International Journal of Pharmaceutics, 22 (1984) 127–130
Elsevier

IJP 00734

Short Communications

Effect of storage on crushing strength, disintegration and drug release from mixed tablet bases

A.M. Molokhia

Dept. of Pharmaceutics, College of Pharmacy, King Saud University, Riyadh (Saudi Arabia)

(Received January 20th, 1984)
(Modified version received May 31st, 1984)
(Accepted June 6th, 1984)

Several studies have been reported (Horhota et al., 1976; Lausier et al., 1977; Chowhan and Palagyi, 1978; Molokhia et al., 1982) on the changes in behavior of tablets upon storage. Such changes were found to be responsible for some bioavailability problems (York, 1977; Gouda et al., 1980). In a previous communication (Molokhia et al., 1982), the effect of two storage conditions 50 °C/50% relative humidity (R.H.) and 40 °C/90% R.H. on crushing strength, disintegration and drug release from single component tablet bases were reported. While lactose-, mannitol- and sorbitol-based tablets were subjected to significant physical changes, tricalcium phosphate and powdered cellulose-based tablets were resistant to changes over a period up to 53 days.

In this study, binary blends of the previously used tablet bases were incorporated with 25% benzoic acid, 4% starch, 2% talc and 1% magnesium stearate. Mixing was carried for 10 min in a tumbling mixer rotating at 60 rpm. The product was then compressed into tablets and examined for the effect of storage at 40 °C/90% R.H. on crushing strength, disintegration and drug release. The tablets, stored in paper bags, were examined at different time intervals over 10 weeks. The crushing strength and disintegration were determined as before (Molokhia et al., 1982). The drug release was determined by following the amount of benzoic acid dissolved as function of time using a USP dissolution apparatus and phosphate buffer 0.05 M, pH 6.0, as solvent. Samples were taken every 5 min for 35 min, filtered through 0.45 μm Millipore filter and assayed by measuring UV absorption at 222 nm.

Fig. 1 shows the effect of storage on the crushing strength of tablets made of lactose and tricalcium phosphate. Similar graphs were obtained for each group of

Correspondence: A.M. Molokhia, Department of Pharmaceutics, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia.

tablets. In general, the lactose-containing tablets showed a decrease in crushing strength of about 30% after 4 days of storage with no significant change after that. The crushing strength of mannitol-containing tablets, however, only decreased by about 15% after 4 days and remained almost constant thereafter. Sorbitol-containing tablets have shown sharp decrease in crushing strength during the first 18 days of storage, after which, the tablets were completely deformed by losing their structure and were discarded. The difference in the effect of storage on crushing strength of tablets made of base blends from that effect on crushing strength of tablets made of single bases (Molokhia et al., 1982) is probably because of the different methods used in making the tablets and the incorporation of tricalcium phosphate or cellulose with the other bases.

Fig. 2 is a representative graph for the effect of storage on tablets disintegration. No significant effect was noticed on the disintegration of tablets containing lactose. The disintegration time of the mannitol-containing tablets did not change during the first 32 days, after which, an increase in the time was observed. Sorbitol-containing tablets showed a dramatic decrease in the disintegration time which correlates well with the observed decrease in crushing strength. Fig. 3 shows a typical benzoic acid dissolution profile from tablets stored for different time intervals. Similar curves were obtained for each group of tablet bases. The lactose-containing tablets showed initial increase in drug release rate upon storage to a maximum after 18 days in presence of tricalcium phosphate (Fig. 3) and 8 days in presence of cellulose. The rate was then decreased until it reached its original value after 50 days in presence of tricalcium phosphate and 32 days in presence of cellulose. Further storage led to further decrease in the rate. The benzoic acid release from mannitol-containing tablets showed similar behavior upon storage except that, the decrease in the release rate towards the end of the storage period was more pronounced, especially in

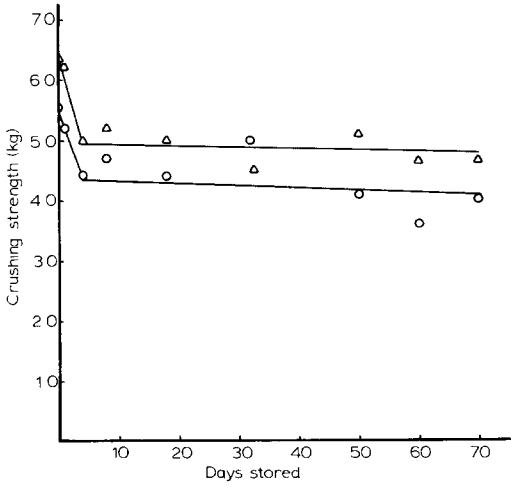

Fig. 1. Effect of storage on the crushing strength of tablets. △, 70% lactose and 30% tricalcium phosphate; and ○, 90% lactose and 10% tricalcium phosphate.

presence of the higher concentration of cellulose. Sorbitol-containing tablets, before losing their structure, showed a significant increase in drug release upon storage. The increase was more pronounced in the presence of cellulose than in the presence of

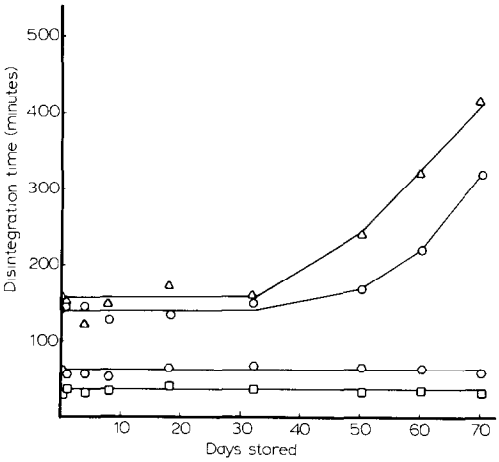

Fig. 2. Effect of storage on the disintegration time of tablets. △, 70% mannitol, 80% cellulose; ○, 90% mannitol, 10% cellulose; ○, 70% lactose, 30% tricalcium phosphate; and □, 90% lactose, 10% tricalcium phosphate.

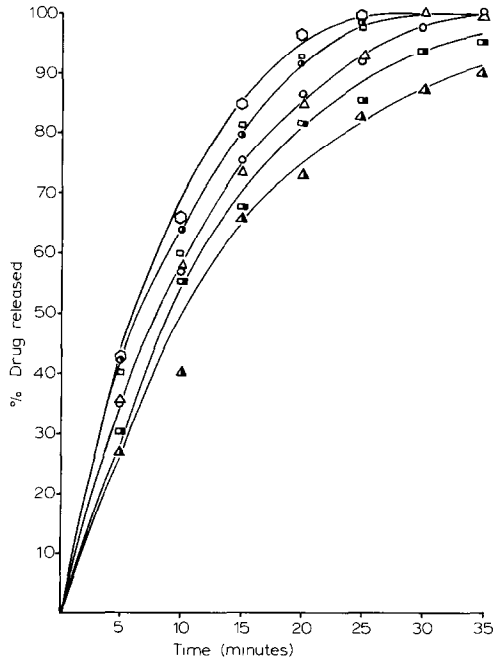

Fig. 3. Drug release from stored tablet made of 70% lactose and 30% tricalcium phosphate. ○, zero days; △, 1 and 45 days; □, 4 days; ◑, 8 days; ○, 18 days; ◨, 60 days; and ▲, 70 days.

tricalcium phosphate. No effect of varying the concentration of tricalcium phosphate or cellulose was observed.

The results of this study when compared with the results of our previous findings (Molokhia et al., 1982) may lead to the following conclusions: (a) tablet bases, when present in mixtures, do not necessarily react to storage conditions similarly to their individual reaction; (b) for each combination of tablet bases, the change in crushing strength, disintegration and drug release may or may not correlate with each other; and (c) long-term storage effect under the same or different conditions used in a study cannot be predicted as tablets' behavior may change during storage. While some questions raised by this study may be answered by the absence of moisture during tabletting, reasons for the decrease of drug release after an initial increase upon storage are still to be sought.

Acknowledgements

The author is grateful to Mr. M. Bazzawi for technical assistance and Mr. K. Abbas for typing the manuscript. This research was supported by the Research Center of the College of Pharmacy, King Saud University.

References

Chowhan, Z.T. and Palagyi, L., Hardness increase induced by partial moisture loss in compressed tablets and its effect on in-vivo dissolution. J. Pharm. Sci., 67 (1978) 1385–1389.

Gouda, M.W., Moustafa, M.A. and Molokhia, A.M., Effect of storage conditions on erythromycin tablets marketed in Saudi Arabia. Int. J. Pharm., 5 (1980) 345–347.

Horhota, S.T., Burgio, J., Lonski, L. and Rhodes, C.T., Effect of storage at specified temperature and humidity on properties of three directly compressible tablet formulations. J. Pharm. Sci., 65 (1976) 1746–1749.

Lausier, J.M., Chiang, C.W., Zompa, H.A. and Rhodes, C.T., Aging of tablets made with dibasic phosphate dihydrate as matrix. J. Pharm. Sci., 66 (1977) 1636–1637.

Molokhia, A.M., Moustafa, M.A. and Gouda, M.W., Effect of storage conditions on the hardness, disintegration and drug release from some tablet bases. Drug Develop. Ind. Pharm., 8 (1982) 283–292.

York, P., The shelf life of some antibiotic preparations stored under tropical conditions. Pharmazie, 32 (1977) 101–104.