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COLOR STABILITY OF ASCORBIC ACID TABLETS MEASURED BY TRISTIMULUS COLORIMETER

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ABSTRACT

The influence of three different tableting diluents and three different forms of ascorbic acid on the color change of vitamin C have been investigated. Ten different direct compression formulations were made and subjected to accelerated stability study. Color changes in tablets were monitored with a Tristimulus Colorimeter. It has been found that lactose and Emdex influenced the color change of direct compression ascorbic acid tablets to a lesser degree than Sorbitol. Further, Calcium Ascorbate brought changes in the color of the tablets at a faster rate than C-90 or Sodium Ascorbate. A good correlation of 0.998 was found for a linear relation of visual color rating against normalized total color difference values of these tablets.

INTRODUCTION

Ascorbic Acid tablets discolor during storage under normal conditions of temperature and humidity. Tablets stored in

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amber colored glass bottles at room temperature gradually change from a white to a yellowish-brown color. This is well evidenced by the fact that vitamin C tablets available in the market differ from white to pale yellow in color. The color stability of ascorbic acid in a tablet dosage form is influenced by environmental conditions as well as excipients used in the formulation (1-4).

In earlier studies, fading of color in tablet formulations was followed by spectrophotometers with light reflectance attachment (5, 6). These studies were mainly aimed at FD&C dyes and their corresponding lakes.

Wort (4) showed the effect of lubricants and glidants on the color stability of ascorbic acid. This report revealed the importance of humidity control in the color stability of ascorbic acid. It was established that the color stability is closely related to chemical stability.

At present, there are at least 17 different forms of ascorbic acid on the market all of which are recommended for various pharmaceutical applications. C-90, Calcium Ascorbate, and Sodium Ascorbate fine granular were chosen for this study.

Ascorbic Acid is widely used in vitamin formulations and in other pharmaeutical preparations. The purpose of this investigation was two-fold: First, it was aimed to study the effect of sweeteners on the color stability of vitamin C chewable tablets; second, the study was extended to evaluate color stability of vitamin C chewable tablets made with three different forms of ascorbic acid.

THEORY

Objects have an appearance when illuminated by light, normally. The color perception of an object varies with a change in the wave length of light. Human eye responds to light energy having wave lengths between 380 mm to 780 mm and thus this range of electromagnetic spectrum is called visible spectrum.

The basis for the tristimulus colorimetry is that any color can be reproduced by three other colors in a controlled experiment. The light source illuminates the sample and the light reflected by the sample is detected and resolved into three signals by the electronics of the instrument. These signals are simultaneously displayed as digital readout.

In the CIE (Commission Internationale de'Eclairage) system, Y, X, and Z are defined as follows:

$$Y = \int_{380}^{750} \bar{y}\ HR\ d \quad ; \quad X = \int_{380}^{750} \bar{x}\ HR \quad ; \quad Z = \int_{380}^{750} \bar{z}\ HR \qquad \text{(Eq 1)}$$

where R is the Ratio of light diffused from the sample, $\bar{y}$, $\bar{x}$, $\bar{z}$, are the wave lengths of the response curve of the standard observer, and H is the wave length of the illuminent. Hunter scale represents the mathematical approximation of the non-linear black white response of the eye. The relationship of this scale and CIE is shown below:

$$L = 10Y^{1/2} \quad \text{(Eq 2)}$$

$$a_L = 17.5\ (1.02\ X-Y)/y^{1/2} \quad \text{(Eq 3)}$$

$$b_L = 7.0\ (y-0\ \ 8467Z)/y^{1/2} \quad \text{(Eq 4)}$$

A plus value a_L indicates redness and a minus value greeness; a plus value of b_L indicates yellowness and a minus value blueness; and the term L is a lightness function and simulates Y.

Total color difference is the magnitude of the resultant vector of three component differences, ΔL, Δa_L, and Δb_L. The total magnitude of color difference, E is a scalar quantity and may be computed from the equation:

$$E = \sqrt{(\Delta L)^2 + (\Delta a_L)^2 + (\Delta b_L)^2} \quad \text{(Eq 5)}$$

EXPERIMENTAL

Materials: Raw materials used in this study are listed in Table 1.

Directly compressible C-90 granulation contains modified food starch and lactose in addition to ascorbic acid. All materials used in this study were obtained directly from the vendors.

Methods:

Tablets were made using direct compression technique on a Rotary

TABLE 1

RAW MATERIAL	GRADE/DESCRIPTION	VENDOR	LOT #
Ascorbic Acid	90% Ascorbic Acid/C-90	Roche	399110
Calcium Ascorbate	82.6% Ascorbic Acid	EM Chemicals	2212524
Sodium Ascorbate	88.9% Ascorbic Acid	Takeda	168
Sorbitol	Crystalline USP (Tablet Type)	Pfizer	691252-S6929
Corn Syrup Solids	Emdex, M5	E.Mendell	
Lactose	USP Regular	Foremost	310
Calcium Stearate	FCC	Mallinckrodt	5853112

Tablet Press* with 7/16" standard cup punches. Weight and thickness of the tablets were adjusted to 600 mg and 6 mm, respectively. Throughout the process, tablets were run at uniform weight and pressure in order to obtain consistent surface properties.

Ten different formulations were made with variations in excipient (sweetener), and type of ascorbic acid. These formulations are shown in Table 2. Formulations made with fructose and/or dextrose anhydrous are now shown in the table because the tablet compression trials were unsuccessful. Tablets made with these two ingredients were extremely friable and thus eliminated from the remaining study.

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* Stokes D3, Press, Stokes-Merril Products, Penwalt Corp., Warminster, PA 98974

TABLE 2

Summary of ten different vitamin C formulations used in Color Stability Study.

	% FORMULA									
RAW MATERIAL	I	AI	AII	AIII	BI	BII	BIII	CI	CII	CIII
Ascorbic Acid *	99.9	18.7			18.7			18.7		
Calcium Ascorbate			20.2			20.2			20.2	
Sodium Ascorbate				18.8			18.8			18.8
Sorbitol		80.3	78.8	80.2						
Corn Syrup Solids					80.3	78.8	80.2			
Lactose								80.3	78.8	80.2
Calcium Stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

*C-90 is a granulation of vitamin C, modified food starch, and lactose.

Tablets were packed in 100 cc glass containers and all the bottles were torqued** down to 20 inch pounds. Then, these bottles were kept in 25°C/75% RH, 35°C/75% RH, and 45°C/75% RH experimental chambers. Samples (one bottle of each) were collected at the end of 1, 2, 3, 4, and 8 week periods and allowed to equilibrate to ambient conditions in the laboratory.

Measurement of Coloration:

Samples collected from the environmental chamnbers at 0 time to 8 weeks were subjected to color evaluation. The surface color of the tablets was quantitatively measured with a Tristimulus Colorimeter*** using the small spot measuring area (10 mm diameter). A specially made aperture plate to hold 7/16" tablets was placed in the sample port of the instrument and then color of the tablets was subsequently measured on Y, X, and Z scale.

At least three tablets (both sides) from each sample were employed in this color measurement experiment.

Efforts were made to check the calibrations of the instru- intermittently during the process of data collection. In order to assure the accuracy of the data, manufacturer's instructions on the use of the instrument were followed very closely. The data collected as chromacity coordinates (Y, X, Z) was reduced to the magnitude of the color difference, E.

** Spring Torque Tester, Owens, Illionois.
*** Gardness XL-23 Tristimulus Colorimeter, Gardner Laboratory, Inc., Bethesda, MD 20014

Sensory Evaluation:

In order to be consistent in the evaluation judgement, the same criteria was given to each score in the scale: 1-No change in color (whtie); 2-Whitish Yellow; 3-Yellowish-White; and 4-Yellowish-Brown. At least three to five tablets from each bottle were checked before a score was assigned to a given condition.

RESULTS AND DISCUSSION

The measured Y, X, Z color coordinate were transformed into L, aL, and bL values with the equations 2, 3, and 4. Then, the value of L, aL, and bL were calculated by comparing zero time values with the test values of various conditions. E-values were derived by plugging these values into equation 5.

E-values for various conditions and formulations were calculated for samples obtained at the end of 1, 2, 3, 4, and 8 weeks storage in environmental chambers. Changes in the magnitude of total color difference were plotted against time. All slopes of the lines were calculated by linear regression analysis (8,9) using an electronic calculator (HP, model 9825B). The number of points on each line is equal to 5. All formulations showed linearity evidenced by a correlation coefficient greater than 0.9 except in a couple of lactose based formulae. Since the plots of E against time are linear, the order of reaction for color change is recognized as zero-order.

Formulations made with lactose as a diluent showed very little change evidenced by smaller E-values compared to Sorbitol and Emdex formulations. The largest E-values for Sorbitol, Emdex and Lactose formulations at 45°C/75% RH were found to be 25, 24, and 8, respectively.

Formulations made with Calcium Ascorbate and Sodium Ascorbate developed color in the tablets at a faster rate than the tablets made with Ascorbic Acid (C-90), which is reflected by larger slopes in the regression equations of Table 3. Nevertheless, it suggests that C-90 coated with modified food starch and lactose has better stability.

Coated Ascorbic Acid is not readily available for chemical reaction with the other ingredients of the formulae studied. It has been reported (4) that the color change in ascorbic acid is directly related to the chemical degradation of this vitamin. Further, the authors monitored the color development as well as the ascorbic acid degradation of formula containing C-90, Sorbitol, and Calcium Stearate. The vitamin C degradation and color development rate constant determined for 25°C/75% RH, 35°C/75% RH, and 45°C.75% RH were compared. The rate of color development is found to be linearly correlated with the rate of vitamin C degradation (Y=0.51+2.1 X) with a correlation coefficient of 0.99.

The thermodynamic parameter, activation energy (Ea), was calculated from Arrhenius plots for each of the formulations. The slopes of the regression equations of Table 3 are the reaction rate constants. These rate constants values were used in

TABLE 3

Stability Data on Ten Different Formulations is Represented in the Form of Linear Regression Equations. The Slopes of These Equations Are The Rate Constants at the Temperature Studied

FORMULA	STORAGE TEMP. with 75% RH (°C)	REGRESSION EQUATION	CORRELATION COEFFICIENT
Ascorbic Acid + Ca Stearate	25	E=0.08t + 3.25	0.85
	35	E=0.15t + 3.39	0.89
	45	E=0.62t + 3.07	0.99
C-90 + Sorbitol + Ca Stearate	25	E=0.29t + 1.43	0.92
	35	E=1.00t + 1.74	0.99
	45	E=2.50t + 2.21	0.99
Ca Ascorbate + Sorbitol + Ca Stearate	25	E=0.91t + 3.53	1.00
	35	E=1.55t + 5.42	0.96
	45	E=2.20t + 9.77	0.84
Na Ascorbate + Sorbitol + Ca Stearate	25	E=0.42t + 2.76	0.96
	35	E=1.32t + 3.65	0.98
	45	E=1.30t + 3.52	0.88
C-90 + Emdex + Ca Stearate	25	E=0.10t + 2.46	0.92
	35	E=0.47t + 2.40	0.98
	45	E=1.52t + 3.50	0.95
Ca Ascorbate + Emdex + Ca Stearate	25	E=0.25t + 2.73	0.71
	35	E=0.86t + 3.02	0.99
	45	E=2.45t + 4.12	0.98
Na Ascorbate + Emdex + Ca Stearate	25	E=0.20t + 2.73	0.91
	35	E=0.86t + 3.02	0.99
	45	E=2.45t + 4.12	0.99
C-90 + Lactose + Ca Stearate	25	E=0.03t + 1.33	0.66
	35	E=0.15t + 1.36	0.97
	45	E=0.47t + 1.25	0.99
Ca Ascorbate + Lactose + Ca Stearate	25	E=0.04t + 2.75	0.71
	35	E=0.15t + 2.55	0.53
	45	E=0.41t + 2.76	0.99
Na Ascorbate + Lactose + Ca Stearate	25	E=0.08t + 1.93	0.65
	35	E=0.27t + 2.08	0.96
	45	E=0.73t + 2.03	0.99

preparing Arrhenius plots. Arrhenius equations obtained for all the formulations showed good linearity with correlation coefficients above 0.9. The effect of temperature on the color change of tablets is expressed by using Arrhenius equation. As shown in Table 4, plots of log K versus 1/T yielded straight-line relationships with negative slope for each of the formulae studied. The activation energy of ascorbic acid calculated by Blaug et. al. (10) in a pH range of 3.5 to 6.6 varied between 23 to 78 K cal/mole.

The Ea values obtained in our study favorably compare with the Blaug's findings.

Tablets were visually rated on a subjective scale of 1 to 4. In several tablets, it was observed that the color devlopment on two faces of the tablet is different. One side is slightly darker than the other.

Normalized E values were compared with sensory socres. Normalization of E values was done by the formula shown below:

$$E_{Normalized} = \frac{E_{Final} - E_{Zero}}{E_{Zero}}$$

Where E Final is the value of E at any time t of a given formula, and E_o is the value of E at time zero of the same formula..

Figure 1 shows the results of this comparison. The bars on the line represent the standard deviation. In this study, the authors found a sensory score beyond 2.5 perceived as a dis-

TABLE 4

Degradation rate constants shown in the previous Table were fitted to Arrhenious Model using Linear regression.

FORMULA	REGRESSION EQUATION	CORRELATION COEFFICIENT	Ea K Cal/ mole	Average Visual Rating
C-90+Ca Stearate	$\log K=-4.195\left(\frac{10^3}{T}\right)+12.922$	0.972	19.20	1
C-90+ Sorbitol+Ca Stearate	$\log K=-4.439\left(\frac{10^3}{T}\right)+14.378$	0.998	20.31	2
Ca Ascorbate + Sorbitol + Ca Stearate	$\log K=-1.820\left(\frac{10^3}{T}\right)+6.079$	0.995	8.33	3
Na Ascorbate + Sorbitol + Ca Stearate	$\log K=-3.058\left(\frac{10^3}{T}\right)+3.058$	0.959	14.00	2
C-90+Emdex + Ca Stearate	$\log K=-4.184\left(\frac{10^3}{T}\right)+13.260$	0.999	19.15	1
Ca Ascorbate + Emdex + Ca Stearate	$\log K=-5.608\left(\frac{10^3}{T}\right)+17.839$	0.998	25.66	1
Ca Ascorbate + Emdex + Ca Stearate	$\log K=-5.165\left(\frac{10^3}{T}\right)+16.656$	0.998	23.64	1
C-90+ Lactose + Ca Stearate	$\log K=-5.672\left(\frac{10^3}{T}\right)+17.539$	0.997	25.96	1
Ca Ascorbate + Lactose + Ca Stearate	$\log K=-4.795\left(\frac{10^3}{T}\right)+14.712$	0.998	21.94	1
Na Ascorbate + Lactose + Ca Stearate	$\log K=-4.553\left(\frac{10^3}{T}\right)+14.192$	0.999	20.83	1

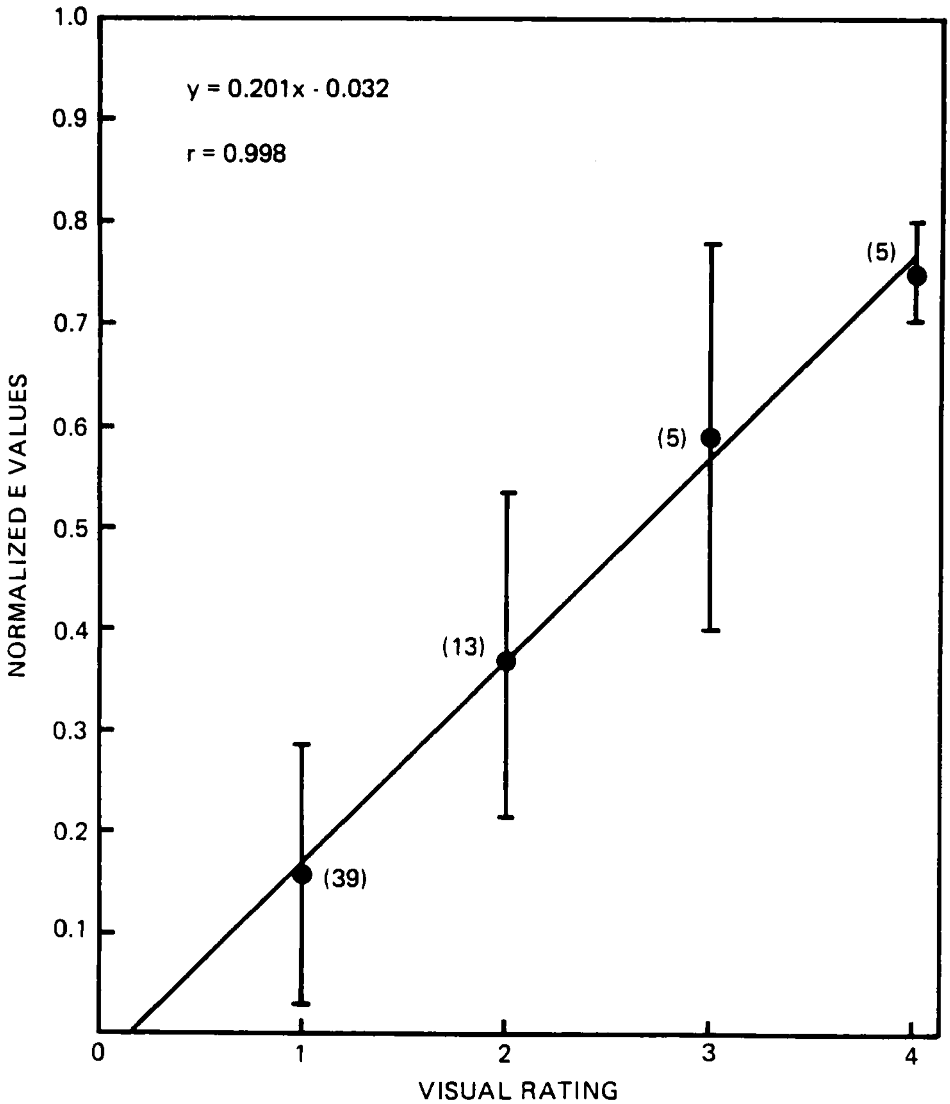

Figure 1: Visual rating of Ascorbic Acid tablets color is compared with the normalized, total colors difference (E) values. The vertical bars on the plot are one standard deviation on the mean. The number in the parenthesis is the sample size for the mean value.

tinct color difference in tablets. At a visual perception of 2.5, the normalized E is found to be 0.48. Assuming 0.48 as normalized E acceptable at the end of two years, predictions were made for all the formulae studied and found them not to meet the set criteria.

Table 4 compares the average scores of visual rating with the activation energy. As expected, when the activation energy is high, the time it took for the tablets to change color was longer than the low activation energy case. Formula containing calcium ascorbate and sorbitol developed a brownish color at a faster rate and was detected both visually and quantitatively.

CONCLUSION

1. The color change in ascorbic acid tablets studied is a zero-order reaction.

2. Lactose and Emdex appear to influence the color change in the tablets to a lesser degree than Sorbitol.

3. Interaction between Calcium Ascorbate and Sorbitol seems to be more pronounced than the interactionsa of Calcium Ascorbate, Emdex, and Lactose.

4. Color changes observed in a subjective evaluation were well correlated with the quantitative measurements. Further, the

use of light reflectance measurements greatly improved the reliability and usefulness of data.

5. The activation energy Ea for vitamin C derived from the color change data compares favorably with known activation energy is determined for chemical degradation of this vitamin.

6. The higher the activation energy, the longer it took the tablets to develop color and vice-versa.

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