CHAPTER VIII

EFFECT OF AGING ON DISINTEGRATING EFFICIENCY OF MODIFIED TAPIOCA STARCH

Influence of storage in different conditions on the performance of disintegrant in tablet product have been studied by a number of researchers.

Khan and Rhodes (1975) have studied water-sorption of disintegrants. They clearly demonstrated that the disintegrants with the highest water uptake are generally the most effective in most tablet system. After aging under humid conditions the tablets containing cation exchange resin and sodium starch glycolate showed a considerable increase in their disintergrating time and a marked reduction in their strength after storage.

Gordon and Chowhan (1987) have studied the effect of tablet composite solubility and hygroscopicity on dissolution efficiency of three super disintegrants. The results indicated that hygroscopic ingredients decreased the effectiveness of super disintegrants.

Sheen and Kim (1989) have studied the water sorption properties of some commonly used disintegrants to evaluate the disintegration and physical mechanical properties of tiaramide hydrochloride tablets containing 5% of disintegrants. They found that the tablets containing sodium starch glycolate changed insignificantly after exposure to humidity. The tablets containing high water sorption disintegrants (croscarmellose sodium, crospovidone and sodium starch glycolate) showed marked decreased in hardness after they were stored in a high humidity atmosphere.

Purpose of the study

The scope of the study in this part is to study the effect of aging on efficiency of modified tapioca starch as tablet disintegrant. The disintegration times and hardness of tablets which prepared using MTS as disintegrant when stored in various percent relative humidity condition were observed.

Materials and Methods

Materials

Paracetamol	(Monsanto, USA)
Explotab[R]	(Mendell, NY, USA, Lot. No E 4222)
Primojel[R]	(AVEBE, Holland)

Methods

Evaluation of the disintegrating property of paracetamol tablets using MTS as disintegrant after aging at various time intervals.

1 Preparation of paracetamol tablets.

The experimental formulation of paracetamol tablet and the procedure of tablet manufacturing were described in the chapter VII . The modified potato starches which are available in market were evaluated to compare their disintegrating efficiency.

2 The tablets were kept in controlled conditions at the relative humidity about 52.0% and 71.3% at constant temperature of 37 ^{o}C.

3 The tablets were randomly selected at various time intervals of 0, 4, 8 and 12 weeks. Then the tablets were subjected to a hardness tester (Schleuniger-2E, model 2E/205). The mean and standard deviation were calculated.

4. The disintegration times of tablet were determined in deionized water using Hanson Research Tablet Disintegration Tester (model 64-700-156, USA). The mean of six determinations and standard deviation were calculated.

5. The dissolution study of paracetamol tablets were conducted using USP dissolution type II method as described in chapter VII. The percent drug dissolved were calculated from absorbance-concentration curve.

Evaluation of disintegrating efficiency of MTS powder after aging at various time intervals.

The MTS powders were kept in bottles which controlled the relative humidity about 52.0% RH and 71.3% RH. The bottles were kept in constant temperature cabinet at 37 ^{o}C. After the end of 4 weeks, 8 weeks and 12 weeks, the storage MTS powder were sampled and incorporated in paracetamol tablet formulation as previously described. The tablet were compressed with compression force about 2800 pounds. Then the hardness, disintegration times and dissolution rate of paracetamol tablets prepared from the storage MTS powder were evaluated.

Results and Discussion

Evaluation of the hardness of paracetamol tablets after aging at various time intervals.

The hardness of tablets containing MTS as disintegrant after aging were insignificant different both in 52.0% RH and 71.3% RH as shown in Table 21.

Table 21 Hardness of Paracetamol Tablets Containing 4% Various Disintegrants, After Aging.

week	MTS		Explotab R		Primojel R	
	52.0% RH	71.3% RH	52.0% RH	11.3% RH	52.4% RH	71.3% RH
0	12.82 (0.48)	12.82 (0.48)	10.11 (0.51)	10.11 (0.51)	10.33 (0.40)	10.3 (0.40)
4	14.63 (0.46)	14.21 (0.36)	16.72 (0.94)	12.46 (0.37)	13.76 (0.35)	14.11 (0.42)
8	14.85 (4.45)	14.35 (0.56)	19.55 (0.49	15.95 (0.49)	14.68 (0.41)	19.05 (0.23)
12	13.33 (0.25)	13.45 (0.53	17.28 (0.64)	13.51 (0.47)	13.58 (0.45)	17.50 (0.76)

While the hardness of tablets containing Explotab^R and Primojel^R as disintegrant increased gradually with the time.

The hardness of tablets using Explotab^R and Primojel^R were maximum after storage for 8 weeks and then declined after storage for 12 weeks both in 52.0% RH and 71.3% RH. This could be explained that it was due to sodium chloride contents (byproduct) in the products which preferred to absorb moisture hence, the tablets absorbed moisture rapidly caused disintegrant within the tablet matrix partially swelled and dissolved to act as a binder, by forming gel and liquid bridge mechanism, resulted increased in tablet hardness. The reduction in strength of tablet after storage 12 weeks could be explained that the excess absorption of moisture by the disintegrant within tablet thus causing swelling and bond disruption.

Evaluation of the disintegration times of paracetamol tablets after aging.

All of the disintegrants studied: MTS, Explotab^R and Primojel^R were affected by the moisture after keeping in the humid atmosphere. The disintegration times of tablets containing various disintegrants which kept in the different relative humidity at various time intervals were shown in Figure 72 and 73. The disintegration times increased as the exposure times increased both in 52.0% RH and 71.3% RH conditions. This could be described that the disintegrants within those tablets have lost some their absorption and swelling ability or disintegrant within the tablet matrix might absorb moisture and swell many times to fill up the porosity of the tablet. It caused reduction of water uptake into the tablet . However, the tablets containing MTS as disintegrant showed less changes of tablet strengths and disintegration times than tablets containing Explotab^R or Primojel^R as tablet disintegrant both in low and high humidity conditions.

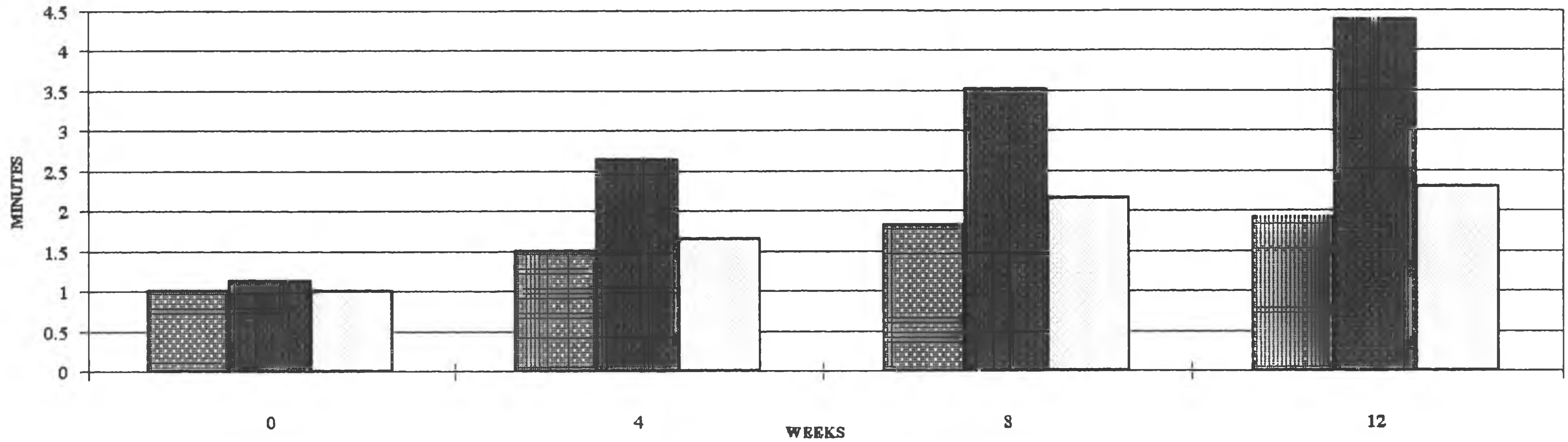
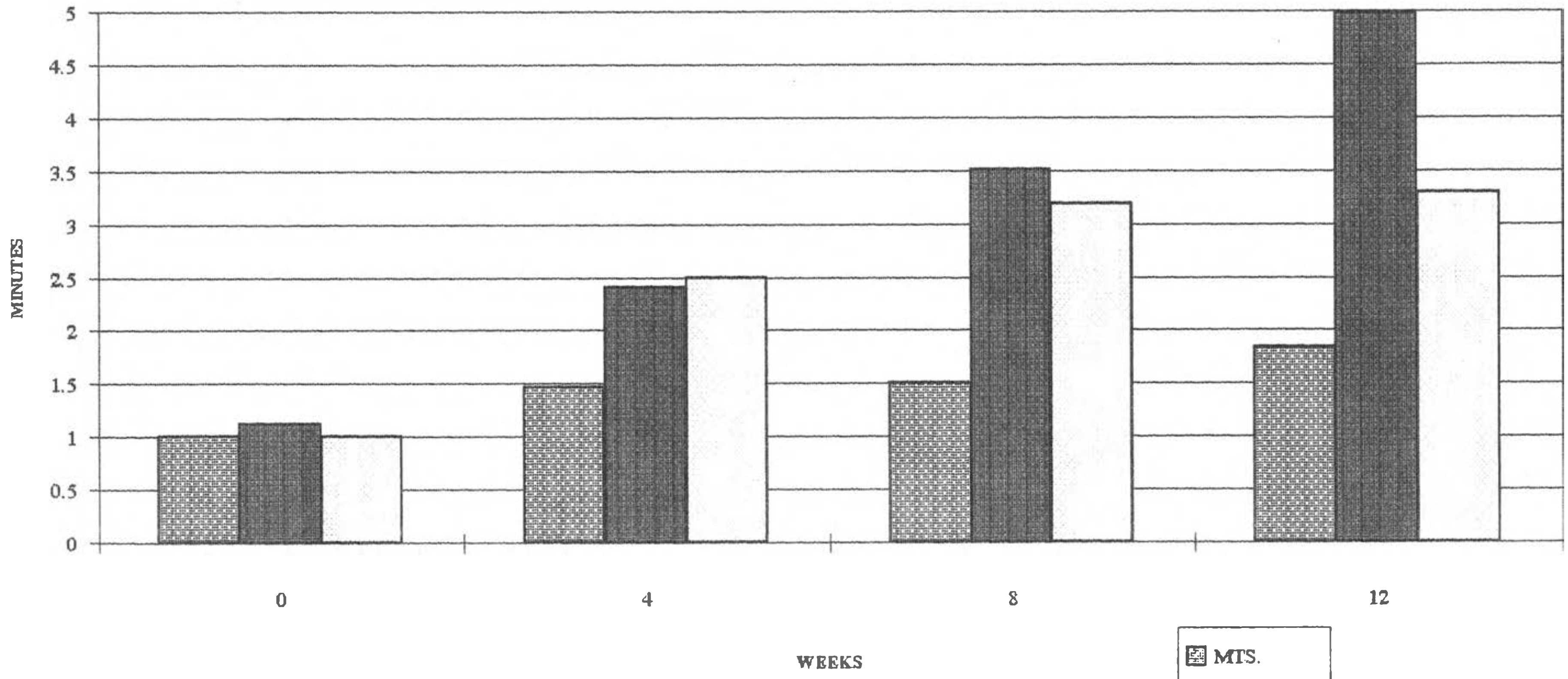


Figure 72 Disintegration Times of Paracetamol Tablets , After Aging (52.0 % RH).



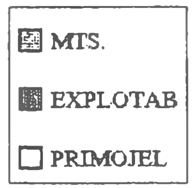


Figure 73 Disintegration Times of Paracetamol Tablets , After Aging
(71.3 % RH)

Dissolution study of aging paracetamol tablets.

The dissolution profiles of paracetamol tablets containing 4% MTS after aging at various time intervals were shown in Figure 74 and Figure 75. Although the disintegration times of paracetamol tablets using MTS as disintegrant increased during keeping in the range of 0-8 weeks , the dissolution rates of tablets were similar both in 52.0% RH and 71.3% RH conditions. However, after aging for 12 weeks the dissolution rates of paracetamol tablets decreased both in the 52.0% RH and 71.3% RH conditions. It was due to MTS within tablet matrix absorbed moisture from atmosphere and lost a swelling ability as previously described.

The comparative study of dissolution rates of paracetamol tablets using various modified starches as disintegrant after aging for 12 weeks were illustrated in Figure 76 and Figure 77. After aging for 12 weeks the paracetamol tablets containing MTS as disintegrant exhibited the dissolution profiles similar to those containing Explotab^{R} and Primojel^{R} as disintegrants.

Evaluation of disintegrating efficiency of MTS powder after aging.

The hardness and disintegration times of paracetamol tablets prepared using MTS powder after aging at various time intervals as disintegrant and tabletting at the same compression force were shown in Table 22.

Table 22 it was indicated that the hardness of paracetamol tablets using MTS powder which were kept in the 52.0% RH condition at various time intervals (4, 8, 12 weeks) did not changed. Nevertheless, the hardness of paracetamol tablets containing MTS powder which were kept in 71.3% RH condition at various time intervals increased as increased in aging time of MTS powder. This could be explained that the MTS absorbed moisture produced partially gel formation in crystal lattice of starch granules resulted MTS also

Table 22 Disintegration Times and Hardness of Paracetamol Tablets, After Aging Powder.

Aging Time	52.0 % RH		71.3 %	
	DT (min)	Hardness (Kp)	DT (min)	Hardness (Kp)
0	1.00 (0.02)	12.8 (0.48)	1.00 (0.02)	12.8 (0.48)
4	1.27 (0.02)	12.8 (0.28)	1.46 (0.12)	16.2 (0.18)
8	1.37 (0.03)	13.0 (0.35)	1.56 (0.02)	16.0 (0.38)
12	1.44 (0.06)	12.9 (0.33)	2.22 (0.05)	16.4 (0.52)

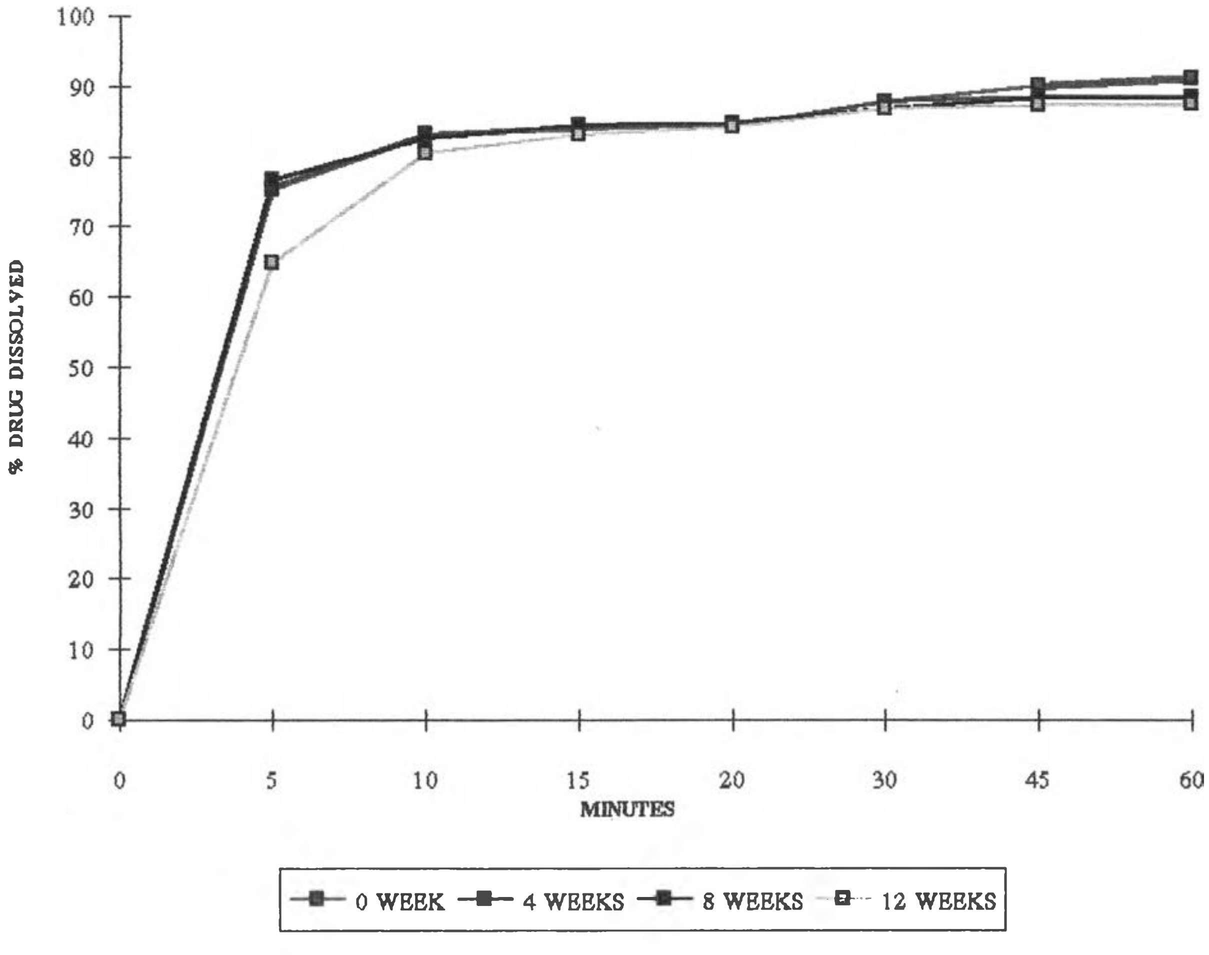


Figure 74 Dissolution Profiles of Paracetamol Tablets Containing MTS as Disintegrant , After Aging (52.0% RH).

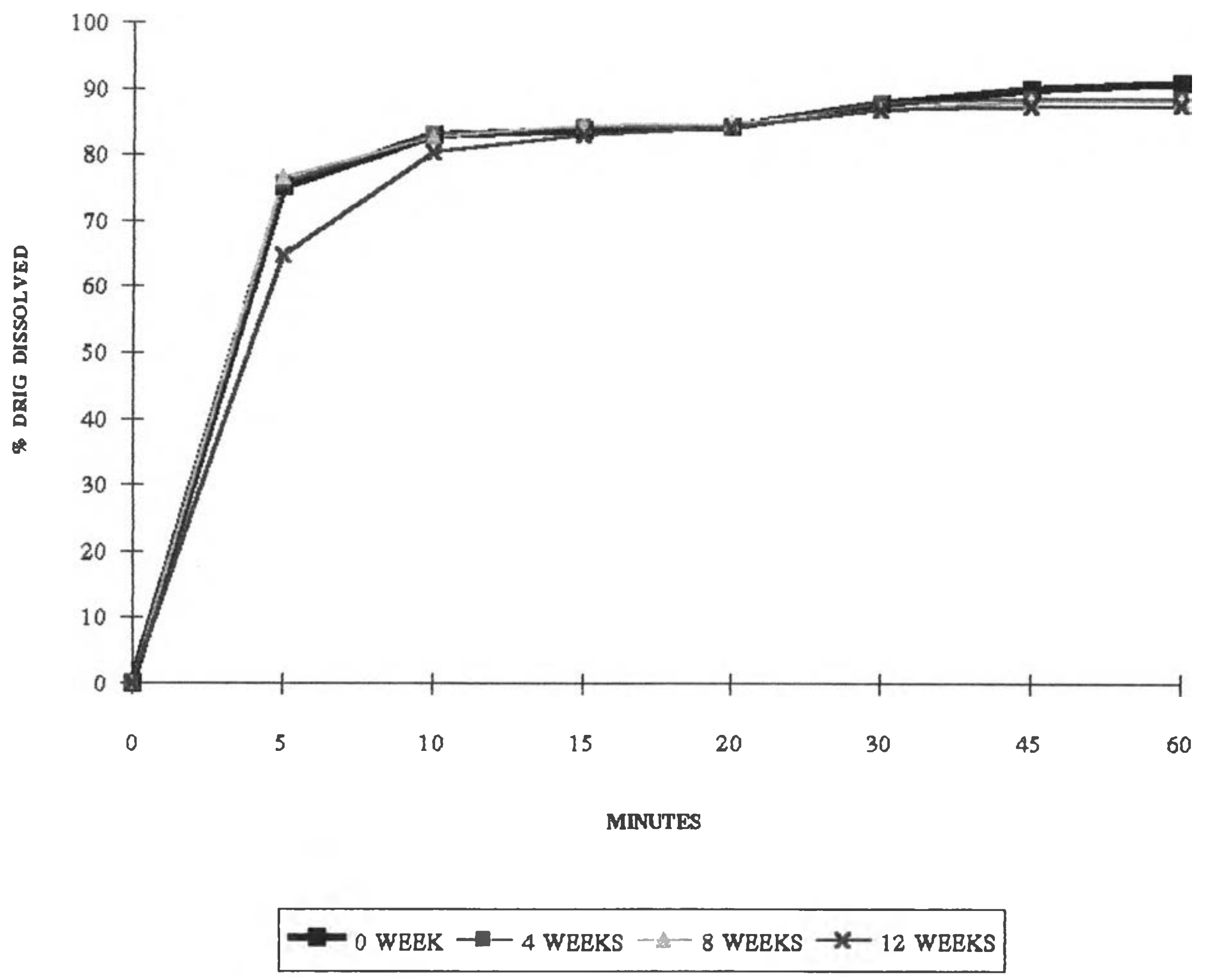


Figure 75 Dissolution Profiles of Paracetamol Tablets Containing 4% MTS as Disintegrant , After Aging (71.3 %).

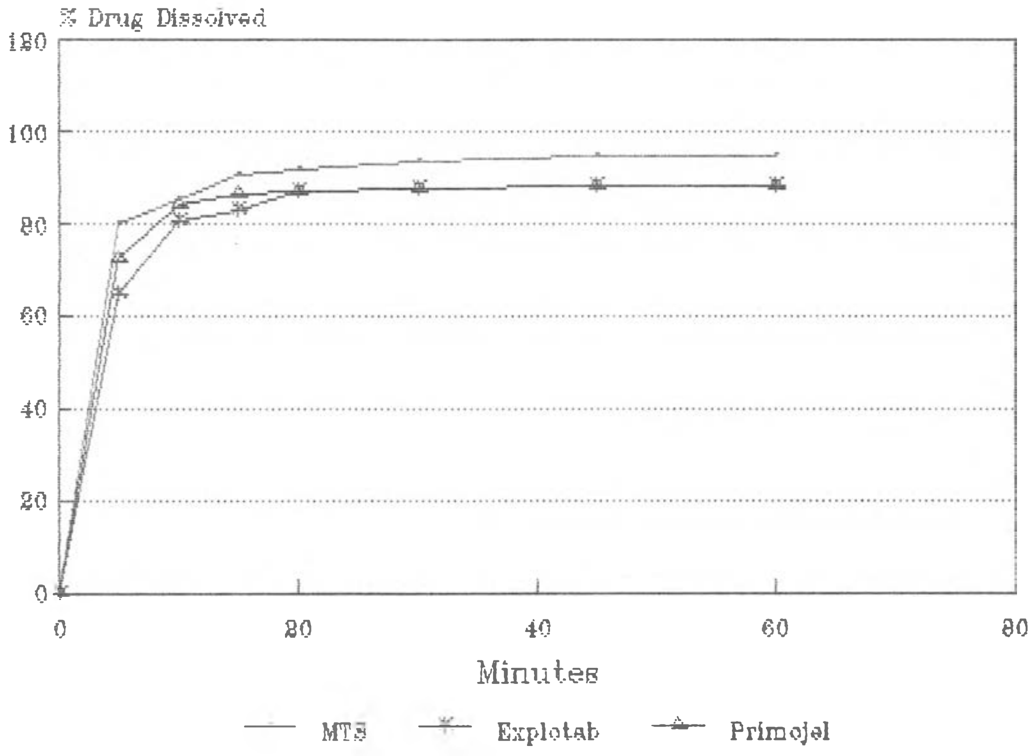


Figure 76 Dissolution Profiles of Paracetamol Tablets Containing 4 % Various Disintegrants, After Aging for 12 weeks. (52.0 % RH)

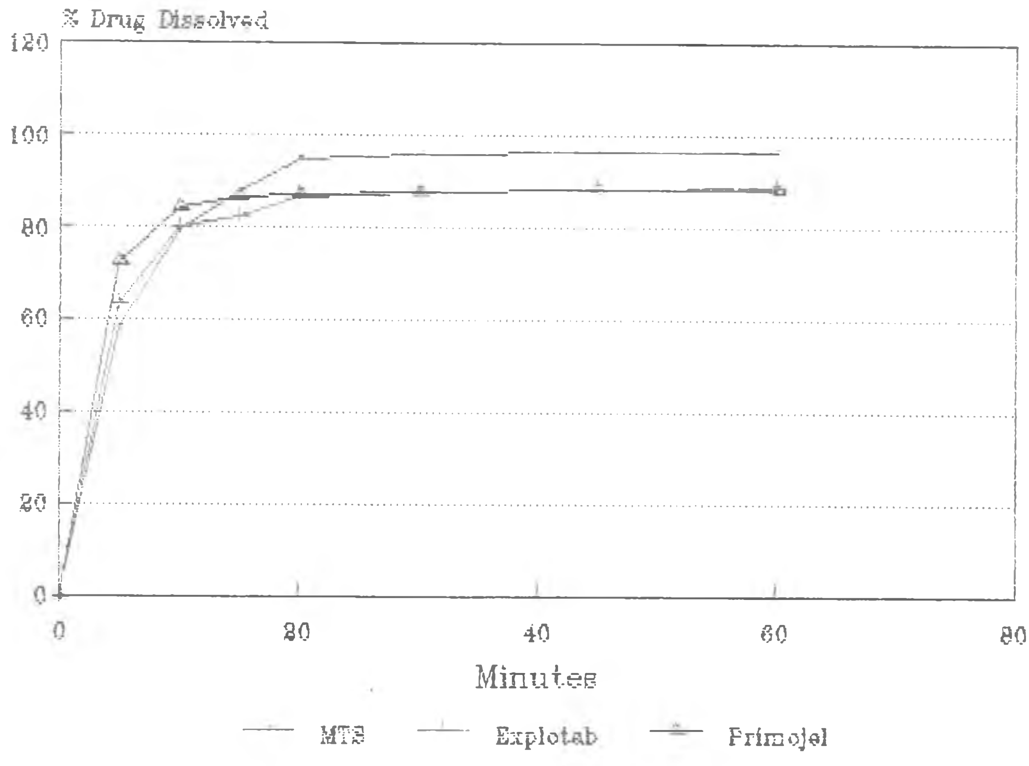


Figure 77 Dissolution Profiles of Paracetamol Tablets Containing 4 % Various Disintegrants, After Aging for 12 weeks. (71.3 % RH)

played a role as a binder and the excess moisture content in MTS powder might strengthen the intergranular liquid-bridge of tablet resulted an increase in tablet hardness.

As the aging time of MTS powder increased, the disintegration times of paracetamol tablets using MTS as disintegrant gradually increased. This could be attributed to moisture absorption of MTS powder might cause reduction in its swelling ability and its disintegrating efficiency of MTS.

Although the disintegration times of paracetamol tablets using 4% MTS powder which were kept at various time intervals increased but the dissolution rates of paracetamol tablets containing those MTS powder more closely resembled as shown in Figure 78. At the high relative humidity condition (71.3% RH) the paracetamol tablets containing 4% MTS which were kept for 12 weeks exhibited a low dissolution rate as shown in Figure 79. This could be explained that the long time exposure of MTS powder to the high relative humidity causing moisture absorption of MTS powder and markedly decreased in swelling capacity which was the important mechanism for tablet disintegration of starch and starch derivatives.

Conclusions

Moisture might affect the tablet strength and disintegration time of the paracetamol tablet containing disintegrant which their swelling are an important mechanism of action to make tablet disintegration such as Explotab^{R}, Primojel^{R} and Modified tapioca starch. Although the moisture affected hardness and disintegration time of tablet using MTS as disintegrant. In fact, the results clearly indicated that moisture less affected the disintegrating efficiency of modified tapioca starch than that of modified potato starches: Explotab^{R} and Primojel^{R}.

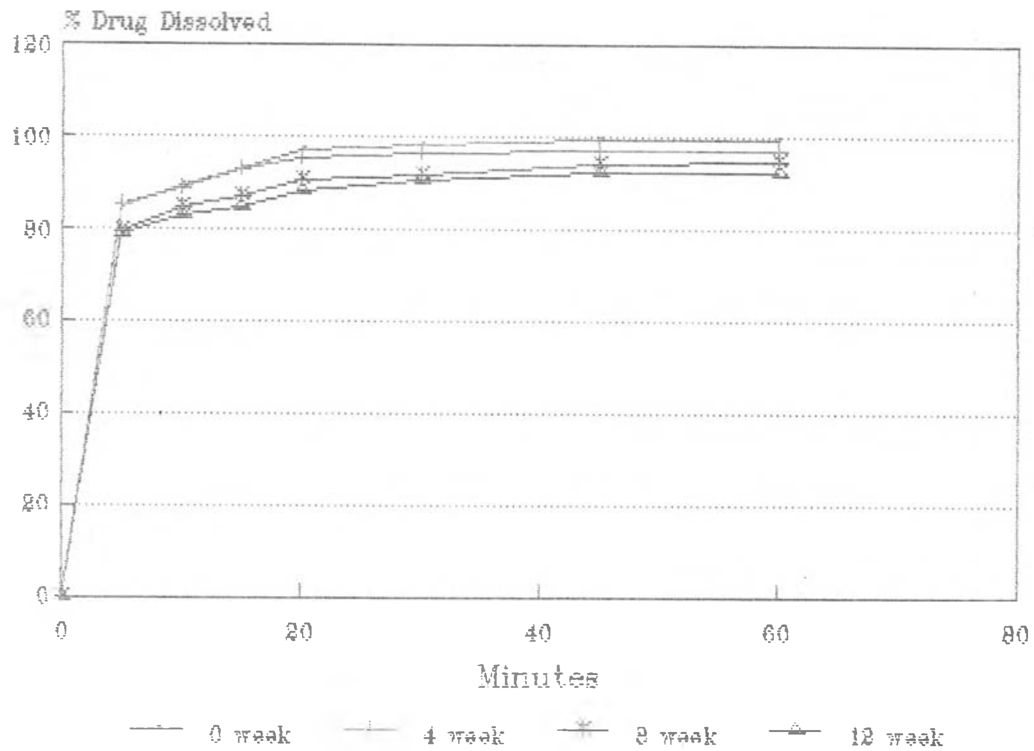


Figure 78 Dissolution Profiles of Paracetamol Tablets Containing 4 % MTS Powder after Aging at Various Time Intervals (52.0 % RH)

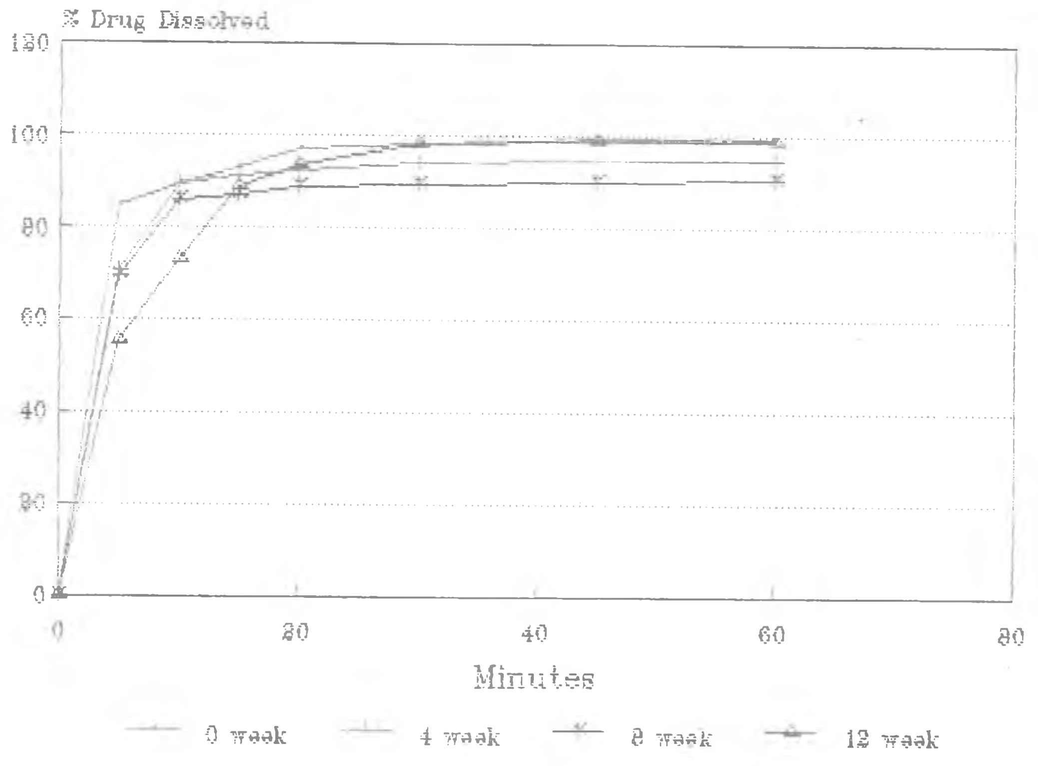


Figure 79 Dissolution Profiles of Paracetamol Tablets Containing 4 % MTS Powder after Aging at Various Time Intervals (71.3 % RH)