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INFLUENCE OF STORAGE UNDER TROPICAL CONDITIONS ON THE STABILITY AND DISSOLUTION OF ASCORBIC ACID TABLETS*

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ABSTRACT

Ascorbic acid tablets stored at 40°C and 90% R.H. demonstrated substantial changes in chemical as well as physical stability including color, disintegration time, hardness and dissolution rate. Tablets stored at 40°C and 35% R.H. showed virtually no change in chemical stability and hardness but measurable changes in disintegration time and dissolution rate. Moisture appeared to be a significant contributing factor to the enhancement of the chemical and physical instability of ascorbic acid tablets.

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INTRODUCTION

Tablet aging can affect not only the chemical stability of the contained drug, but also certain physical parameters such as color, hardness, disintegration time and dissolution rate. Storage of tablets under tropical conditions is expected to enhance chemical instability of the drug as well as physical instability of the tablet dosage form.

Aged tetracycline tablets have been found to demonstrate decreased chemical stability (1) and increase dissolution time (2) during storage. Retardation of dissolution rate due to aging has been reported for tablets of sodium salicicylate (3), acetaminophen (4), phenylbutazone (5), prednisone (6), hydrochlorothiazide (7), and aspirin (8).

The problem of tablet aging with accompanying changes in stability, disintegration time and dissolution rate has received increasing attention (9,10).

The purpose of this study therefore, was to investigate the influence of storage under tropical conditions on the stability and in-vitro availability of ascorbic acid from commercial tablets produced and marketed in one of the African countries where tropical climate predominates.

EXPERIMENTAL

Materials: Ascorbic acid, glacial acetic acid, metaphosphoric acid, 2,6 dichlorophenol-indophenol sodium,

sodium bicarobonate were obtained from commercial sources in pharmaceutical or reagent grade and were used without further purification. Ascorbic acid tablets, freshly made and having the same batch number were obtained from a pharmaceutical company in an African country and used in this investigation.

Equipment: The following equipment were used: Incubators with controlled temperature and humidity; USP tablet disintegration apparatus; USP tablet dissolution apparatus; Erweka tablet hardness tester.

Procedure:

Tablet Storage: The freshly made tablets were placed in loosely capped plastic vials and placed in desiccators containing saturated solutions of either monobasic ammonium phosphate or magnesium chloride hexahydrate. The desiccators were then placed in incubators maintained at 40°C ±. These solutions produced relative humidity of 90% and 35% respectively at 40°C. Tablets were withdrawn periodically and evaluated for appearance, drug content, hardness, disintegration time and dissolution rate.

Assay of Ascorbic Acid: Analysis of ascorbic acid in the tablets was carried out on duplicate samples at different time intervals using the official dichlorophenolindophenol method (11).

Content Uniformity: The USPXXI-NFXVI (12) general procedure was followed. Ascorbic acid content was determined by the dichlorophenolindophenol method (11).

Disintegration: Disintegration time was determined by the USPXXI-NFXVI (13) method using distilled water as the disintegration medium. Six tablets were used for each determination.

Dissolution: Dissolution profiles of ascorbic acid tablets were determined by the USPXXI-NFXVI (13) rotatingbasket method at 100rpm. A volume of exactly 900 ml of distilled water maintained at 37 $\pm$ 0.5^{o}C was used as the dissolution medium. A 4-ml sample from the dissolution vessel was withdrawn at various time intervals by means of a filtering pipet into a 50-ml volumetric flask containing a 6-ml of metaphosphoric -acetic acid mixture and titrated against 2,6 dichlorophenolindophenol using appropriate blank. Four milliliters of distilled water was introduced to the dissolution vessel to replace the sample withdrawn. A cumulative correction was made for the previously removed samples in determining the total amount of drug released according to the equation used by Sciarra and Patel (14). Six tablets were used for each determination.

Hardness: Tablet hardness was determined on 10 tablets using the Erweka tablet hardness tester.

TABLE 1

Ascorbic Acid Content of Tablets Stored under Tropical Conditions

Storage Time (Days)	% Ascorbic Acid in Tablets Stored at: 40°C & 90% R.H.		40°C & 35% R.H.	
	Avg.	± S.D.	Avg.	± S.D.
0	100.01	4.3	100.01	4.3
20	100.74	2.9	99.3	3.2
48	94.0	3.5	100.2	2.2
105	76.7	7.4	101.7	7.6
164	62.4	1.8	101.7	4.2

DISCUSSION OF RESULTS

Content uniformity of Fresh Tablets:

The tablets were found to comply with the official requirements for content uniformity since average ascorbic acid content was found to be 100.01 ± 4.3%.

Chemical Stability:

It is evident from Table 1 that the chemical instability of ascorbic acid was enhanced during storage of the tablets at 40°C and 90% R.H. On the other hand, tablets stored at 40°C and 35% R.H., were found to be chemically stable. It appears therefore, that the moisture was a significant contributing factor

TABLE 2

Hardness and Disintegration of Ascorbic Acid Tablets Stored under Ttopical Conditions

Storage Time (Days)	40°C & 90% R.H.				40°C & 35% R.H.			
	Hardness Kg.		Disintegration (Min.)		Hardness Kg.		Disintegration (Min.)	
	Avg.	± S.D.	Avg.	± S.D.	Avg.	± S.D.	Avg.	± S.D.
0	6.53	0.85	145	36	6.53	0.85	145	36
20	1.78	0.43	201	50	5.6	0.92	247	34
48	Too soft		>240		6.2	0.76	>240	
105	Too soft		>240		6.2	0.35	>240	
164	Too soft		>240		5.4	0.43	>240	

to the enhancement of the chemical instability of ascorbic acid tablets.

Physical Stability:

Tablets stored at 40°C and 90% R.H. were found to discolor progressively from white to yellow, tan, dark brown and then almost black. However, tablets stored at 40°C and 35% R.H., demonstrated only a very slight change in color at the end of the storage period when they assumed only a light buff color.

Tablets stored at 40°C and 90% R.H. demonstrated decreasing hardness on storage, whereas the hardness of

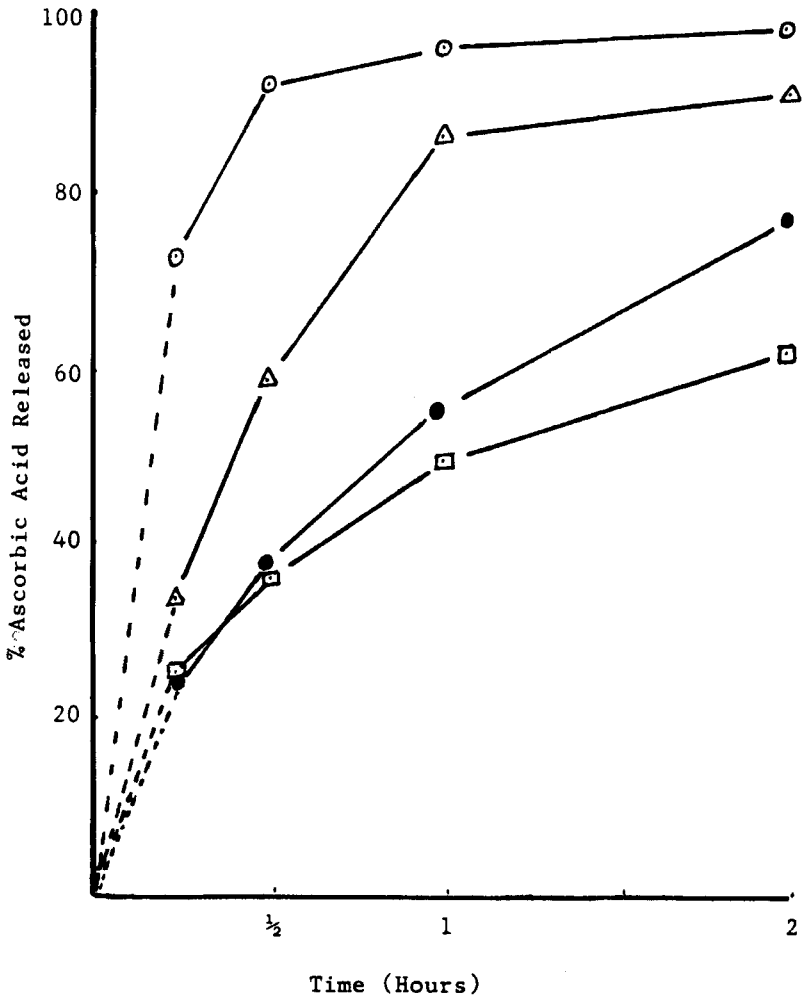

FIGURE 1

Dissolution Profiles of Ascorbic Acid from Tablets Stored at 40°C and 90% R.H. Key: ⊙ -Fresh tablets, ▲ -Tablets stored for 20 days, ● -Tablets stored for 48 days, ⊡ -Tablets stored for 125 days

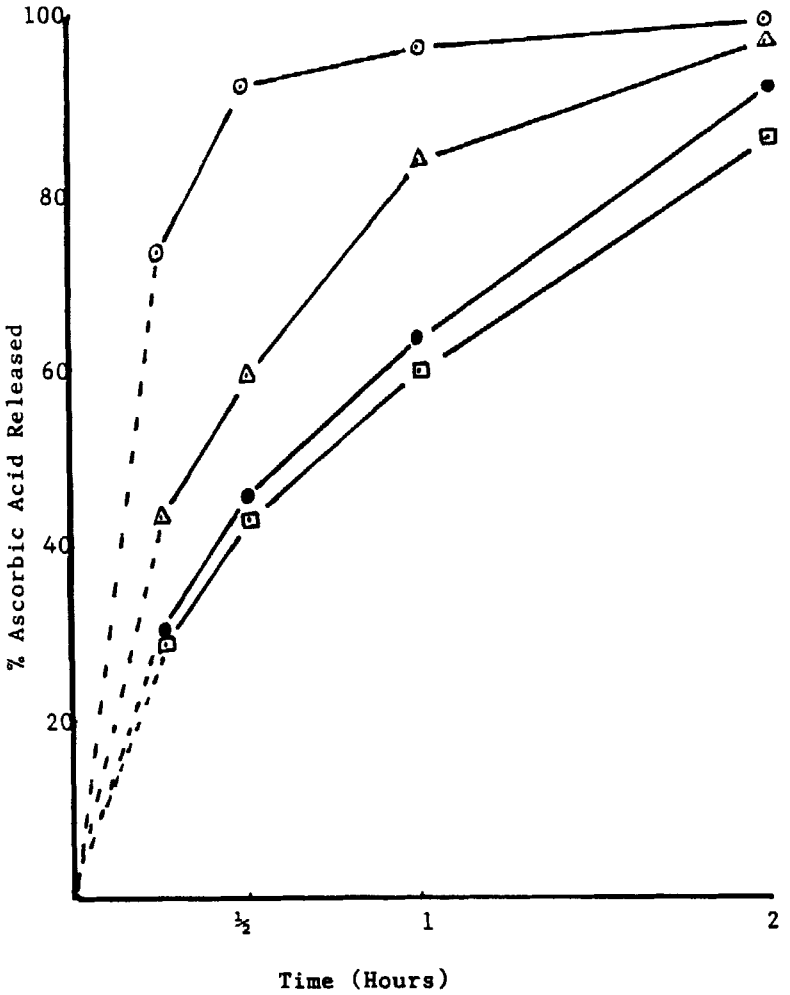

FIGURE 2

Dissolution Profiles of Ascorbic Acid from Tablets Stored at 40°C and 35% R.H. Key: ⊙ -Fresh tablets, △ -Tablets stored for 20 days, ● -Tablets stored for 48 days, ⊡ -Tablets stored for 133 days

the tablets stored at 40°C and 35% R.H. remained virtually unchanged as evidenced from Table 2.

Disintegration time was found to increase substantially during storage under either dry or wet conditions as can be seen from Table 2. This may be attributed to thermal gelation of the cellulose ester coat applied to the ascorbic acid particles used in the manufacture of the tablets.

Figures 1 and 2 illustrate the influence of storage conditions on the release of ascorbic acid from the tablets. It is evident that the decrease in dissolution rate was more pronounced for tablets stored at 40°C and 90% R.H. This again can be attributed to thermal gelation of the cellulose ester coat of the ascorbic acid particles.

CONCLUSIONS

The study has shown that storage under tropical conditions can substantially affect chemical as well as physical stability of ascorbic acid tablets. Moisture appeared to be a significant contributing factor to the enhancement of tablet instability.

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