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EFFECT OF STORAGE CONDITIONS ON THE HARDNESS, DISINTEGRATION AND DRUG RELEASE FROM SOME TABLET BASES

Abdulla M. Molokhia, Mamdouh A. Moustafa and M. Wafik Gouda,
Department of Pharmaceutics, College of Pharmacy,
University of Riyadh, Riyadh,
Saudi Arabia.

ABSTRACT

The effect of storage at relatively high temperature and humidity on tablets prepared from different bases was studied for up to eight weeks. Drug release from tablets was followed by measuring the concentration of a marker (amaranth) in the dissolution medium. Lactose and mannitol based tablets showed an increase in hardness and disintegration time, and a decrease in the initial rate of drug release. Sorbitol based tablets, stored under 50°C/50% relative humidity (R.H.), showed a decrease in hardness and slower disintegration and dissolution. When stored under 40°C/90% R.H., the tablets were completely deformed within three days. Tricalcium phosphate and cellulose-based tablets did not show any storage related changes in hardness, disintegration or drug release.

INTRODUCTION

Excipients used in tablet formulation constitute, in most cases, the greater part of the tablet weight. Directly compressi-

ble bases are widely used in tablet manufacturing since they provide the properties sought in the mixed tablet ingredients, in particular, ease of compaction. A good tablet base should not only be inert and compressible but should also be resistant to storage. Physical changes in tablet excipients during and/or after tablet manufacturing were reported in several publications (1-11). Some of the changes which took place in the tablet bases were found to be responsible for many of the bioavailability problems experienced with drugs taken in tablet form (5, 7, 8). A marked decrease in the rate of drug dissolution has been observed when some antibiotic and sulfonamide tablets were stored at relatively high temperature and humidity (12). Similar storage effects have also been observed in our laboratories for erythromycin tablets (13).

In this investigation, the effects of storage at 50°C/50% relative humidity (R.H.) and 40°C/90% R.H., on tablets prepared from different bases were studied. The changes in hardness, disintegration and release rate of a marker were followed for up to eight weeks.

EXPERIMENTAL

Preparation of Tablets

Lactose monohydrate[14], cellulose[15], tricalcium phosphate[16], sorbitol[14] and mannitol[17] powders were granulated[18] with a hydroalcoholic solution of amaranth. The wet granules were dried at 50°C in a hot air oven and sieved through a number 16 sieve. The granules were then thoroughly mixed with 2% W/W of magnesium stearate powder as a lubricant and the blend was compressed[19] into tablets (12 mm diameter, 1 gm each).

Storage Conditions

Tablets in paper bags were stored in two climatic chambers[20] adjusted at 50°C/50% R.H., and 40°C/90% R.H. Samples of tablets

of each base were taken at various time intervals over 8 weeks for hardness determination, disintegration and drug dissolution testing.

Hardness

Hardness was determined using an Erweka hardness tester[21]. Six tablets were used for each determination from which the mean was calculated.

Disintegration

Disintegration was determined[22] using the U.S.P. method. Phosphate buffer, 0.05 M, pH 6.5 at 37 $\pm$ 0.2°C was the disintegration medium. Six tablets were used for each determination.

Dissolution

Dissolution rates of amaranth were determined[23] in phosphate buffer, 0.05 M, pH 6.5. The apparatus was essentially of U.S.P. specifications. Exactly 900 ml of solvent at a temperature of 37 $\pm$ 0.1°C and a stirring rate of 50 r.p.m. were used for each determination. The rotating basket was 1.8 cm from the bottom of the dissolution vessel. Samples were withdrawn at various time intervals, filtered through a 0.45 µm millipore filter, appropriately diluted with phosphate buffer. The amounts of amaranth dissolved were determined by measuring its absorbance at 526 nm. Three tablets were used for each determination.

RESULTS AND DISCUSSION

Tables 1 and 2 summarize the effects of storage on tablet hardness and disintegration time. Figs. 1 through 4 show the dissolution patterns of amaranth as a function of storage time.

Lactose and mannitol based tablets showed an increase in hardness (Table 1) and disintegration time (Table 2), and a decrease in the initial rate of drug release upon storage

(Figs. 1 & 2). This effect which was more pronounced under 40°C/90% R.H., is probably due to increased inter-particle bonding through partial surface solution and recrystallization of the base.

Sorbitol based tablets, when stored under 50°C/50% R.H., showed a decrease in hardness (Table 1) and slower disinteg-

TABLE 1

Effect of Storage at 50°C/50% R.H. and 40°C/90% R.H. on Tablet Hardness

Tablet Base	Storage Condition	Hardness (kgm) of Tablets Stored for (days)					
		0	3	10	21	38	53
Lactose	50°C/50% R.H.	13.2	13.9	14.3	14.7	>15.0	>15.0
	40°C/90% R.H.	13.2	14.9	>15.0	>15.0	>15.0	>15.0
Mannitol	50°C/50% R.H.	7.2	8.8	9.7	9.9	11.2	11.5
	40°C/90% R.H.	7.2	7.9	8.8	9.4	11.9	12.3
Sorbitol	50°C/50% R.H.	14.2	11.2	9.0	8.9	8.5	8.3
	40°C/90% R.H.	14.2	----	----	----	----	----
Tri-calcium phosphate	50°C/50% R.H.	11.5	10.3	10.7	11.6	11.9	11.6
	40°C/90% R.H.	11.5	10.9	10.8	10.8	10.9	10.9
Cellulose	50°C/50% R.H.	7.3	6.7	6.7	7.3	7.1	7.3
	40°C/90% R.H.	7.3	6.5	6.7	7.3	7.1	6.9

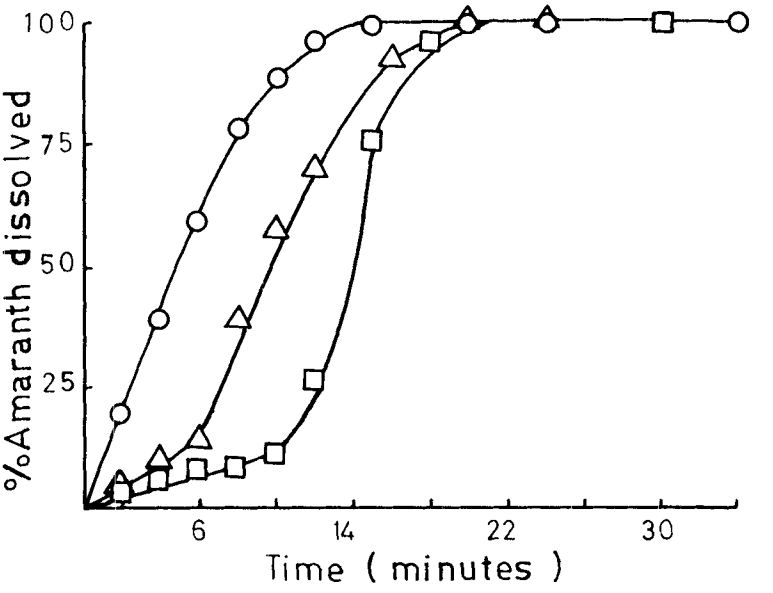

FIGURE 1

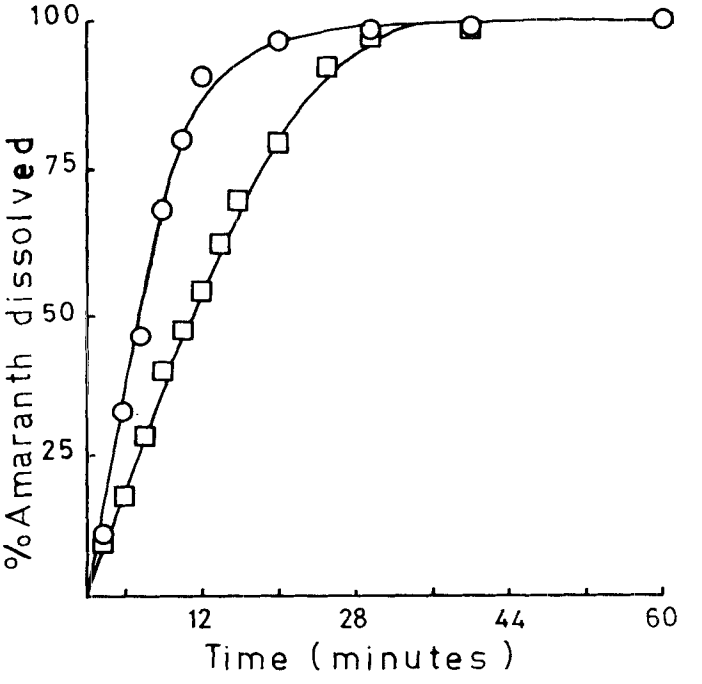

FIGURE 2

ration (Table 2) and dissolution (Fig. 3). When stored under 40°C/90% R.H., the tablets were completely deformed, within three days, due to moisture absorption.

Tricalcium phosphate and cellulose-based tablets did not show any storage related change in hardness (Table 1), disintegration time (Table 2) or drug release (Fig. 4). Although

TABLE 2

Effect of Storage at 50°C/50% R.H. and 40°C/90% R.H. on Tablet Disintegration Time

Tablet Base	Storage Condition	Disintegration Time (min) of Tablets Stored for (days)					
		0	3	10	21	38	53
Lactose	50°C/50% R.H.	1.67	2.0	2.0	2.3	2.67	3.0
	40°C/90% R.H.	1.67	2.33	3.0	4.33	6.0	6.33
Mannitol	50°C/50% R.H.	2.67	3.67	3.67	4.0	4.33	4.33
	40°C/90% R.H.	2.67	3.0	3.67	4.67	5.33	5.67
Sorbitol	50°C/50% R.H.	4.33	4.0	3.0	2.33	2.33	2.33
	40°C/90% R.H.	4.33	----	----	----	----	----
Tricalcium phosphate	50°C/50% R.H.	167	172	175	169	180	175
	40°C/90% R.H.	167	167	175	162	179	170
Cellulose	50°C/50% R.H.	0.50	0.40	0.50	0.40	0.40	0.50
	40°C/90% R.H.	0.50	0.55	0.50	0.55	0.45	0.45

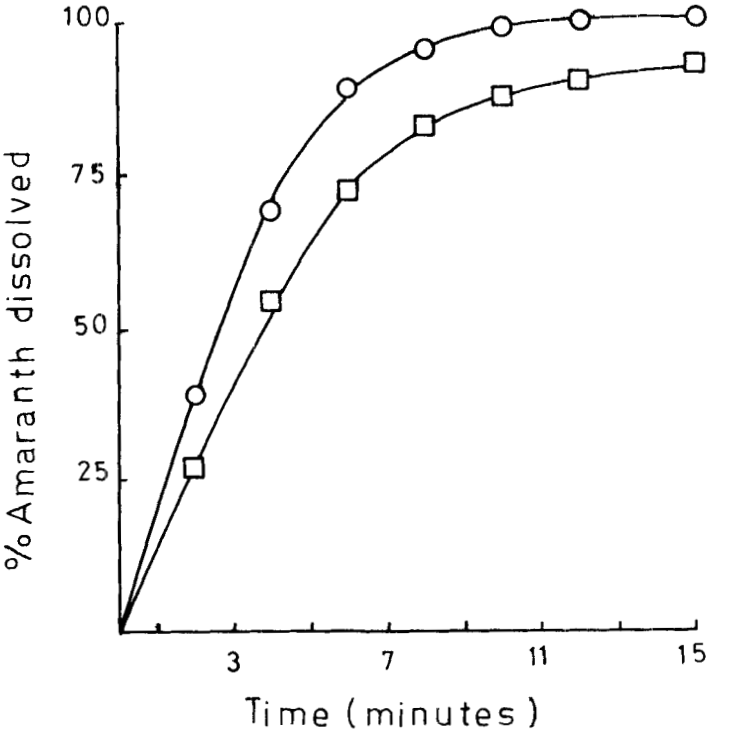

FIGURE 3

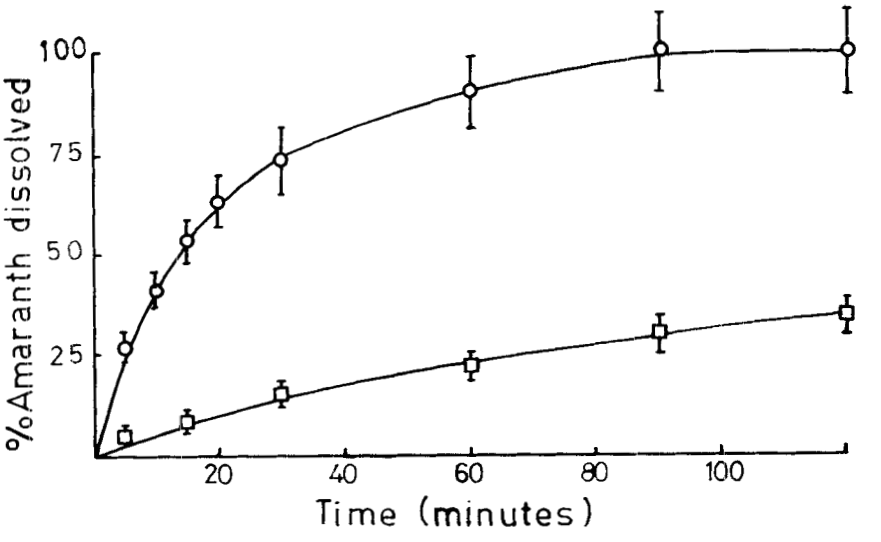

FIGURE 4

the disintegration of cellulose tablets was very fast (∿ 0.5 min.), complete release of amaranth was delayed to about 90 minutes. This can be due to sorption of amaranth on the porous cellulose powder. Tricalcium phosphate, on the other hand, is a very slightly soluble material and unless a disintegrant is included in the tablet formulation, drug release would be slow because of the limited surface area exposed to the dissolution medium.

In tropical as well as other countries, where drugs are sometimes stored under extremes of temperature and humidity, a tablet base which retains good pharmaceutical qualities is of prime importance. Results of the present investigation should help with the selection of tablet bases for the manufacture of tablets which satisfy this requirement. Among the five tablet bases examined in this study, tricalcium phosphate and cellulose proved to be quite resistant to storage under high temperature and/or high humidity.

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