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Short Communication

Effect of storage conditions on erythromycin tablets marketed in Saudi Arabia *

M. WAFIK GOUDA, MAMDOUH A. MOUSTAFA ** and ABDULLA M. MOLOKHIA

Dept. of Pharmaceutics, College of Pharmacy, University of Riyad, Riyad (Saudi Arabia)

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In a solid dosage form, the nature of the active ingredient, its dissolution rate and the type of excipients added in the formulation, among other factors, were shown (Fincher, 1968; Aguiar et al., 1968; Aguiar and Zelmer, 1969; Chowhan and Palagyi, 1978) to affect the bioavailability of drugs. Erythromycin was reported (Nightingale et al., 1976) to have serious bioavailability and/or quality assurance problems. In order to optimize its stability and bioavailability, a large number of derivatives and formulations have been prepared. Those formulations, while reasonably stable under normal storage conditions, cannot be expected to remain so when the conditions are extreme. In Saudi Arabia, as well as other parts of the world, prolonged exposure of dosage forms to extremes of temperature (up to 50°C) and humidity (up to 90% relative humidity) may take place. York (1977) reported a dramatic decrease in shelf-life and dissolution rate of some antibiotics when stored under tropical conditions.

In this report, two brands (A and B) of film-coated erythromycin stearate tablets and one brand (C) of enteric-coated tablets of erythromycin base were examined physicochemically for the effect of two storage conditions; namely, 50°C/50% relative humidity (R.H.) and 40°C/90% R.H. Tablets were stored in paper bags, plastic dispensing bottles used in local hospitals and in glass-bottles for comparison.

Disintegration and dissolution methods adopted essentially followed USP specifications. Dissolution rates were measured at 30 ± 0.2°C in a sodium chloride/hydrochloric acid medium, pH 1.2, which was changed after one hour to pH 7.5 by addition of dibasic sodium phosphate and sodium hydroxide. Erythromycin was determined by a spectrophotometric method (Tepe and St. John, 1955) which was found to produce results comparable to those obtained from the USP microbiological assay.

Table 1 summarizes average values (of 6 tablets) for hardness, disintegration, tablet weight, dimensions and content of active material of all 3 brands. Apart from an increase in hardness by storage at 40°C/90% R.H. for tablets of brand C and a decrease in disinte-

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** To whom correspondence should be addressed.

TABLE 1

AVERAGE TABLET WEIGHT, DIMENSIONS, HARDNESS, DISINTEGRATION TIME AND DRUG CONTENT OF ERYTHROMYCIN TABLETS

	Brand		
	A	B	C
Tablet weight (g)	0.790	0.632	0.935
Thickness (cm)	0.637	0.620	0.770
Diameter (cm)	1.335	1.348	1.410
Hardness (kg)	14.5	10.0	12.5 [a]
Disintegration time (min)	8 [b]	15	7.5
Drug concentration (% of labelled amount)	95.2	95.7	98.1

[a] Exceeded the maximum value on scale (15 kg) by storage for 41 days at 40°C/90% R.H.
[b] Decreased to 3 min after storage for 18 days at 40°C/90% R.H.

gration time of tablets of brand A under the same conditions, little or no changes were otherwise observed. Dissolution rates were, however, significantly decreased by storage of all tablets under both conditions (Fig. 1).

High temperature and/or humidity, through their effects on the physical and mechanical properties of tablets, lead to the marked decrease in dissolution of the stored tablets. Tablets of brand A developed sticky external coats and mottling. Disintegration time and dissolution rate were decreased by storage particularly at 40°C/90% R.H. Although the decrease of disintegration time would be expected to increase dissolution rate, opposite effects were observed. This lack of correlation may be attributed to changes in the per-

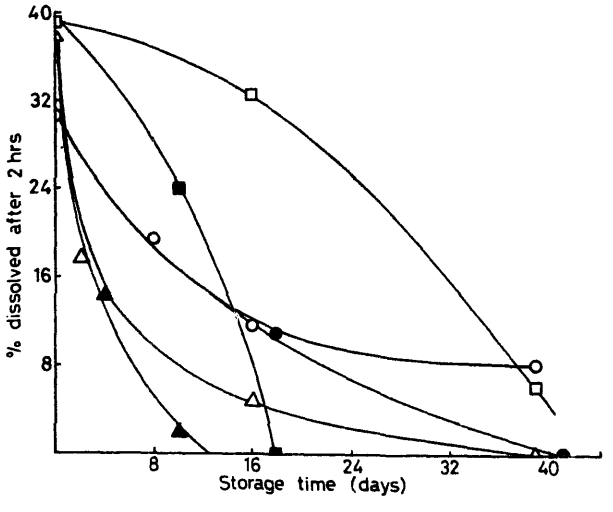

Fig. 1. Effect of storage on the percentage of erythromycin dissolved after 2 h; ○ Brand A 50°C/50% R.H.; ● Brand A 40°C/90% R.H.; □ Brand B 50°C/50% R.H.; ■ Brand B 40°C/90% R.H.; △ Brand C 50°C/50%.R.H.; ▲ Brand C 40°C/90% R.H.

TABLE 2

EFFECT OF TYPE OF CONTAINER ON THE DISSOLUTION OF STORED ERYTHROMYCIN TABLETS

Brand, storage conditions	% drug dissolved after 2 h, unstored tablets	% drug dissolved after 2 h, tablets stored for 40 days		
		Paper bags	Plastic containers	Glass bottles
A, 40°C/90% R.H.	30	0	7	25
B, 50°C/50% R.H.	38	3	5	34

meation characteristics of the polymer mixed with tablet granules. While the disintegration time of tablets of brand B was not significantly decreased upon storage, the general pattern of changes observed was similar to that for tablets of brand A.

The decrease in dissolution of the enteric coated tablets (brand C) is believed to be due to drug entrapment within the enteric coat. The presence of the tablet core during dissolution together with the slight increase in hardness of tablets stored at 40°C/90% R.H. suggest hardening of the enteric coat which prevented it from dissolving and consequently inhibited the release of erythromycin.

The effect of type of container on the change in dissolution rate by storage is shown in Table 2. Throughout the study, glass containers offered greater protection and consequently the tablets retained higher dissolution rates as compared to the tablets stored in plastic containers or paper bags.

The marked decrease observed in dissolution rates warrants detailed in vivo bioavailability studies of stored tablets and possible adjustments of formulae, storage recommendations, expiration dates and dispensing conditions.

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