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EFFECT OF TEMPERATURE AND HUMIDITY ON HARDNESS AND FRIABILITY OF PACKAGED PARACETAMOL TABLET FORMULATIONS

IQBAL AHMAD AND RIAZ HUSSAIN SHAIKH
Department of Pharmaceutical Chemistry,
Faculty of Pharmacy, University of Karachi,
Karachi-75270, Pakistan

ABSTRACT

The influence of various temperature and relative humidity conditions on changes in hardness and friability of five commercial brands of packaged paracetamol tablets stored over a period of six months has been investigated. At 75% RH all sample show deterioration in hardness at 25° (5-10%) and at 45° (10- 39%). At 100% RH there is a little difference in deterioration in hardness at 25° (16-24%) and 45° (20-28%) suggesting that once the critical moisture content is reached by the tablets, further increase in relative humidity has little effect on changes in hardness. Under the same conditions, all tablets show an increase in friability ranging from 2.83 to 8.02%. The over-all increase in friability with an increase in temperature from 25° to 45° at 75% and 100% RH is 0.0 to 25.2%. The results indicate that moisture sorption by tablet matrix through certain packaging materials may adversely affect the hardness and friability characteristics.

Introduction

Various official and unofficial tests are used to evaluate the tablet dosage forms during in-process controls. These tests include physical appearance, colour, odour, thickness, diameter, hardness, friability, weight variation, content uniformity and disintegration time, and are designed to ensure the control of problems that can arise during tablet granulation or compression. Tablets must be fabricated to withstand chipping, abrasion, and breakage during the expected tablet life under conditions of storage, transportation and handling. An important physical property of tablets is their mechanical strength which is expressed in terms of hardness (Seth, 1956; Brook and Marshall, 1968) and friability (Smith, 1949, Burlinson and Pickering, 1950; Webster and Van Abbe, 1955), and manufacturers normally employ such tests to ensure that the tablets would withstand the rigours of handling and transportation, and would maintain the desired physical characteristics during storage.

The hardness of a tablet is a function of how much pressure has been exerted in making it (Carstensen, 1993), and it varies with the composition, thickness, shape and

diameter of tablets (Guisel, 1980). Tablet hardness is not an absolute indicator of strength since some formulations, when compressed into very hard tablets, tend to 'cap' on attrition, losing their crown portions. Therefore, friability, another measure of a 'tablet's strength' or 'wearing quality is often determined. Adequate tablet hardness and resistance to friability are necessary requisites for consumer acceptance. The monitoring of tablet hardness is especially important for pharmaceutical products having potential bioavailability problems (Banker and Anderson, 1986).

The hardness of a tablet may be influenced by moisture (Nakabayasbi, 1980), and long-term deterioration in hardness may occur when the tablets containing the most effective disintegrants are subjected to high humidities (Reier and Shangraw, 1966; Khan and Rhodes, 1971). For example, starches show a great affinity for water (In-gram and Lowenthal, 1966) and high starch level often result in a loss of bonding, cohesion, and hardness in tablets (Banker *et al.,* 1980). The influence of temperature and humidity on tablet hardness and friability has been studied by several workers (Duvall *et al.,* 1965; Lee *et al,* 1965, Seitz and Flessland, 1965; Jamil, 1972; Nakabayashi *et al.,* 1980; Fulcoly, 1984; Wang, 1985; Marshall and Rudnic, 1990). The purpose of this investigation is to evaluate the effect of various temperature and humidity conditions on the hardness and friability of five commercial brands of pack-aged paracetamol tablet formulation during storage over a period of six months.

Materials and Methods

The details of commercial paracetamol tablet formulations (A and B, 200mg; C, D, and E, 500mg) used in this study and the various temperature (25°C, 37°C and 45°C) and humidity (75% and 100% RH) conditions employed for their storage have been reported (Ahmad and Shaikh, 1993).

Determination of hardness

The hardness of various brands of paracetamol tablets was determined during storage using a Schleuniger (Model 2E) hardness tester and the values were recorded in kP units. The measurements were performed on ten tablets in all instances, and the average values were recorded.

Determination of friability

The abrasion loss of paracetamol tablets was measured by weighing twenty tablets (Wo), subjected them to 100 revolutions in an Erweka friabilator for four minutes and then reweighing the tablets (W). The friability, f, is given by:

$$F = 100 \frac{(1 - Wo)}{W}$$

Results and Discussion

Changes in tablet hardness

The hardness values determined on sample A-E initially and on five/six months storage, under various conditions of temperature and humidity, are given in Table 1. In all cases paracetamol tablets show a decrease in hardness except at 37°/75% RH where samples A, B, C and E indicate no change in hardness. The percent decrease in hardness of the tablets at various temperature- humidity condition after five/six months storage is reported in Table 2 and the plots of percent decrease in hardness versus temperature at 75% and 100% RH are shown in Fig. 1.

The decrease in harness of sample A, B (200mg), and C, D, E (500mg) with an increase in temperature from 25° to45° at 75% and 100% RH is 28.60, 5.56, 5.26, 8.66 and 5.85% and 8.57, 6.43, 0.0, 0.0 and 3.34% respectively. At 75% RH, all samples appear to lose hardness (5-10%) at room temperature (25°), whereas there is no change in hardness on storage at 37^0 except a little decrease for sample D at five months. After this period the tablet tend to become fragile or moistened. On further increase in temperature to 45°, sample A (polycoated paper packaging) shows 39% decrease in hardness and sample B-E, 10-18% decrease indicating the ineffectiveness of polycoated paper to provide enough protection to tablets from moisture sorption beyond the equilibrium moisture content (EMC).

At 100% RH, the decrease in hardness of tablets (16-25% stored at 25° is more significant for all the samples. Under the same conditions at 37°, the decrease in hardness (5-18%) appears to be relatively small and at 45°, the loss in hardness amounts to 20-29%, with the highest values reached at five months for samples A (28.57%) and C (28.57%) packaged in polycoated paper, followed by sample B (22.22%) at four months) packaged in viscose film (cellophane), D (23.81%) packaged in PVC/AC/aluminium foil and E (20.0%) packaged in PVC/PVDC/aluminum foil. The pattern of these data is in accordance with the behaviour of the packaged samples with regard to the effect of temperature and humidity under the same conditions on the disintegration time (Ahmad and Shaikh, 1994) of paracetamol tablets. The better moisture barrier properties of aluminium foil (Lee et at, 1965; Hanna, 1982) and PVC/PVDC material (Hanlon, 1984; Fulcoly and Liebe, 1983), used in the packaging of samples D and E are due to their relative impermeability to moisture vapours and therefore good protection from moisture damage.

The relatively high decrease in hardness of samples (5-29%) on increasing the temperature from 25° to 45° at 75% RH compared to that (1-9%) at 100% RH may indicate that as soon as the EMC at a particular relative humidity is attained and the moisture content of tablet has reached the level of critical moisture content (CMC), their

physical properties are liable to change. In fact the dependence of EMC on relative humidity has been well established and once the tablets attain CMC, the hardness would reach below the manufacturer's specifications (Nakabayashi et al, 1980).

The moisture adsorption capacity of compressed tablet formulations in various packagings affects the stability of the drugs and is d'rectly related to the interrelation-ship of moisture sorption and tablet hardness (Lee *et al,* 1965). The highest moisture sorption by some excipients in tablet matrix causes greatest deterioration in tablet hardness and the formulator may need improvement in product design to preserve the physical characteristics of tablets.

Changes in tablet friability

The percent increase in friability of samples A-E stored under various conditions of temperature and relative humidity is given in Table 3. All samples show an increase in friability ranging from 2.83 to 8.02% which is more than the generally regarded upper level of acceptable friability (0.8-1.0%) for pharmaceutical products. The increase in friability values for samples A, C, D, E at 45°(75% RH is 4.72, 4.72, 4.24, 4.72% and at 45°/100% RH is 4.72, 5.66, 5.18, 4.72% respectively. The values for sample B could not be determined due to paste formation by excessive moisture sorption. The overall increase in friability with an increase in temperature from 25° to 45° at 75% RH is 0.0 to 25.2%. Further increase in humidity to 100% RH has no effect on friability indicating that beyond CMC of the product (Nakabayashi et al., 1980), moisture has no effect on the extent of deterioration in physical characteristics of the tablets.

The hardness and friability of conventional tablets are interrelated depending on the formulation components. Friability depends on particle size distribution (Lantz et at, 1975, Banker and Anderson, 1986), moisture content (Seitz and Flossland, 1965; Nakabayashi et al, 1980), and other factors. Moisture may bring about the disruption of interparticulate bonds and increase porosity to alter the tablet strength and thus cause changes in hardness and friability. Modified tests based on 'Brinell' hardness measurements have been devised to provide information on the surface hardness or friability of tablets, as well as a measure of their plasticity versus brittleness (Hiestand and Smith, 1984; Holman and Leuenberger, 1988). It should be noted that friability tests are meaningful only when they can be correlated to the effect of packaging equipment on the tablets. Therefore, actual packaging trials should be conducted on pilot batches and finished package standards should be established on the basis of these trials.

Overall temperature-humidity effects

It is now well recognised that the behaviour of solid dosage forms on storage at constant temperature and humidity is a function of equilibrium moisture content. Once the tablets attain the critical moisture content (Cartensen, 1993), their physical properties

e.g. hardness and friability are liable to deterioration (Nakabayashi. 1980). The package moisture transmission rate under known environmental conditions would determine to reach CMC and hence the expected change in tablet characteristics. The USP (1985) water-vapour permeation test could provide guidelines to ascertain the suitability of a chosen material for unit-dose packaging of solid dosage forms. Since the physiomechanical properties of tablets are moisture dependent, which is a function of permeability of packaging material at ambient temperature, it is necessary to develop a tripartite relation of the product, the package and the environment for the design of packaging material with superior moisture barrier properties.

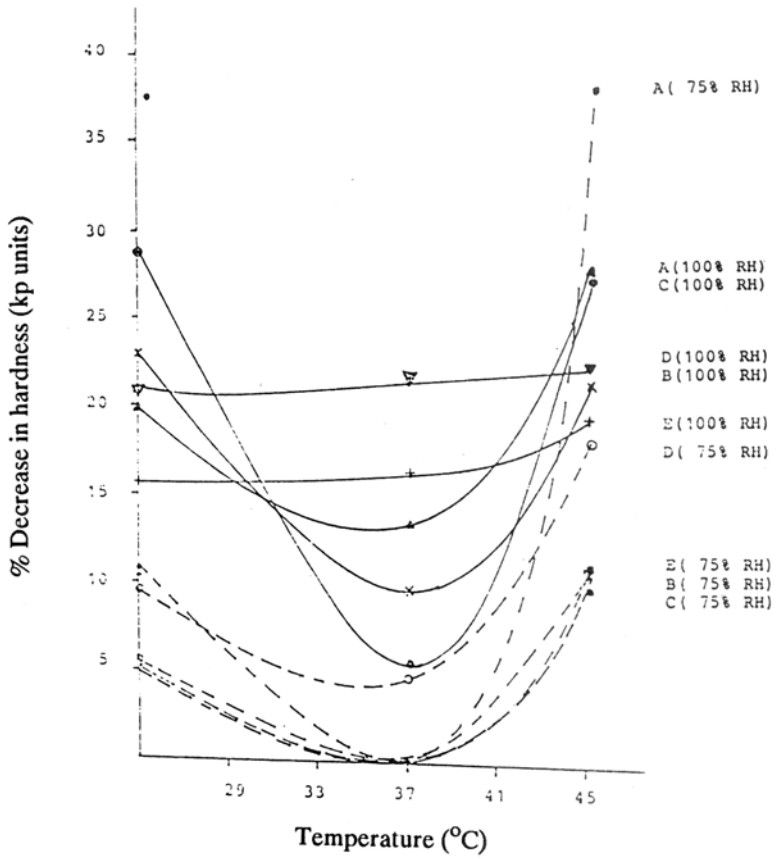

Fig. Plots of percent decrease in hardness of paracetamol tablets vs temperature at 75% and 100% RH.

TAble 1
Hardness (kP Units) of paracetamol tablets stored at various temperatures and humidities*

Sample	25°C/100% RH		25°C/75% RH		37°C/75% RH		37°C/100% RH		45°C/75% RH		45°C/100% RH	
	0 initial	6 month	0 initial	6 month	0 initial	6 month	0 initial	6 month	0 initial	6 month	0 initial	6 month
A	9.5	8.5	10.0	8.0	10.5	***10.5	10.5	***9.0	11.5	7.0	10.5	***7.5
B	9.0	8.5	9.5	***7.5	9.0	***9.0	9.0	***7.0	9.0	***8.0	9.0	**7.0
C	9.5	9.0	10.5	***7.5	10.0	***10.0	9.0	***8.5	9.5	***8.5	10.5	***7.5
D	10.5	9.5	10.5	***8.0	10.0	9.5	10.0	***9.0	11.0	***9.0	10.5	***8.0
E	9.5	9.0	9.0	***7.5	10.5	***10.5	11.0	***9.0	9.0	***8.0	10.0	***8.0

*Values reported at four ** or five months *** due to later tablet fragility or paste formation

Table 2
Percent decrease in hardness (kP units) of paracetamol tablets stored for six months at various temperatures and humidities*

Storage condition	Overall decrease	Percent decrease in samples A	B	C	D	E
25°C/75% RH		10.53	5.55	5.26	9.52	5.26
37°C/75% RH		***0.0	***0.0	***0.0	5.0	***0.0
45°C/75% RH		39.13	***11.11	***10.52	***18.18	***11.11
	25-45°C/75% RH	28.60	5.56	5.26	8.66	5.85
25°C/100% RH		20.0	***21.05 **15.79	***28.57	***23.81	***16.66
37°C/100% RH		***14.28	***22.22	***5.55	***10.0	***18.18
45°C/100% RH		***28.57	**22.22	***28.57	***23.81	***20.0
	25-45°C/100% RH	8.57	6.43	0.0	0.0	3.34

*Values obtained at four ** or five months***

Table 3

Friability (Percent) of paracetamol tablets at six months on storage at various temperatures and humidities*

Sample	25°C/75% RH	25°/100% RH	37°C/75% RH	37°C/100 RH	45°C/75% RH	45°C/100% Rh
A	3.77	4.24	4.72	4.24	4.72 ***(+0.95)	4.72 ***(+0.48)
B	5.81	7.55	8.02	7.07	**--	**--
C	3.77	4.72	3.77	3.77	4.72 ***(+0.95)	5.66 ***(+0.94)
D	3.77	4.72	3.30	3.77	4.24 ***(+0.47)	5.18 ***(+0.46)
E	4.72	4.72	4.24	2.83	4.72 ***(0.0)	4.72 ***(0.0)

*Values were nil for fresh samples A-E.

**Values could not be determined due to paste formation.

***Values indicate overall change at 25-45°C/75% and 100% RH.

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