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THE EFFECT OF ENVIRONMENTAL MOISTURE AND TEMPERATURE ON THE PHYSICAL STABILITY OF EFFERVESCENT TABLETS IN FOIL LAMINATE PACKAGES CONTAINING MINUTE IMPERFECTIONS

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ABSTRACT

The effect of environmental moisture on the physical stability of effervescent tablets in foil laminate packages containing microscopic imperfections (openings) was examined. Packaged tablets were stored at different relative humidity (RH) and temperature conditions and evaluated for physical stability at predetermined time intervals. Physical stability was assessed by noting if the tablet components reacted prematurely to yield soft tablets during storage. A penetrating dye solution test was used to determine if the foil packages contained imperfections which might allow transmission of moisture. The results of the investigation indicated that absolute moisture integrity of the foil package is required for product stability.

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INTRODUCTION

Occassional batches of an effervescent potassium supplement tablet had evidenced physical instability. The instability manifested itself as a premature reaction of the ingredients required for effervescence, i.e., packaged tablets became physically deteriorated and would not effervesce in water. The tablets were always packaged in individual foil/polyethylene/paper laminate packets.

It was known that package imperfections could result in physical instability of effervescent tablets (1). Gross examination of the less stable batches, however, did not reveal an excessive number of package defects. A technique for leak testing in water under vacuum also did not indicate excessive defects. However, microscopic examination revealed an excessive number of minute imperfections in the foil portion of the laminate in less stable batches. A more sensitive leak test was therefore developed which utilized a dye solution. Results with this test correlated with microscopic observations.

The following study demonstrates the effect of minute imperfections in laminate packaging material on the stability of an effervescent product held in moist environments.

EXPERIMENTAL

The effervescent tablets used in this study were round, 2.54 centimeters (cm) in diameter, flat face, and had a thickness of approximately 0.61 cm. The dimensions of the foil laminate package were 5.59 cm by 5.59 cm. The laminate

consisted of 11.3 kilogram (kg) pouch paper, over 3.2 kg polyethylene, over 0.003 cm aluminum foil, over 6.8 kg polyethylene.

Procedure:

The effect of several humidity conditions at room temperature was assessed by placing packaged tablets in desiccator jars containing appropriate salt solutions to maintain environments of 32% RH, 43% RH and 81% RH at 25°C. The investigation was performed to determine if humidity at a controlled temperature of 25°C influenced physical stability.

The effect of temperature at high humidity was also studied. Packaged tablets were placed in a humidity cabinet set at 80% RH/38°C and in desiccator jars containing appropriate salt solutions to maintain environments of 78% RH and 81% RH at 30°C and 25°C, respectively.

The effect of exposure time to high humidity was also studied. Samples were placed in an environment of 80% RH/38°C. One portion of the packaged tablets was removed after one month of storage and placed in a dry environment (25°C) for 5 months. These samples were then examined for tablet softening and compared with samples left at 80% RH/38°C for the total time period of six months.

Samples stored at dry conditions served as controls for the other storage conditions using temperatures of 25°C, 30°C, and 40°C. The humidity of the environment at these conditions was not monitored, however, the areas were assumed to be relatively dry because they were incubators or air conditioned rooms. Occasional checks of the 30°C area showed the relative humidity never exceeded 32%.

The sample size for each storage condition was 400 packets.

Test Methods:

The foil packets were tested for imperfections by use of an oil soluble dye dissolved in an organic solvent (2). Using a sharp cutting edge, a circle was cut in the face of the package just large enough to remove the tablet. A few drops of the dye solution were then placed into the packet, swirled and allowed to stand for 30 minutes or until the outside surface of the package showed leakage of the dye. Samples of packaged tablets (approximately 700) were tested for leaks in this manner prior to the study and 55% of the packets were found to leak.

Softened tablets were detected by pressing each packaged tablet between the thumb and index finger at predetermined time intervals (up to 24 months). All packets that contained soft tablets were immediately tested for leaks. All remaining packages, except those held at 40°C and 25°C, were tested for leaks at the termination of the study.

RESULTS AND DISCUSSION

As shown in Figure 1, storage at humid room temperature conditions had an adverse effect on physical stability. Approximately 45% of the packaged tablets became soft after storage for six months at 81% RH/25°C while none was softened after nine months at 43% RH/25°C or 24 months at 32% RH/25°C. A substantial number (29%) of tablets softened, however, after storage for 24 months at 43% RH/25°C.

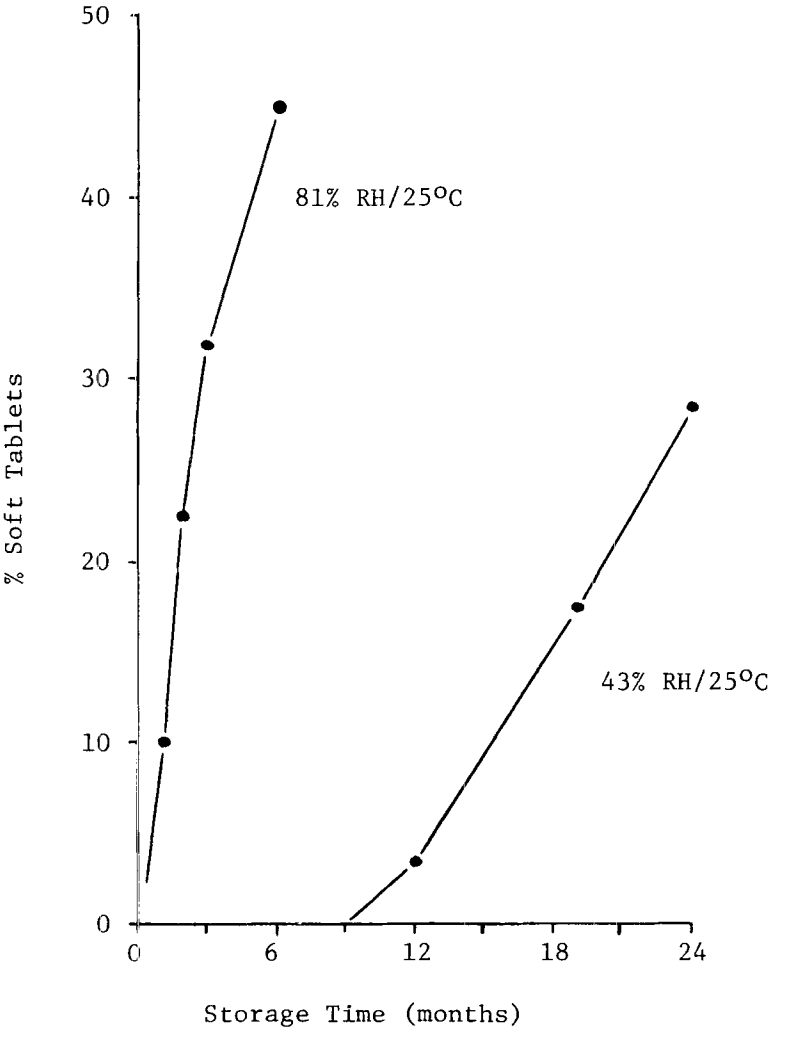

FIGURE 1

Effect of High and Moderate Humidity at Room Temperature on the Number of Tablets Softening During Storage.

Higher temperatures accelerated deterioration of the tablets stored at high humidity conditions as shown in Figure 2. The number of and rate at which tablet softening occurred at 78% RH/30°C and 81% RH/25°C after six months were similar but appreciably less than that found at 80% RH/38°C. On the other hand, temperature had no perceivable effect on tablets which were held for up to 24 months under dry conditions as evidenced by the absence of softened tablets in packages stored at 25°C, 30°C or 40°C in dry areas.

The plot in Figure 3 demonstrated that exposure to high temperature/humidity conditions for a relatively short period of time initiated physical instability which continued even after tablets were removed to dry conditions at room temperature. Here, approximately 23% to 26% of the tablets deteriorated after one month at 80% RH/38°C. Tablets left at this condition continued to deteriorate until approximately 55% of the tablets softened after six months. Tablets transferred to dry room temperature conditions continued to deteriorate but at a greatly reduced rate. A total of only 35% softened after six months storage. However, all tablets were stable when held for 24 months at dry room temperature conditions. These data suggest that when sufficient moisture is present during the first month of storage, effervescence will occur even after removal to cooler and dryer conditions.

The figures illustrate that exposure of poorly packaged tablets to humid conditions caused physical deterioration. More important, perhaps, is the observation that deteriorated tablets were rarely found in packets which did not have detectable imperfections. At the conclusion of the study, the packets were tested for leaks and approximately 54% of the total were found to leak. This was in good agreement with the

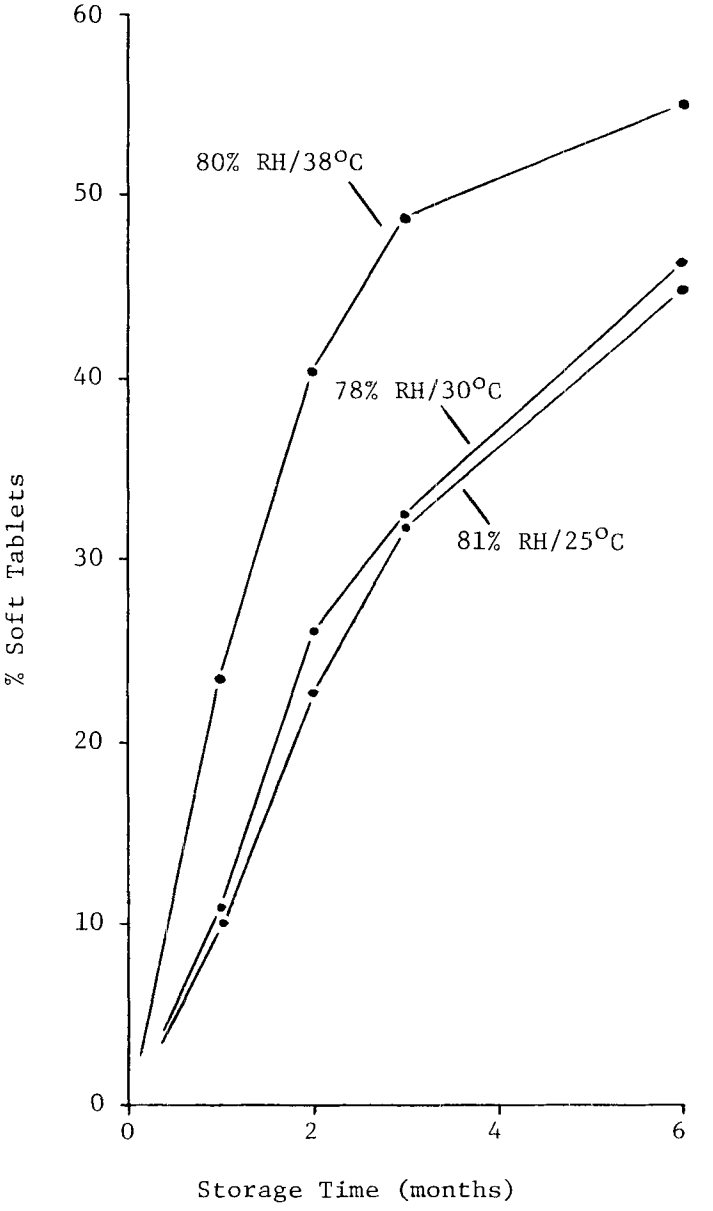

FIGURE 2

Tablet Softening During Six Months of High Humidity Storage at Various Temperatures.

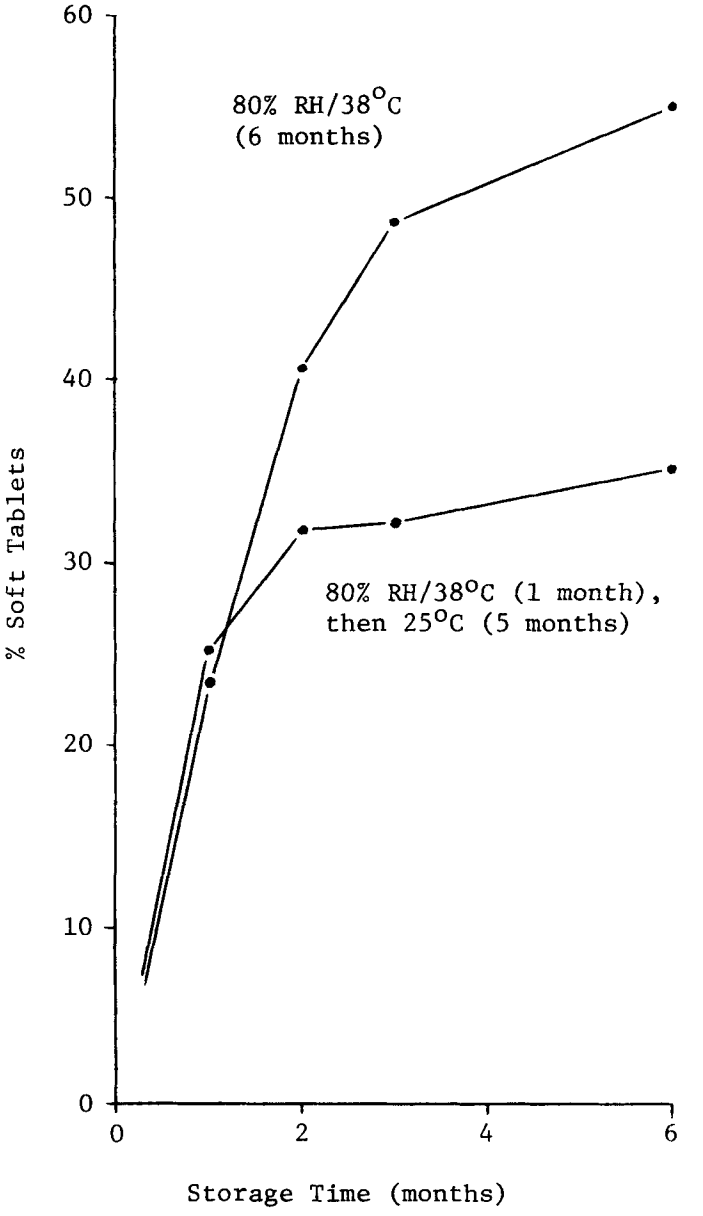

FIGURE 3

Effect of Interrupted High Humidity/High Temperature Storage on the Incidence of Tablet Softening.

TABLE I

Leak Test Results

Storage Condition	(months)	Percent of Packets which Failed Leak Test: Packets with Soft Tablets	Packets with Firm Tablets
80% RH/38°C	6	99.1	7.9
78% RH/30°C	6	99.5	14.2
81% RH/25°C	6	100.0	12.2
43% RH/25°C	24	99.2	38.5

incidence of 55% found prior to starting the study. Results from leak testing of packets which contained deteriorated tablets, however, showed that over 99% of these packets had imperfections (Table I). The results in Table I also show that some samples held at moist conditions (43% RH or higher) contained firm tablets even though the packets had imperfections. This is especially obvious after storage for 24 months at 43% RH/25°C. Storage at the higher humidity conditions, however, resulted in a smaller percentage of samples which contained firm tablets in packets that had imperfections. This illustrates again that high humidity accelerates the physical deterioration of effervescent tablets when stored in packets of poor integrity.

CONCLUSIONS

Absolute integrity of foil laminate packaging is critical for the stability of effervescent products when exposure to elevated humidity is experienced, even for relatively short

periods of time. The dye penetration test was able to detect the minute imperfections in the laminate which led to the physical deterioration of the tablets.

ACKNOWLEDGEMENTS

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