

EFFECT OF MOISTURE ON THE STABILITY OF PACKAGED PARACETAMOL TABLET FORMULATIONS

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ABSTRACT

The stability of four commercial brands of packaged paracetamol tablet formulations stored at $25\pm 1^{\circ}\text{C}$ and $75\pm 2\%$ RH for a period of six months has been studied and the effect of moisture on the degradation of paracetamol has been evaluated. PVC/PVDC/Al foil and polycoated paper packagings offer maximum protection to paracetamol tablets against moisture induced degradation. Moisture transmission of polymeric material appears to decrease with an increase in drug concentration and hence a relatively slow rate of degradation under controlled conditions.

INTRODUCTION

Drug substances in tablet formulations are susceptible to degradation by moisture, heat, light and other stimuli (Wadke and Jacobson, 1980; Nakabayashi *et al.*, 1981; BP, 1993) and various models have been proposed to predict the product-package shelf-life under specified storage conditions (Liebe, 1990). Paracetamol tablets are sensitive to moisture (Koshy and Lach, 1961; Connors *et al.*, 1986; Amareshwar and Radha Kishan, 1999) and many deteriorate under adverse storage conditions. Several studies have been conducted on the prediction of shelf-life and the effect of temperature and humidity on the disintegration time, and hardness and friability of packaged paracetamol tablet formulations (Ahmad and Shaikh, 1993, 1994a, 1994b, 1994c). The object of this work is to study the effect of moisture on the stability of these formulations.

MATERIALS AND METHODS

The details of various brands of commercial packaged paracetamol tablet formulations (B, 200 mg; C, D and E, 500 mg) stored at $25\pm 1^{\circ}\text{C}$ and $75\pm 2\%$ RH in a Hot Pack climatic chamber and the assay method used (B.P., 1993) have been described previously (Ahmad and Shaikh, 1993).

The moisture content of the packaged tablets was determined under the prevailing storage conditions by subtracting the initial weight of the tablets from that of the stored material at various time intervals. The determinations were performed in duplicate in all instance and the results were averaged.

RESULTS AND DISCUSSION

Fig. 1 shows the moisture uptake of sample B (2.5%), C (1.2%), D (3.2%) and E (2.2%) stored at $25\pm 1^{\circ}\text{C}$ and $75\pm 2\%$ RH for a period of six months. It appears that the sample B, C and E

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achieve the equilibrium moisture content (EMC) after about four months whereas sample D continues to gain moisture up to six months. EMC is a function of the surrounding relative humidity and may differ for various materials under the same conditions. These differences are due to the manner in which the water is held by the material, for example, in fine capillary pores or molecularly bound form (Lachman *et al.*, 1986).

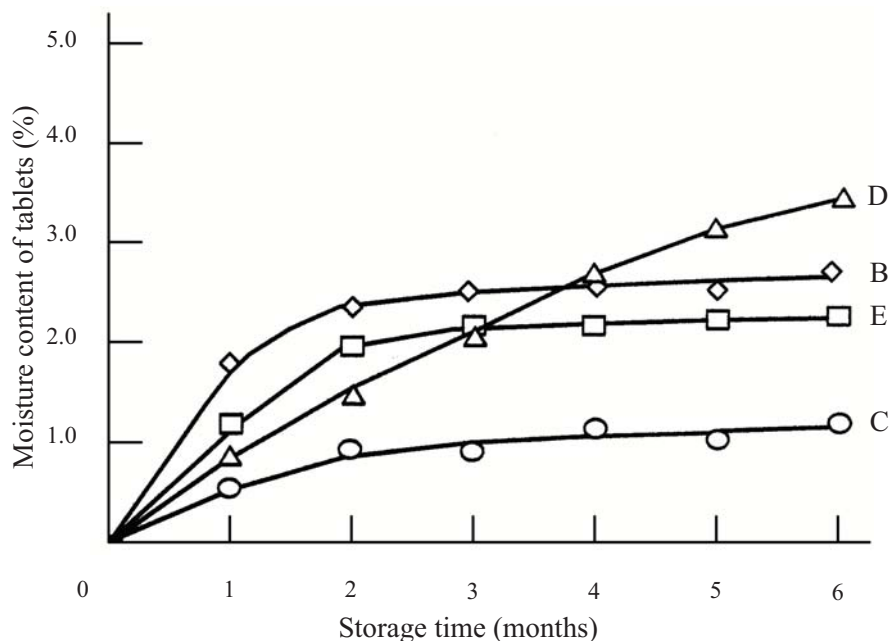


Fig.1: Moisture content of paracetamol tablets (B-E) stored at 25°C and 75% RH.

The variations in moisture content of the samples B-E during storage may depend upon several factors such as the moisture permeabilities of the packaging materials, physicochemical properties of the dosage form and moisture sorption characteristics of disintegrating agents. It is advisable to use packaging materials with low water vapour transmission rates. The rate of moisture uptake, under controlled conditions, is a function of packaging material thickness (Khan and Rhodes, 1975; Ahmad and Shaikh, 1994b, 1994c).

The stability of solid dosage forms at constant temperature is considered as a function of EMC which, in turn, is dependant on relative humidity (Wang, 1985; Liebe, 1990). The quality of packaging material would determine the moisture permeation to achieve EMC and hence, the rate of degradation of the active ingredient in the tablet.

Fig. 2 shows the plots of moisture uptake versus paracetamol degradation for the samples B-E indicating that a relationship exists between the moisture content of tablets and the rate of degradation of paracetamol. After the initial phase an EMC is achieved and the drug continues to degrade steadily under specified storage conditions.

Sample B (200 mg) shows maximum degradation of paracetamol up to the extent of 7.3% whereas sample C, D and F (500 mg) show 4.5%, 5.0% and 4.4% degradation, respectively, on storage for six months. The values are in accordance with the shelf-lives of tablets determined

under the same storage conditions (Ahmad and Shaikh, 1993) and reflect the influence of moisture transmission characteristics of the packaging material (Liebe, 1990) on paracetamol degradation in the samples. It may be concluded from the present study that the packaging material of sample C (polycoated paper) and sample E (PVC/PVDC/Al foil) offer maximum protection to paracetamol tablets against moisture induced degradation. Moisture vapour transmission of polymeric material used in packaging appears to decrease with an increase in drug concentration and hence a relatively slow rate of degradation under controlled conditions. A Kinetic model to predict the effect of moisture and heat on the aging of packaged tablets has been proposed (Nakabayashi *et al.*, 1981).

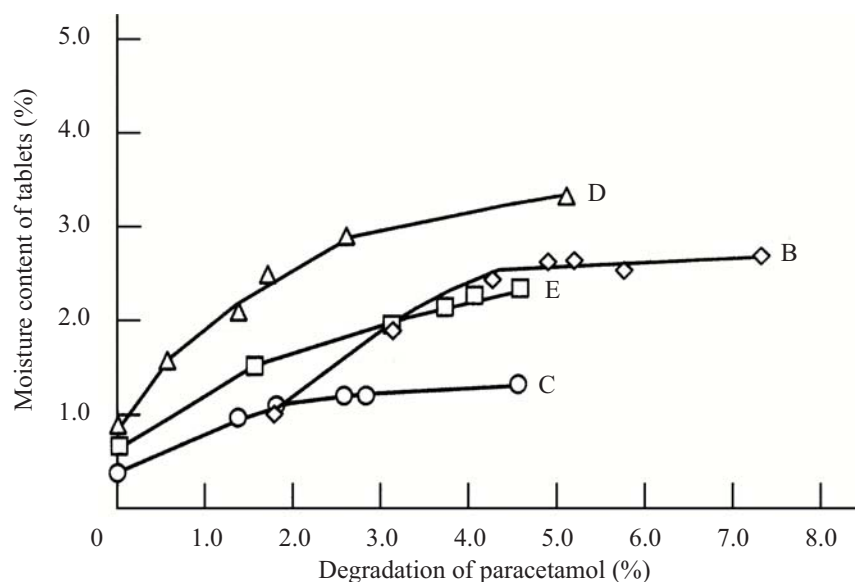


Fig. 2: Dependence of paracetamol degradation on moisture content of tablets (B-E).

In view of the fact that the formulation characteristics of the individual samples and the moisture permeability and thickness of the packaging material are not known, it would not be appropriate to draw definite conclusions as to the effect of moisture on the stability of paracetamol tablets. However, the present study provides a general correlation between the moisture content of tablets and paracetamol degradation (%) for a particular packaging material under specified storage conditions.

REFERENCES

- Ahmad, I. and Shaikh, R.H. (1993). Stability of paracetamol in packaged tablet formulations. *Pak. J. Pharm. Sci.* **6**(2): 37-45.
- Ahmad, I. and Shaikh, R.H. (1994a). Prediction of shelf-life of packaged paracetamol tablet formulations. *Pak. J. Pharmacol.* **11**(1): 53-58.
- Ahmad, I. and Shaikh, R.H. (1994b). Effect of temperature and humidity on the disintegration time of packaged paracetamol tablet formulations. *Pak. J. Pharm. Sci.* **7**(1): 1-7.
- Ahmad, I. and Shaikh, R.H. (1994c). Effect of temperature and humidity on hardness and friability of packaged paracetamol tablet formulations. *Pak. J. Pharm. Sci.* **7**(2): 69-78.

- Amareshwar, P. and Radha Kishan, M. (1999). Effect of moisture vapour transmission rate through polymeric films coated on to tablets, *The Eastern Pharmacist* (New Delhi), **42**: 121-123.
- British Pharmacopoeia (1993). Vol.2, HMSO, London, p.1042.
- Connors, K.A., Amidon, GL. and Stella, V.J. (1986). *Chemical Stability of Pharmaceutical*, 2nd Edn, John Wiley & Sons, New York, pp.163-168.
- Khan, K.A. and Rhodes, C.T. (1975). Water-sorption properties of tablet disintegrants. *J. Pharm. Sci.* **64**: 447-451.
- Koshy, K.T. and Lach, J.L. (1961). Stability of aqueous solutions of N-acetyl-p-aminophenol. *J. Pharm. Sci.* **50**: 113-117.
- Lachman, L., Liberman, H.A. and Kanig, J.L. (1986). *The Theory and Practice of Pharmacy*, 3rd Edn, Lea & Febiger, Philadelphia, p.54.
- Liebe, D.C. (1990). *In: Modern Pharmaceutics* (Banker, G.S. and Rhodes, C.T., Eds.), 2nd Edn, Marcel Dekker, New York, Chapter 18.
- Nakabayashi, K., Shimamoto, T., Mima, H. and Okada, J. (1981). Stability of packaged solid dosage forms. V. Prediction of the effect of aging on the disintegration of packaged tablets influenced by moisture and heat. *Chem. Pharm. Bull. (Japan)*. **29**: 2051-2056.
- Wadke, D.A. and Jacobson, H. (1980). *In: Pharmaceutical Dosage Forms: Tablets*, Vol.1 (Liberman, H.A. and Lachman, L., Eds.). Marcel Dekker, New York, Chapter 1.
- Wang, M.J. (1985). Prediction of Moisture Content of a Packaged Moisture Sensitive Pharmaceutical Product Stored under Fluctuating Temperature and Humidity Environments, M.S. Thesis, School of Packaging, Michigan State University, East Lansing.