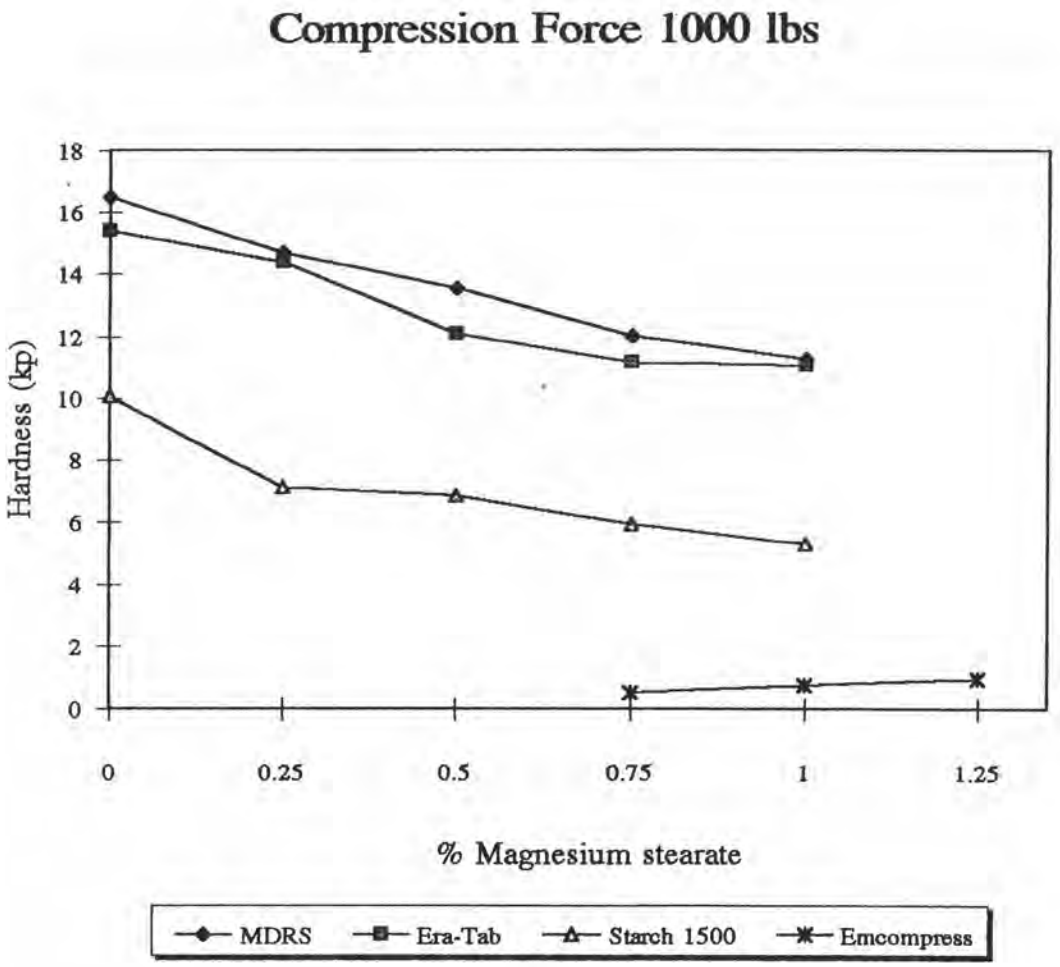



Figure 41 Comparative evaluation of magnesium stearate on hardness of various diluents and MDRS compressed at 1,000 lbs

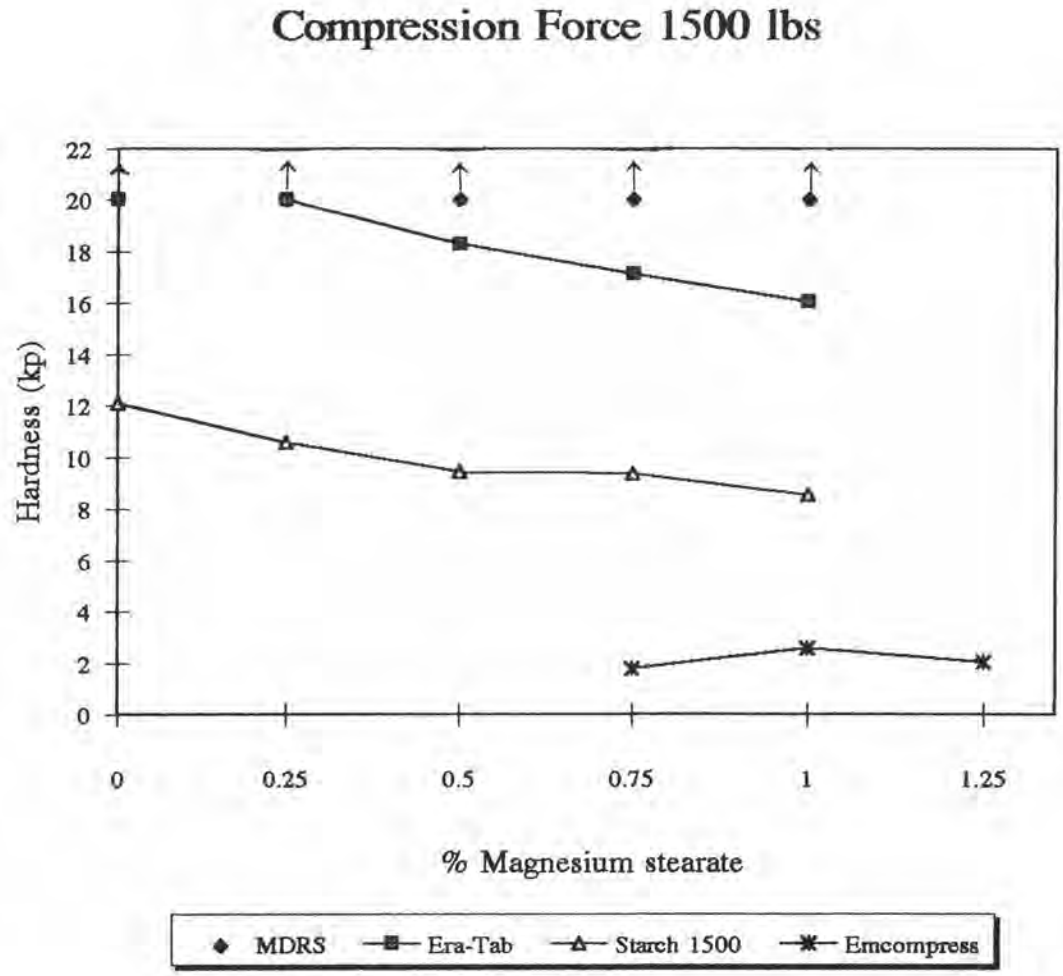



Figure 42 Comparative evaluation of magnesium stearate on hardness of various diluents and MDRS compressed at 1,500 lbs ( The arrow signs indicate that the hardness of tablets were more than 20 kps.)

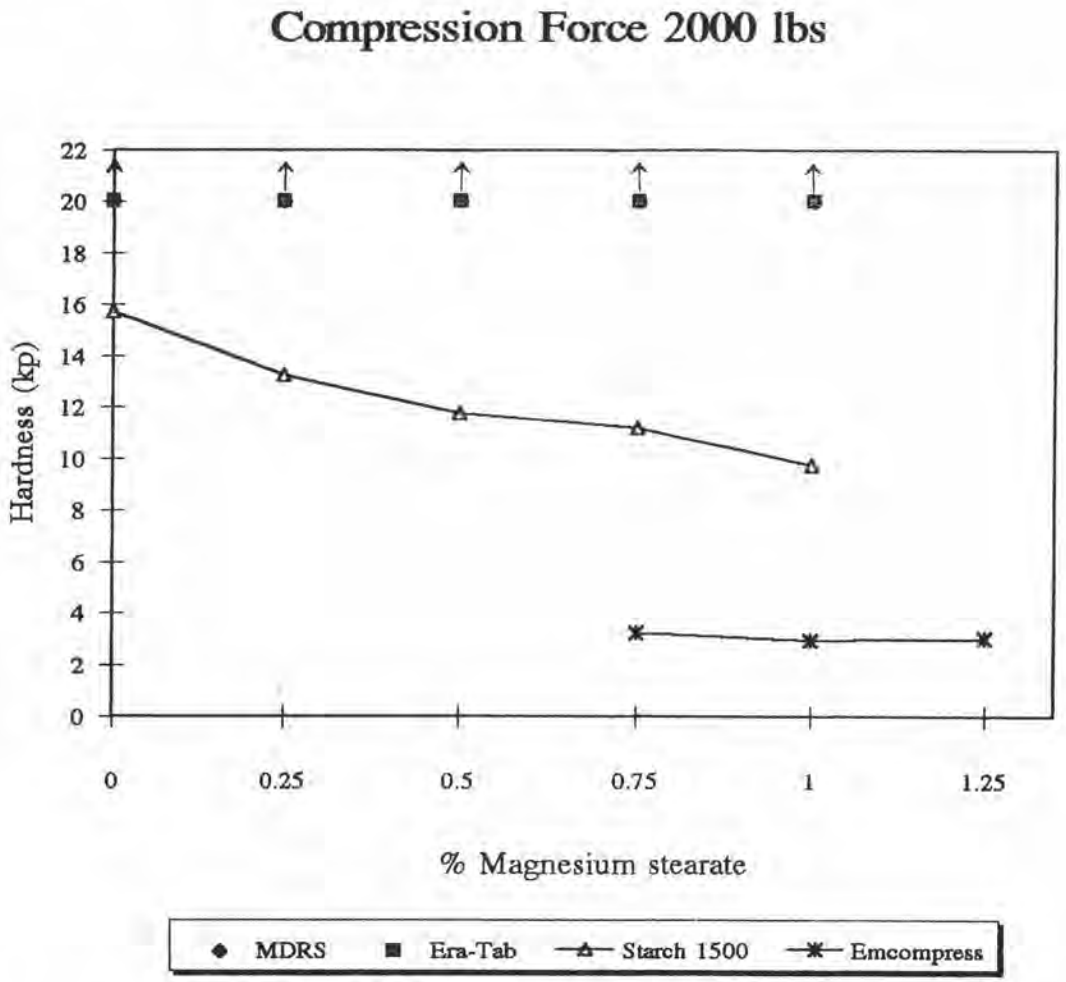



Figure 43 Comparative evaluation of magnesium stearate on hardness of various diluents and MDRS compressed at 2,000 lbs ( The arrow signs indicate that the hardness of tablets were more than 20 kps.)

except 1.0 % magnesium stearate of Era-Tab$^{R}$ tablets. The hardness of modified rice starch tablets at compression force of 2,000 pounds were higher than 20 kps at any given lubricant but that of Era-Tab$^{R}$ tabletswere approximately 20 kps at the lubricant levels of 0.75 % and 1.0 %.

At 1,500 pounds, the hardness of modified rice starch tablets were roughly 20 kps but that of Era-Tab$^{R}$ tablets were 20, 18.267, 17.120 and 16.05 kps at the levels of 0.25 %, 0.50 %, 0.75 %, 1.00 % magnesium stearate, respectively.

Avicel PH 102$^{R}$ was also affected by the presence of the lubricant; however, the decrease in the hardness was not noticeable.

**Disintegration Time**

Table 17-21 and Figure 44-51 show the effect of lubricant on disintegration time of tablets prepared from various diluents at different compression forces

It was generally accepted that the disintegration time of tablets increased with compression force or the levels of lubricant. For the same level of compression force and lubricant concentration, the disintegration time of various tablets increased in the following orders: Era-Tab$^{R}$ < Avicel PH 102$^{R}$ < Modified rice starch < Starch 1500$^{R}$. With Emcompress$^{R}$, for any level of compression force and lubricant concentration, the disintegration time of them was more than 1 hrs. As the concentration of magnesium stearate was increased for each tablet, the disintegration time was simultaneously increased. For modified rice

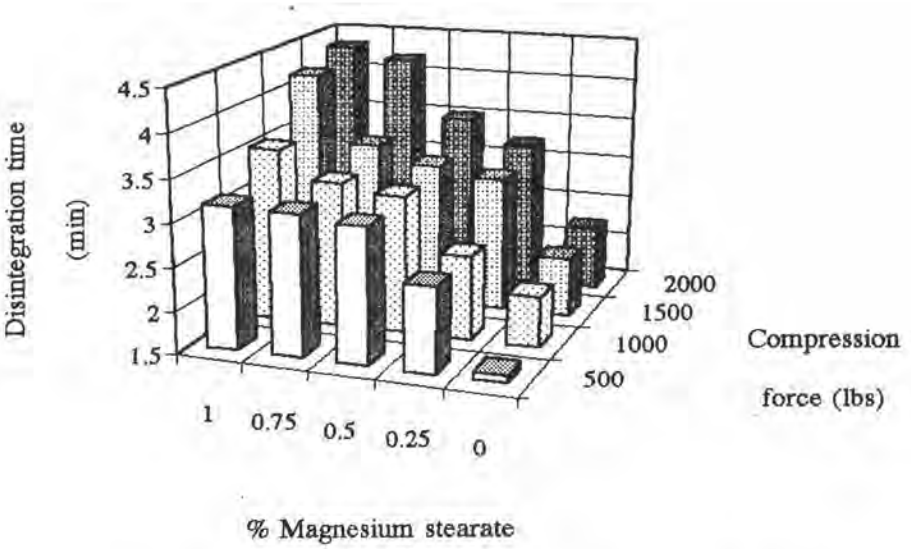



Figure 44 Effect of magnesium stearate on disintegration time of MDRS tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

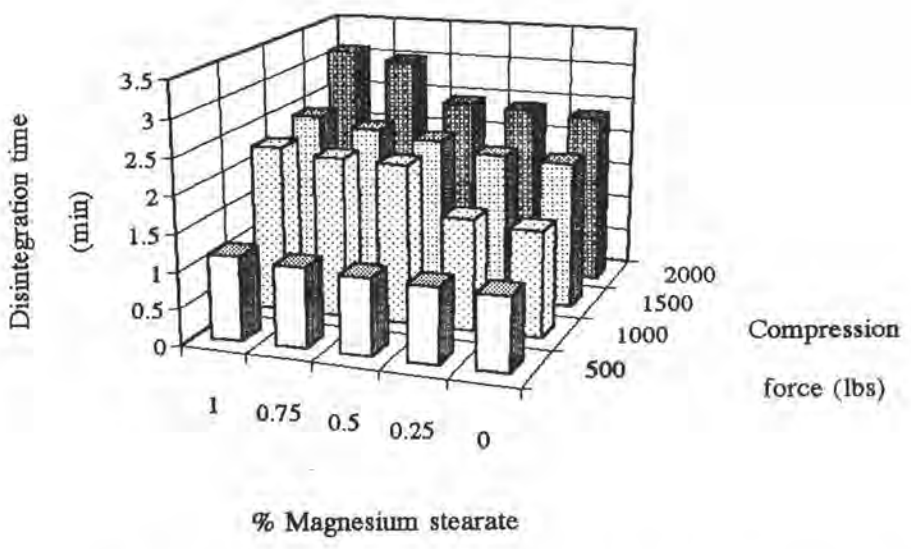



Figure 45 Effect of magnesium stearate on disintegration time of Era-Tab$^{R}$ tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

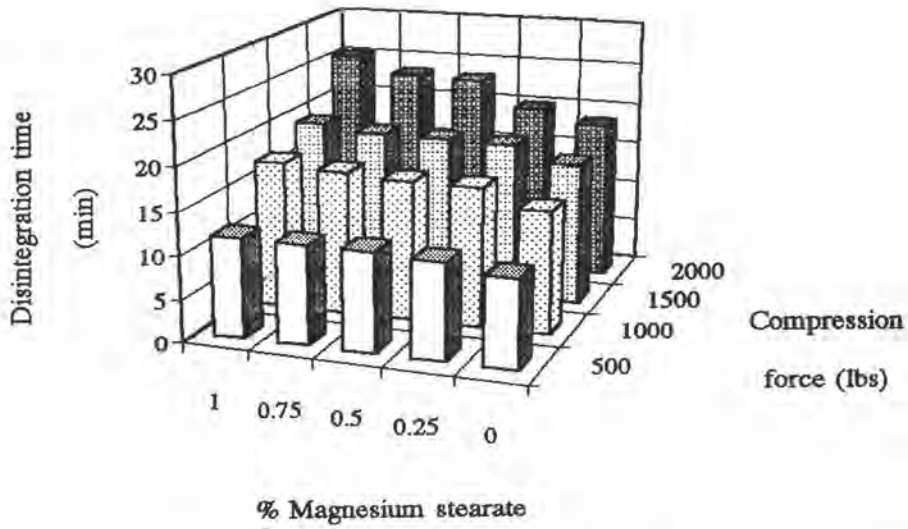



Figure 46 Effect of magnesium stearate on disintegration time of Starch 1500$^{R}$ tablets compressed at 500, 1,000, 1,500 and 2,000 lbs

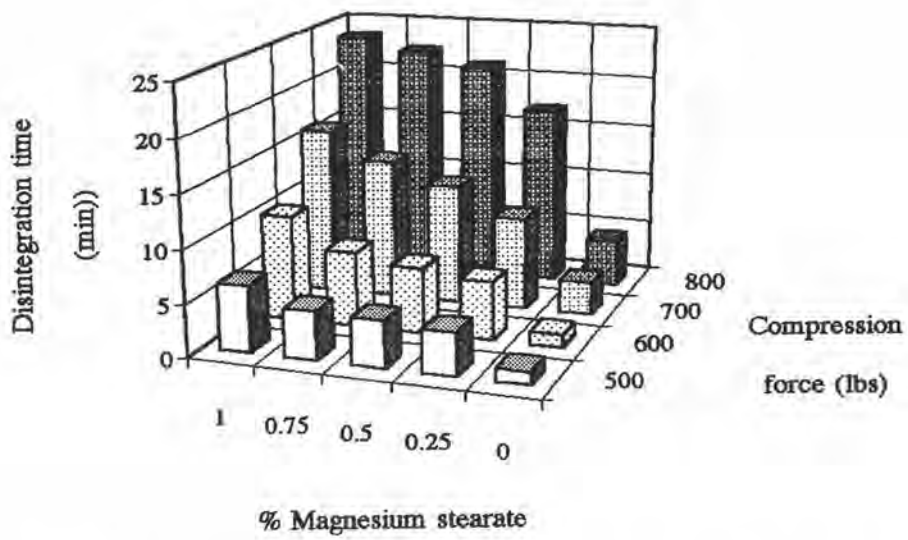



Figure 47 Effect of magnesium stearate on disintegration time of Avicel PH 102$^{R}$ tablets compressed at 500, 600, 700 and 800 lbs

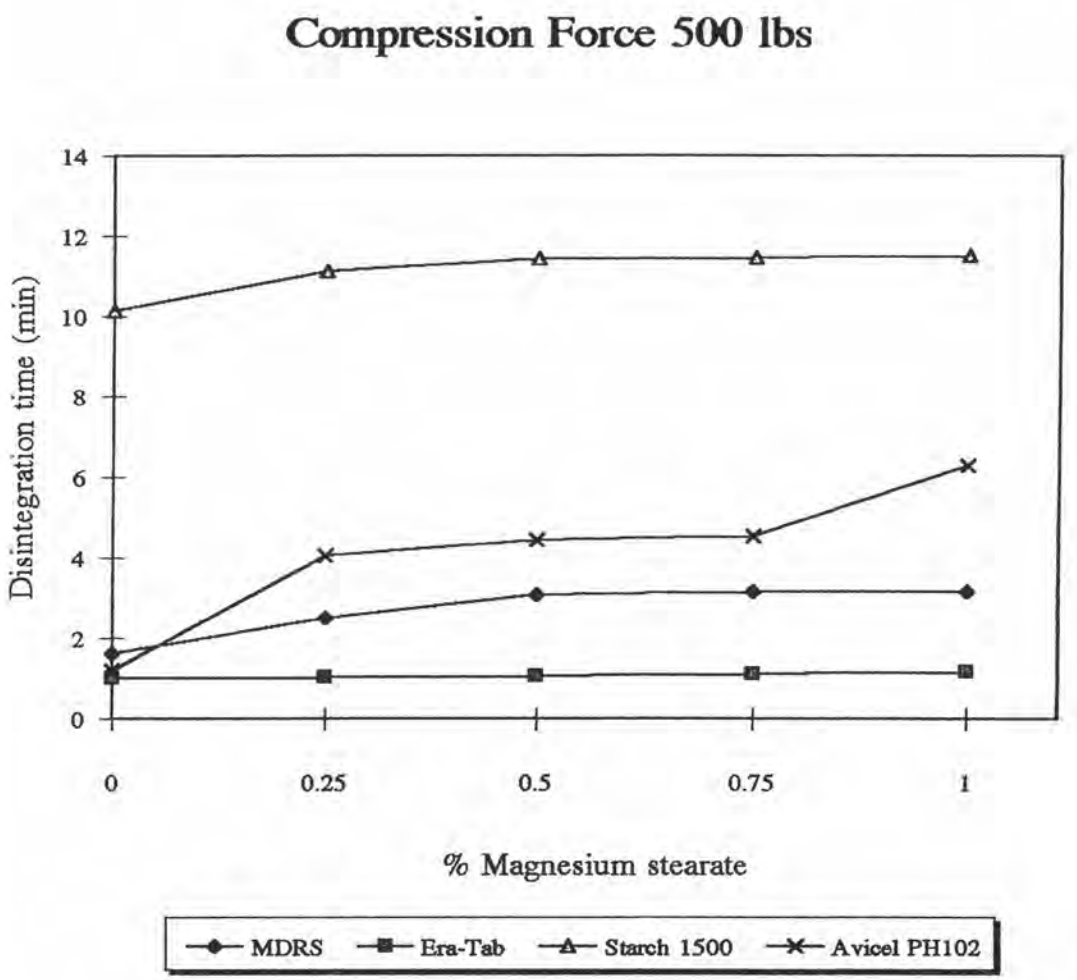



Figure 48 Comparative evaluation of magnesium stearate on disintegration time of various diluents and MDRS compressed at 500 lbs

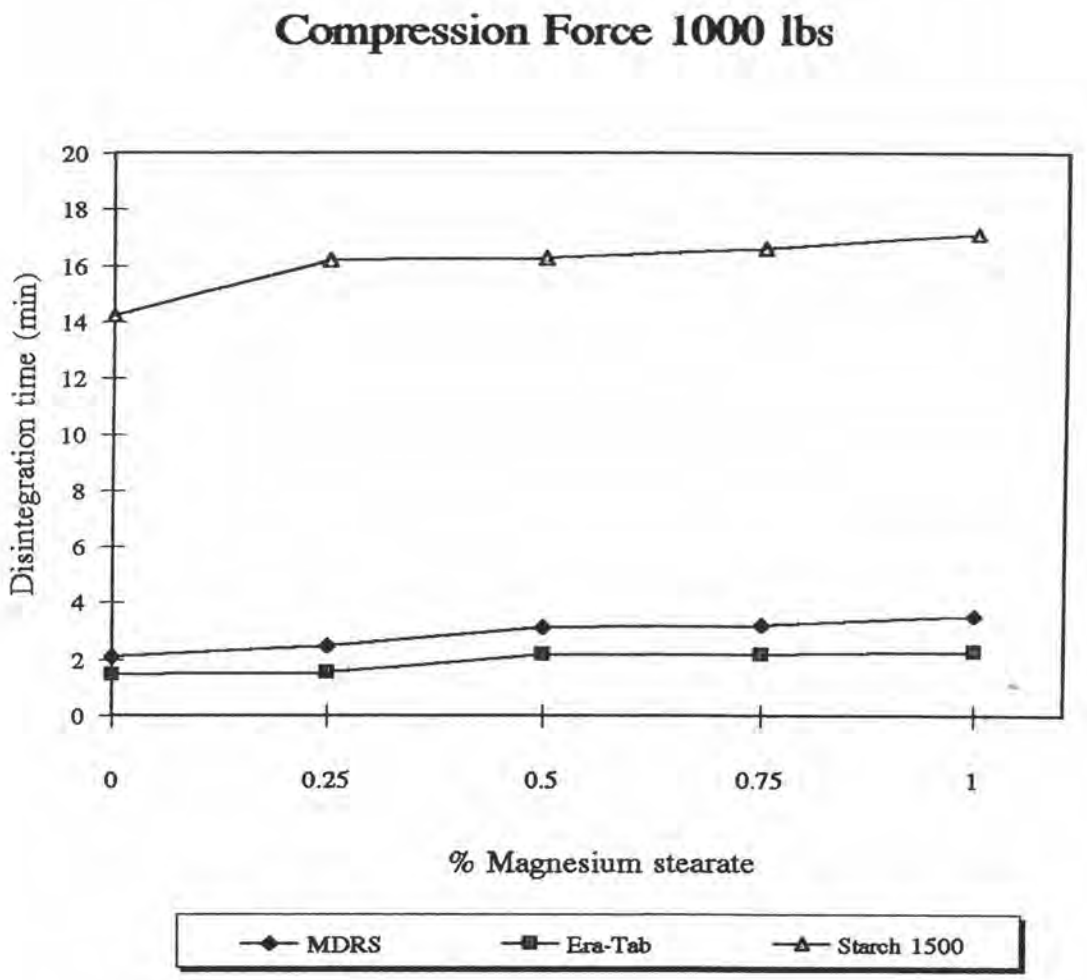



Figure 49 Comparative evaluation of magnesium stearate on disintegration time of various diluents and MDRS compressed at 1,000 lbs

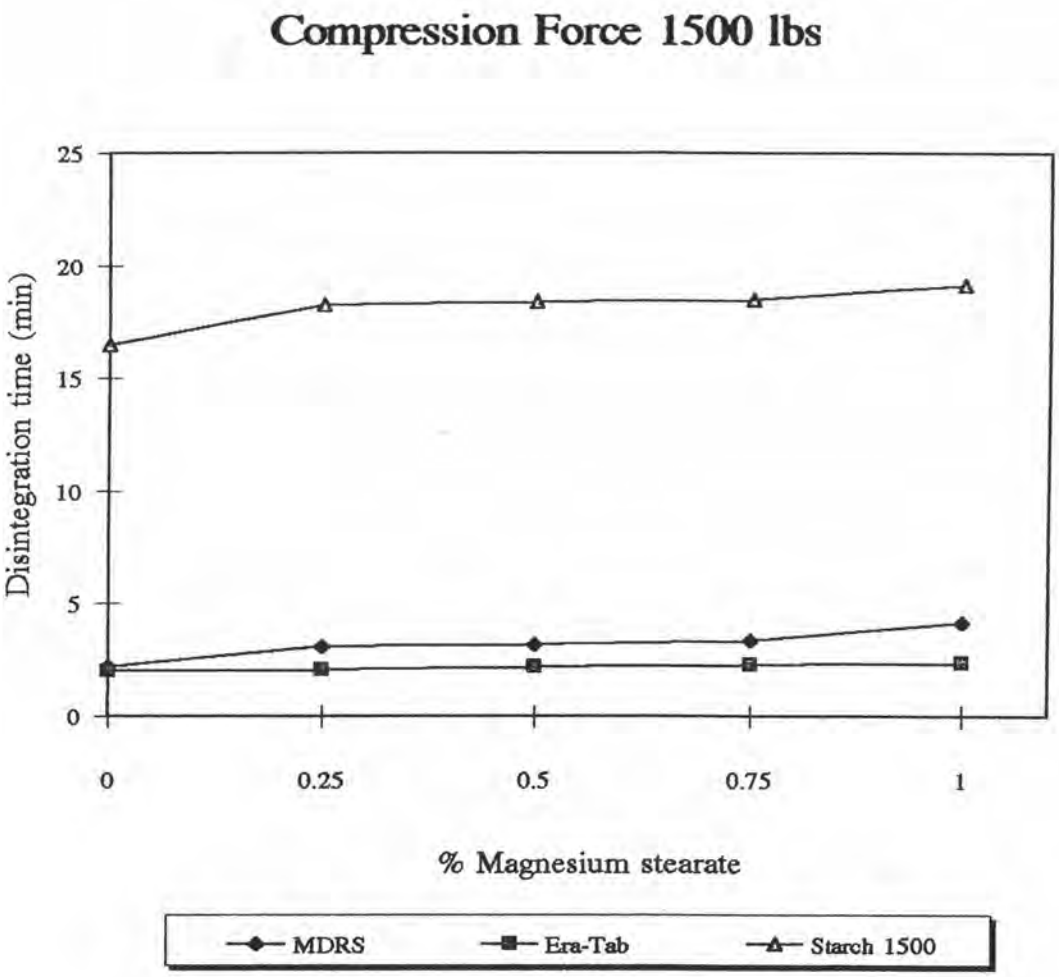



Figure 50 Comparative evaluation of magnesium stearate on disintegration time of various diluents and MDRS compressed at 1,500 lbs

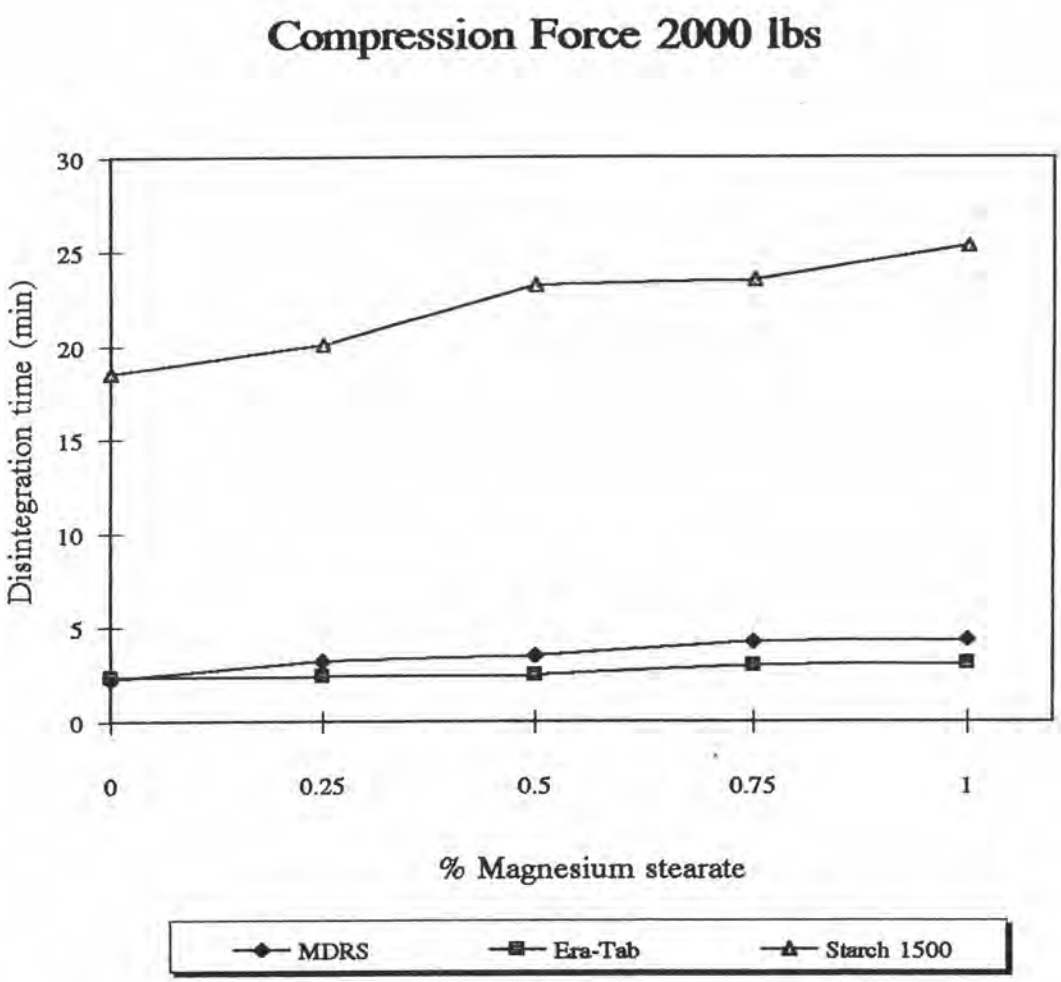



Figure 51 Comparative evaluation of magnesium stearate on disintegration time of various diluents and MDRS compressed at 2,000 lbs

starch and Era-Tab$^{R}$ tablets, the disintegration time of these tablets were less than 5 mins at any level of compression force or lubricant concentration.

## Application in Manufacture of Tablet Products

The flowability and compressibility of modified rice starch suggested that it would be a direct compression diluent. Thus model tablet formulations were designed to evaluate the properties of tablet containing active ingredient. Model drugs studied in this experiment were isoniazid and hydrochlorothiazide. Two kinds of tablets were prepared using single punch tablet machine. In the formula containing Starch 1500$^{R}$ or Avicel PH 102$^{R}$, talc was mixed for improving of flow properties. Each formula was produced at different compression forces to obtain hardness value about 4-5 kps.

### Isoniazid

### 1. Weight Variation

The results of average weight and standard deviation of isoniazid tablets are illustrated in Table 22. Weight variation of isoniazid tablets prepared from various diluents were within the limit of USP standard.

### 2. Thickness

The average thickness and standard deviation of isoniazid tablets prepared from various diluents are shown in Table 22. Thickness values decreased in the following orders: Avicel PH 102$^{R}$ > Modified rice starch > Era-Tab$^{R}$ > Starch 1500$^{R}$.

Table 22 Physical properties of isoniazid tablets prepared with commercial diluents and MDRS

| Diluents | Physical Properties of Tablets | | | | $T_{80\%}$ (min:sec) | % Label Amount (±SD) |
|---|---|---|---|---|---|---|
| | Wt. (mg±SD) | TN. (mm±SD) | HN. (kp±SD) | D.T. (min±SD) | | |
| MDRS | 351.4 (1.051) | 4.005 (0.02) | 4.130 (0.368) | 2.450 (0.213) | 9:45 (0.987) | 99.01 (0.587) |
| Era-tab | 349.5 (0.976) | 3.662 (0.034) | 4.788 (0.331) | 2.252 (0.156) | 9:15 (1.025) | 99.35 (0.751) |
| Starch 1500 | 351.7 (1.125) | 3.4301 (0.023) | 4.008 (0.351) | 13.078 (0.301) | 10:45 (1.103) | 101.45 (0.934) |
| Avicel PH102 | 352.3 (1.067) | 4.278 (0.033) | 4.211 (0.493) | 0.156 (0.038) | 10:25 (0.847) | 99.06 (1.057) |

Wt. = Weight TN. = Thickness

HN. = Hardness D.T. = Disintegration time

## 3. Hardness

The average hardness and standard deviation of isoniazid tablets are presented in Table 22. All the cases, the hardness of tablets were within the range of 4-5 kps.

## 4. Disintegration Time

As can be seen in Table 22 and Figure 52, the disintegration time isoniazid tablets could be ranked the following: Starch $1500^R$ > Modified rice starch > Era-$Tab^R$ > Avicel $PH102^R$. The statistical differences ($p < 0.05$) are depicted in Table 42 and 43 (Appendix V).

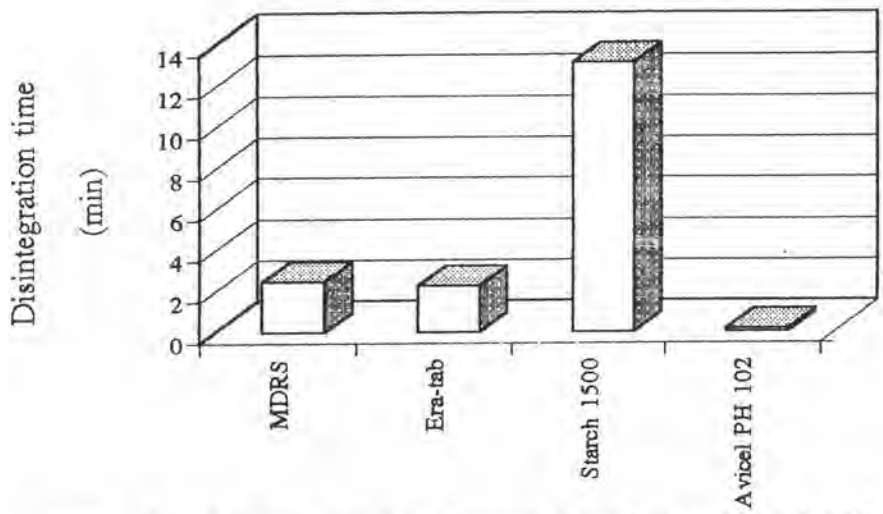



Figure 52 Comparison disintegration time of isoniazid tablets containing various diluents and MDRS

**5. Percent Label Amount**

The average of percent label amount of isoniazid tablets are presented in Table 22. The percent label amount of various diluents were within the limit of USP XXIII standard (90-110 %).

**6. Dissolution of Tablets**

According to Figure 53, the dissolution time profiles of isoniazid tablets prepared from various diluents were seemed not different. The . plot of $T_{80\%}$ (the times at 80 % drug released) were ranked as in the following: Starch $1500^R$ > Avicel PH $102^R$ > Modified rice starch > Era-$Tab^R$ and met the requirement of the test for dissolution of tablets (Table 22, Figure 54 ). The statistical differences are illustrated in Table 46 and 47 (Appendix V). It showed that no significant differences of $T_{80\%}$

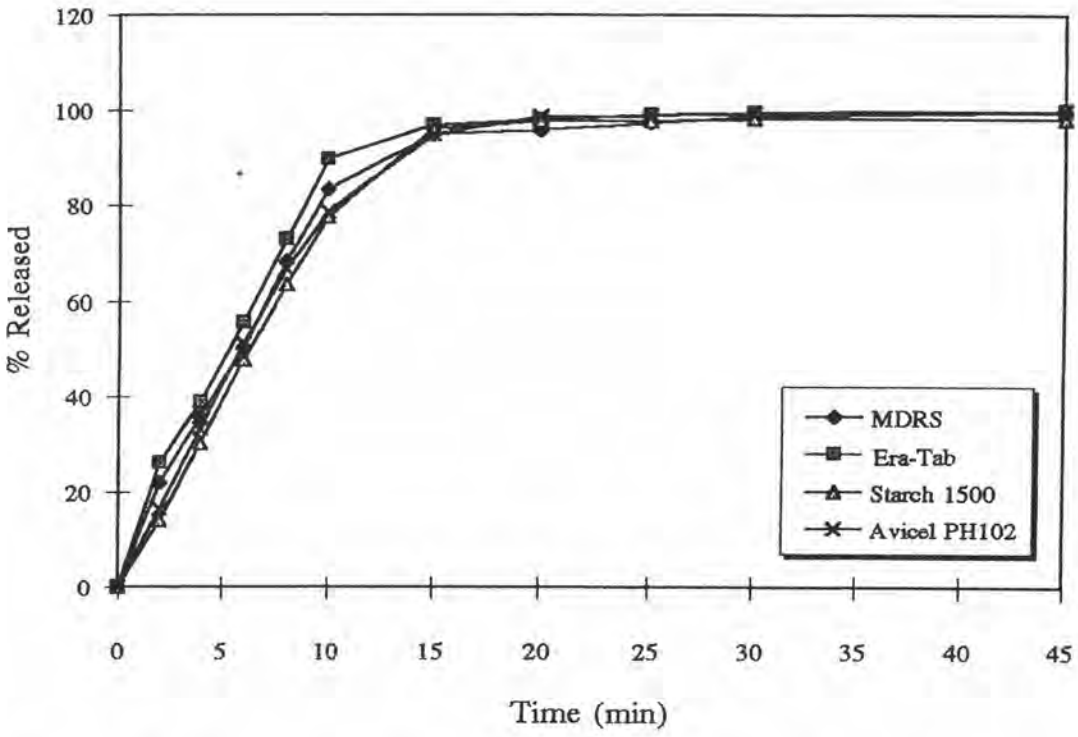



Figure 53 Comparison dissolution profiles of isoniazid containing various diluents and MDRS

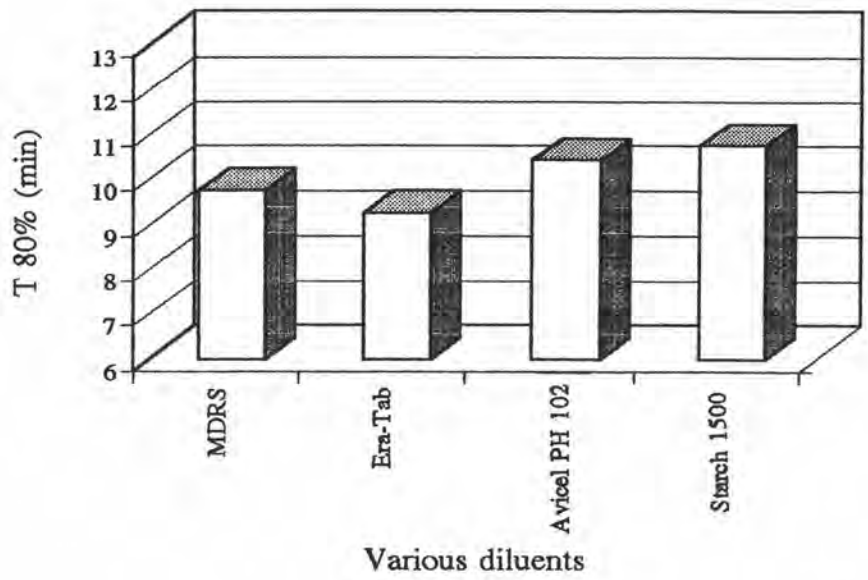



Figure 54 Comparison $T_{80\%}$ of isoniazid containing various diluents and MDRS

were observed in the groups of diluents: Modified rice starch and Era-Tab$^R$, Avicel PH 102$^R$ and Starch 1500$^R$. At 45 minutes interval, the amounts of isoniazid dissolved were 99.92 %, 100.00 %, 98.31 % and 99.93 % in tablet containing modified rice starch, Era-Tab$^R$, Starch 1500$^R$ and Avicel PH 102$^R$, respectively.

**Hydrochlorothiazide**

**1. Weight Variation**

The mean and standard deviation of hydrochlorothiazide tablets prepared from various diluents are presented in Table 23. In all cases, weight variation of tablets were within the limit of USP XXIII standard.

**2. Thickness**

The results of average thickness and standard deviation of hydrochlorothiazide tablets are illustrated in Table 23. They were ranked as follow: Avicel PH 102$^R$ > Modified rice starch > Era-Tab$^R$ > Starch 1500$^R$.

**3. Hardness**

From the data in Table 23, the hardness of tablets were all within the range of 4-5 kps.

**4. Disintegration Time**

The disintegration time of hydrochlorothiazide tablets are presented in Table 23 and Figure 55. They could be ranked as follow: Starch 1500$^R$ > Modified rice starch > Era-Tab$^R$ > Avicel PH 102$^R$. The

Table 23 Physical properties of hydrochlorothiazide tablets prepared with commercial diluents and MDRS

| Diluents | Physical Properties of Tablets | | | | $T_{d0\%}$ (min:sec) | % Label Amount (±SD) |
|---|---|---|---|---|---|---|
| | Wt. (mg±SD) | TN. (mm±SD) | HN. (kp±SD) | D.T. (min±SD) | | |
| MDRS | 351.9 (0.985) | 4.272 (0.037) | 4.980 (0.743) | 2.275 (0.285) | 15:03 (1.107) | 98.87 (0.935) |
| Era-tab | 352.6 (0.785) | 3.662 (0.035) | 4.788 (0.035) | 1.030 (0.215) | 12:31 (1.217) | 100.43 (0.860) |
| Starch 1500 | 351.7 (1.002) | 3.522 (0.020) | 4.700 (0.588) | 3.435 (0.123) | 17:15 (0.954) | 99.65 (0.947) |
| Avicel PH102 | 348.5 (1.056) | 4.278 (0.036) | 4.211 (0.352) | 0.148 (0.017) | 10:30 (1.412) | 101.58 (1.103) |

Wt. = Weight TN. = Thickness

HN. = Hardness D.T. = Disintegration time

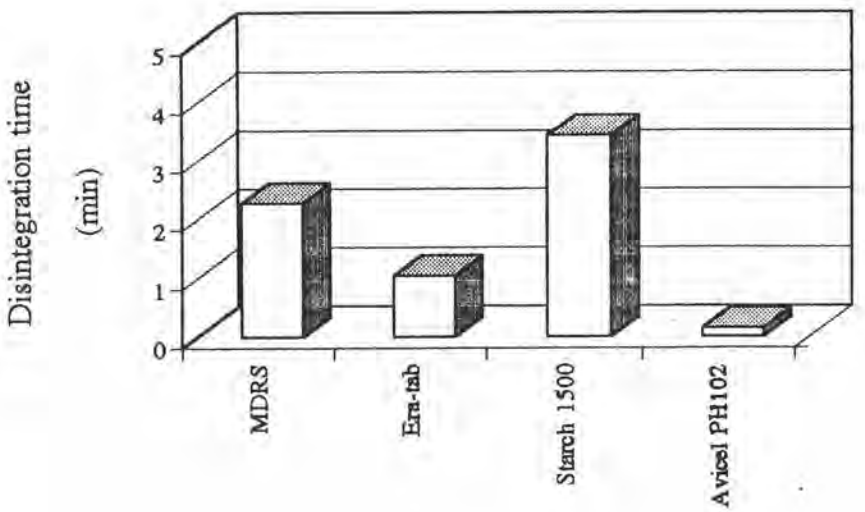



Figure 55 Comparison disintegration time of hydrochlorothiazide tablets containing various diluents and MDRS

statistical differences ($p < 0.05$) are presented in Table 44 and 45 (Appendix V).

**5. Percent Label Amount**

The results of the mean and standard deviation of percent labelamount of hydrochlorothiazide tablets are presented in Table 23. The data were within the range of USP XXIII standard (90-110 %).

**6. Dissolution of Tablets**

Figure 56 shows the dissolution time profiles of hydrochlorothiazide tablets prepared from various diluents. For the first 10 minutes, the results showed that dissolution rate decreased in the following orders: Era-Tab$^R$ > Avicel PH 102$^R$ > Starch 1500$^R$ > Modified rice starch. However, about 10 minutes later, dissolution rate of Avicel PH 102$^R$ and modified rice stach were higher than that of Era-Tab$^R$ and Starch 1500$^R$, respectively. The plots of $T_{60\%}$ versus various diluents are shown in Figure 57 (see data in Table 23 ). It was found that $T_{60\%}$ decreased in the following orders: Starch 1500$^R$ > Modified rice starch > Era-Tab$^R$ > Avicel PH 102$^R$. The statistical differences ($p < 0.05$) are illustrated in Table 48 and 49 (Appendix V). $T_{60\%}$ of all tablet formulas were accepted according to the USP XXIII requirement. At 60 minutes interval, the amounts of hydrochlorothiazide dissolved were 80.75 %, 80.09 %, 77.88 % and 86.55 % in tablet containing modified rice starch, Era-Tab$^R$, Starch 1500$^R$ and Avicel PH 102$^R$, respectively.

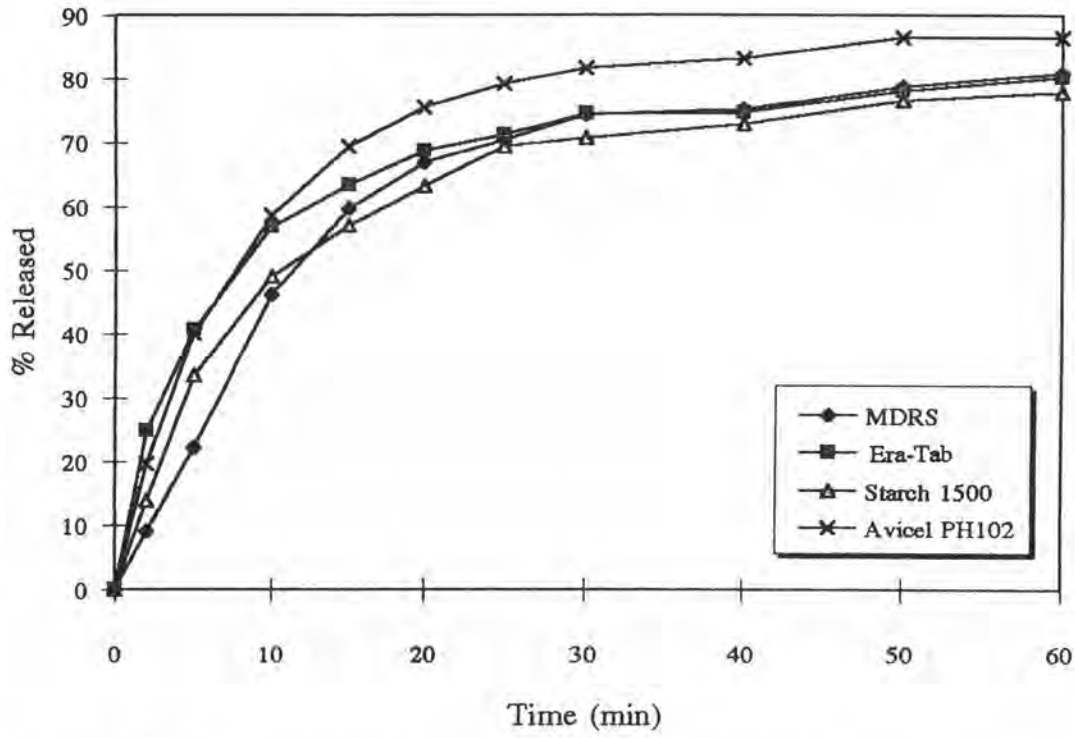



Figure 56 Comparison dissolution profiles of hydrochlorothiazide tablets various diluents and MDRS

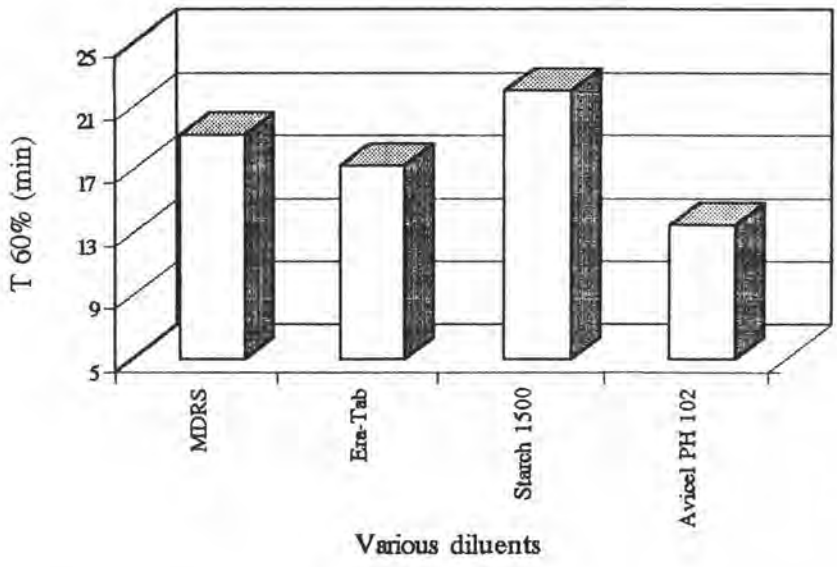



Figure 57 Comparison $T_{60\%}$ of hydrochlorothiazide containing various diluents and MDRS