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EFFECT OF TEMPERATURE AND HUMIDITY ON THE DISINTEGRATION TIME OF PACKAGED PARACETAMOL TABLET FORMULATIONS

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ABSTRACT

A study of the effect of various temperature and humidity conditions on the disintegration time of different brands of packaged paracetamol tablet formulations has been made over a period of six months. Under all the storage conditions paracetamol tablets show an increase in disintegration time ranging from 9.1 to 65.5% (200 mg tablets) and 1.2 to 150.0% (500 mg tablets) on increasing the temperature from 25 to 45°C (75% RH). The increase in disintegration time on increasing the temperature from 25 to 45°C (M)% RH) ranges from 14.3 to 157.7% (200 mg tablets) and 15.3 to 92.3% (500 mg tablets). The overall increase in disintegration time from 25-45°C at 75% and 100% RH is 36.4 to 56.4° (201 mg tablets) and 10.0 to 1405% (500 mg tablets) and 101.3 to 122.9% (200 mg tablets) and 2.6 to 46.8% (500 mg tablets) respectively. These results indicate that PVC/PVDC/A1 foil packaging cause relatively less change in disintegration time of the tablets compared to that of the polvcoated paper and viscose film.

Introduction

The importance of tablet disintegration has been recognized as a first step towards achieving rapid bioavailability of the active ingredients (Lowenthal. 1972). Tablets must undergo the process of disintegration and dissolution prior to drug absorption and delivery l o the site of pharmacological activity. Proper disintegration of a tablet and deaggregation of the tablet fragments are often critical to the optimum performance of the dosage form. As the solubility of the drug decreases, rapid tablet disintegration becomes increasingly important for compressed tablets (Banker and Anderson, 1986). The formulation of the product can have a significant effect on the rate of disintegration and dissolution and may be influenced by the physicochemical properties of the active

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ingredients and excipients as well as the manufacturing process (Racz, 1989). Faulty, ineffective or inappropriate packaging can invalidate even the most stable formulation under excessive temperature and humidity environments and can alter the physical characteristics of tablets such as disintegration and hardness to hinder the desired effect. Several studies have been conducted on the influence of temperature and humidity on tablet disintegration and other characteristics (Duval *et* at, 1965; Lee *et al.* 1965; Carstensen *et al.,* 1966; Maekawa et *al.,* 1966; Ogawa *et at,* 1975; Nakabayashi et *al.,* 1981; Jamil, 1972; Jamil *et al.,* 1983a, 19836; Jamil and Ahmad, 1984). The present work is based on a study of the effect of temperature and humidity on the disintegration time of different brands of paracetamol tablet formulations to evaluate the efficacy of packaging materials in maintaining the designed characteristics during prolonged storage.

Materials and Methods

The details of commercial paracetamol tablet formulations (A and B, 2110 mg; C, D and E, 500 mg) used in this study and the various temperature (25°, 37° and 45°C) and humidity (75% and 100% RH) conditions employed for their storage have been reported (Ahmad and Shaikh, 1993).

Disintegration test:

The disintegration test on various brands of paracetamol tablets during storage was carried out according to the procedure of BP (1993) using a Manesty disintegrator.

One tablet was introduced into each cylindrical glass tube of the basket-rack assembly. The assembly was suspended in the beaker containing the specified liquid. The apparatus was operated at 37 ± 1°C for the specified time (30 minutes). The assembly was removed from the liquid and the disintegration time of the tablets was noted.

Results and Discussion

The disintegration time (minutes) recorded for sample A-E at zero time and on six months storage under various conditions of temperature and humidity is given in Table 1. Under all the storage conditions paracetamol tablets show an increase in disintegration time in sample A-E indicating ineffectiveness of the packaging material to varying degrees. The percent increase in disintegration time at various temperature-humidity conditions during six months is reported in Table 2 and the plots of percent increase in disintegration time versus temperature at 75% and 100% RH are shown in Fig.l.

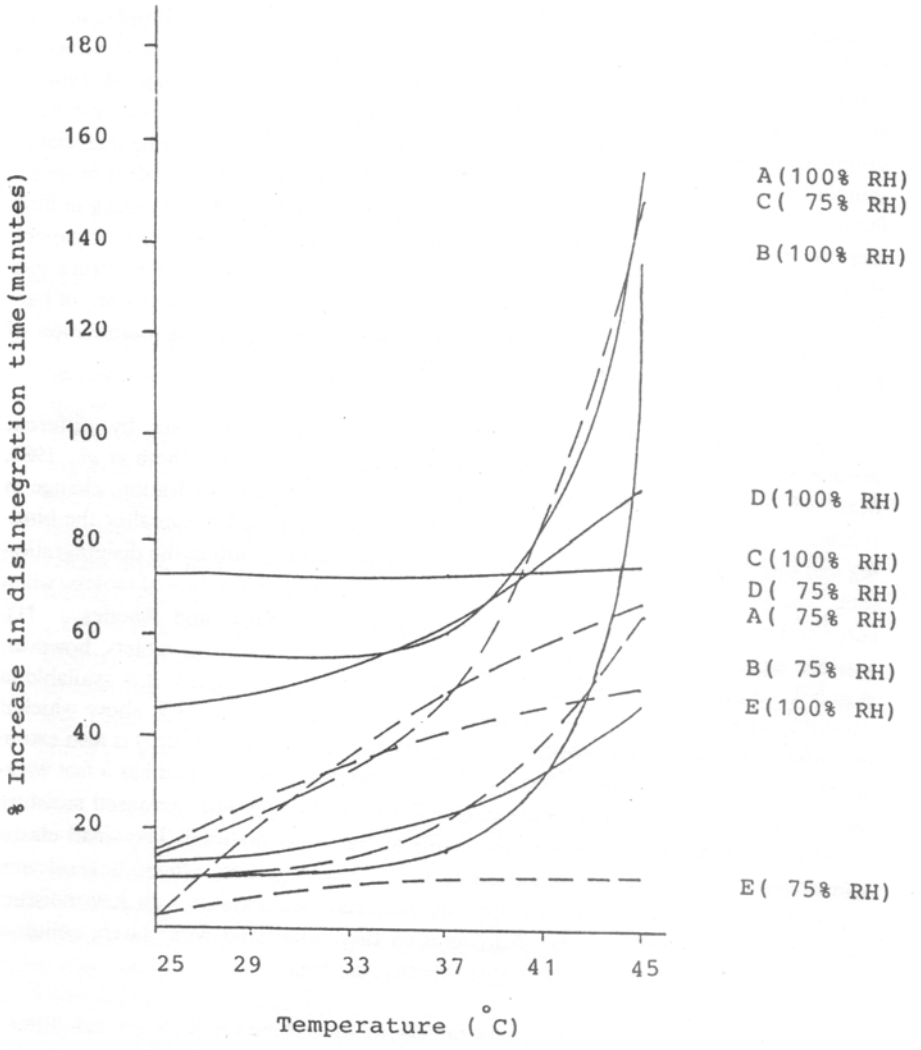

Figure 1: Plots of % increase in disintegration time of paracetamol tablets vs temperature at 75% and 100% RH.

The increase in disintegration time of sample A, B (200 mg) and C, D, E (500 mg) with an increase in temperature from 25 to 45° at 75% RH is 56.4, 36.4 and 140.5, 65.3, 10.1% respectively. While the increase in disintegration time of these samples on increasing the temperature from 25 to 45° at 100% RH is 101.3, 122.9 and 2.6, 46.8, 31.7% respectively. The plots in Fig. 1 show that there is relatively little effect of temperature on disintegration time at 75% RH, while further increase in relative humidity to 100% causes drastic change in sample A and B and to a lesser extent in sample C, sample D and E appear to be least affected. Thus the packaging material of sample D (PVC/AC/Aluminium foil) and E (PVC/PVDC/Aluminium foil) is more effective in controlling the permeation of moisture by the tablet matrix resulting in little increase in the disintegration time compared to that of sample A (polycoated paper), B (viscose film) and C (polycoated paper). The rate of permeation of moisture into the tablet matrix depends on the thickness of the diffusion pathway, the nature of barrier material (i.e., the more hydrophobic the material the slower the permeation of moisture) and on the porosity of the barrier (Richards, 1972).

Several types of disintegrants are used in tablets which act by different mechanisms (Lowenthal, 1972a, 1972b; Khan and Rhodes, 1975; Sheth et al., 1980; Marshall and Rudnic, 1990) including capillary action, swelling, hydration, change in volume or position and gas releasing. Excessive moisture sorption can alter the binding and disintegrating properties of tablet excipients and thus affect the disintegration time. The long-term deterioration in hardness and disintegration time of tablets, when subjected to high humidities, has been demonstrated (Khan and Rhodes, 1971). Various types of disintegrants may be used in the manufacture of tablets, however, starch is the most widely employed and best established disintegrant. It is available in various grades and modified forms with a moisture content of 3 to 12%, above which it may lose its disintegrating properties. Microcrystalline cellulose (Avicel) is also extensively used as a disintegrant. It has a moisture content of upto 3% and has a fast wicking rate for water. It has a tendency to develop static charges with increased moisture content and does not disintegrate as readily as the dried material. The small elastic deformation of Avicel also contributes to its disintegration effect. Several new polymeric agents have been developed as potential disintegrants with low moisture sorption tendency and reduced disintegration time compared with starch, cellulose and other commonly used disintegrants (Sheth *et al.,* 1980).

The relative uptake of moisture by tablets, under a given set of storage conditions, will depend upon the nature of the *active* ingredients and excipients present in the formulation. The equilibrium moisture content (EMC) of tablet excipients may vary at different temperatures and relative humidities and can thus affect the tendency to pick up moisture and so influence disintegration time. The sorption isotherms of different

excipients indicate that upto a certain level, i.e. 70% RH, the EMCs are apparently dependent upon the initial moisture content (IMC) of the material, above 80% RH, however, there is a rapid pick up of moisture indicating the diminishing influence of the IMC (Daruwala, 1980; Carstensen, 1993), as observed in the case of paracetamol formulations A-C (Fig.1) and the resultant disintegration behaviour. Wagner (1971) has written as excellent review of the disintegration test applied to tablet formulations. The test is still used as a guide to the formulator in the preparation of an optimum tablet formula and as an in-process control test to ensure lot-to-lot uniformity. It also enables the formulator to evaluate the physical characteristics of tablet formulations during storage under extreme climatic conditions.

Table 1

Disintegration time (Minutes) of paracetamol tablets stored at various temperatures and humidities

Sample	25°C/ 75% RH		25°C/ 100% RH		37°C/ 75% RH		37°C/ 100% RH		45°C/ 75% RH		45°C/ 100% RH	
	0 month	6 month	0 month	6 month	0 month	6 month	0 month	6 month	0 month	6 month	0 month	6 month
A	1.42	1.55	1.45	2.30	1.19	1.45	1.50	2.40	1.45	2.40	1.30	3.35
B	2.20	2.50	2.10	2.40	2.50	3.50	1.55	2.30	2.10	3.15*	2.15	5.10*
C	2.10	2.30	1.45	2.50	2.10	2.40	1.30	2.25	1.20	3.00	2.00	3.50
D	2.45	2.50	2.18	3.15	2.18	3.25	2.00	3.25	2.45	4.10	2.30	4.40
E	4.30	4.35	4.51	5.20	4.10	4.50	4.45	5.40	4.00	4.45	4.15	6.10

*Values obtained at five months.

Table 2

Percent increase in disintegration time (minutes) of paracetamol tablets stored for six months at various temperatures and humidities

Storage condition	Overall increase	Percent increase in samaple A	B	C	D	E
25°C/75% RH		9.1	13.6	9.5	2.0	1.2
37°C/75% RH		21.8	40.0	14.3	49.1	9.8
45°C/75% RH		65.5	50.0	150.0	67.3	11.2
	25 - 45°C/ 75% RH	56.4	36.4	140.5	65.3	10.0
25°C/100% RH		58.6	14.3	72.4	44.5	15.3
37°C/100% RH		60.0	48.4	73.0	62.5	21.3
45°C/100% RH		157.7	137.2	75.0	91.3	47.0
	25 - 45°C/ 100% RH	101.3	122.9	2.6	46.8	31.7

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