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Investigation of Colorant FD&C Yellow No. 5 Stability in Pharmaceutical Syrup Containing Ascorbic Acid and the Optimal Storage Condition

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Original Research Article

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ABSTRACT

Stability of colorant FD&C Yellow No. 5 and ascorbic acid (AA) in pharmaceutical KndCold syrup under different storage conditions (Standard conditions, temperature variation, sunlight presence, and sodium hydroxide addition) have been investigated. Under the standard conditions, 18.6% of ascorbic acid in solution converted, while pulling the samples out to indirect sunlight, color intensity was increased by 53%., and AA loss was recorded as 19.1%. Storage temperature was had a harsh effect on AA degradation and color intensity, specifically the loss of AA and color intensity boost was 2.1%, 16.8%, 24.7% and 2.8%, 40%, 53.1%, at 0, 20, and 40℃, respectively. Subsequently, the role of pH was investigated by adding a base such as NaOH. The addition of the base produces the different pH syrups: 4.5, 5.8, and 7.4. A sample of pH 7.4 fulfills the lowest AA degradation rate, nearly 5.7%, similarly for color intensity change. In conclusion, ascorbic acid degradation in KndCold syrup has a direct influence on the concentration of the yellow color. The optimal conditions for processing the yellow colored pharmaceutical syrups, which contains ascorbic acid, could be a temperature below 10℃, the completely a bsence of sunlight, and basic solution pH.

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Keywords: Ascorbic acid; FD&C yellow No.5; degradation; storage.

ABBREVIATIONS

AA	*: Ascorbic Acid*
SC	*: Standard Conditions*
EDTA Disodium	*: Edetate disodium*
FD&C	*: Federal Food, Drug, and Cosmetic*
NaOH	*: Sodium Hydroxide*

1. INTRODUCTION

Utilization of ascorbic acid (Vitamin C) in pharmaceuticals manufacturing has beneficial effects on human body [1-6]. The most popular function of ascorbic acid is an effective antioxidant [1,7]. Numerous pharmaceutical forms involve ascorbic acid as an individual active ingredient or combined with other ingredients [8,9]. However, degradation is one of the major drawbacks of ascorbic acid in liquids due to several factors. Scrutinizing of Ascorbic acid degradation in liquids is reported in the literature [10-14]. All of the cited studies tackled decomposition kinetic of ascorbic acid in simple solutions and fruit juices. Not only in the pharmaceutical liquids, pH of solution enhances the degradation rate of ascorbic acid [15]. Besides, photosensitizing environment, the presence of sugar, storage temperature, the presence of oxygen, and storage period have demonstrated to be a decomposition motivator [12,16-18].

Ascorbic acid pharmaceuticals, which include liquids, tablets, drops, etc., are utilized as nutritional supplements or/and to overcome particular health issue [9,19]. KndCold is a yellow colored syrup contains ascorbic acid, paracetamol, chlorpheniramine maleate, and pseudoephedrine HCl as active ingredients. After a month of syrup manufacturing, a significant boost in the color concentration has been observed, and not in another acid-free ascorbic syrup. According to the pharmaceuticals assessment criteria, occasionally, a defect in drug composition can lead to a significant alteration in color. Analytically, the yellow color intensity of syrup is proportional to the degradation rate of ascorbic acid.

The effects of ascorbic acid ($C_6H_8O_6$) degeneracy on FD&C yellow No. 5 ($C_{16}H_9N_4Na_3O_9S_2$) in pharmaceutical liquids have not been studied yet. Therefore, this study has been carried out to figure out the optimal environment for ascorbic acid syrup (KndCold) manufacturing and storage. Yellow No. 5 colorant intensity and ascorbic acid concentration in KndCold has been determined based on sunlight presence, storage temperature variation, and alkaline solution addition. The alkaline solution was used is a sodium hydroxide, to control pH of the solution.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 KndCold syrup

As mentioned earlier, KndCold syrup is a combination of ascorbic acid 55 mg, paracetamol 120 mg, chlorpheniramine maleate 2 mg, and pseudoephedrine HCl 15 mg per 5 ml of syrup. Hence, this medicine is used to treat cold & flu and allergy. The inactive excipients in KndCold syrup consist of sugar, EDTA Disodium, Sodium metabisulfite, sodium saccharin, propylene glycol, ethanol (96 mL/100 mL water), glycerin, sorbitol, FD&C yellow no.5 ($C_{16}H_9N_4Na_3O_9S_2$), and pineapple flavor. Table 1 shows the standard specifications of KndCold syrup. The size of the industrial KndCold batch is 2000 liter, which produces 20000 bottles of the syrup. About 200 shaded bottles have been taken from random batch to perform the tests.

2.1.2 Reagents

Dilute H_2SO_4 (5.7 mL/100 mL water), starch as an indicator, iodine solution (0.05 mole/L), and deionized water, all of these reagents except DW have been prepared by [20].

2.1.3 Sodium hydroxide additive

Reagent grade, ≥98% purity, pellets (anhydrous) was purchased from Sigma-Aldrich Co. Ltd.

Table 1. Standard specification of KndCold syrup

Specification	Value
pH	3.5
Specific gravity	1.17
Alcohol content	8 vol.%
Color intensity (reading at 400 nm)	0.35

2.2 Methods

2.2.1 Determination of color intensity

FD&C yellow No. 5 concentration in the syrup was determined as a light transmittance using a spectrophotometer (SPECORD® 210 PLUS, Analytik Jena AG, Germany) at wavelength 400 nm against a cell of deionized water.

2.2.2 Determination of ascorbic acid

Ascorbic acid retention in KndCold syrup was determined using an iodometric titration, which involves the following steps:

i. A 10 ml aliquot of sample is placed into a 250 ml conical flask.
ii. A 20 ml of 5.7 vol. % H_2SO_4 solution and 20 ml of DW are added to above flask.
iii. A 2 ml of the starch indicator is added then the solution is filtered through a Filtropa size four filter papers.
iv. The filtered solution is titrated, using class A 100 ml burette, with 0.05 mole/L iodine solution to the first light green shade.
v. Each ml of 0.1 N iodine solution is equivalent to 8.806 mg ascorbic acid [20]. Ascorbic acid content was calculated as mg ascorbic acid per 5 ml of KndCold Syrup.

3. RESULTS AND DISCUSSION

3.1 Yellow No. 5 Stability in the Standard Conditions

The term of "standard conditions" refers to additives-free KndCold formula and customary pharmaceuticals storage conditions, which include 25°C, humidity >15%, and dark circumference. The aforementioned problem of KndCold colorant instability has been determined over two months, the color and ascorbic acid content were tested every five days. In a manufacturing day, ascorbic acid content and color intensity was 55.8 mg/5 ml and 0.35, respectively.

3.2 Effects of Indirect Sunlight on Yellow No. 5 Stability and Ascorbic Acid Loss

Placing about 40 diaphanous bottles of KndCold syrup in front of the transparent window that allows passing sufficient sunlight. Based on the results, sunlight slightly promotes ascorbic acid degradation, as well as, color intensity boosts. Fig. 1.a and 1.b depict the comparison of effects of indirect sunlight and standard storage condition on ascorbic acid content and color intensity.

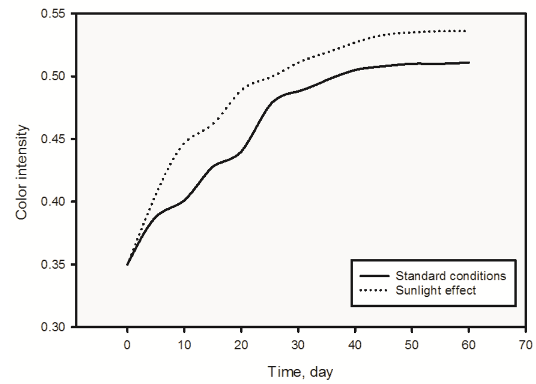

Fig. 1.a. Yellow color intensity change with time stored under SC and under sunlight

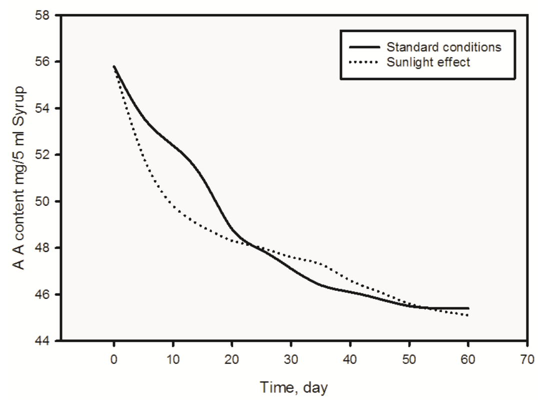

Fig. 1.b. AA concentration fall with time stored under the Standard Conditions and under sunlight

3.3 Effects of Storage Temperature on Yellow No.5 Stability and Ascorbic Acid Loss

The color stability and ascorbic acid loss due to storage temperature in the KndCold syrup have been investigated at three different temperatures: 0, 20, and 40℃. Shaded sample bottles of KndCold have been stored in three stability chamber (Thermolab Scientific) for 60 days. At 0℃, the sample is completely frozen; thereby it needs to be molten before the test. The degradation rate of ascorbic acid is much slower than higher storage temperatures. Unfortunately, the storage of KndCold syrup up to two months at 0℃ after manufacturing poses uneconomic procedure. While, ascorbic acid retention encounter a higher level of degradation when prone to a higher temperature as 40℃. Fig. 2.a and 2.b illustrate the loss of ascorbic acid retention and color intensity outgrowth during storage at 0, 20, and 40℃.

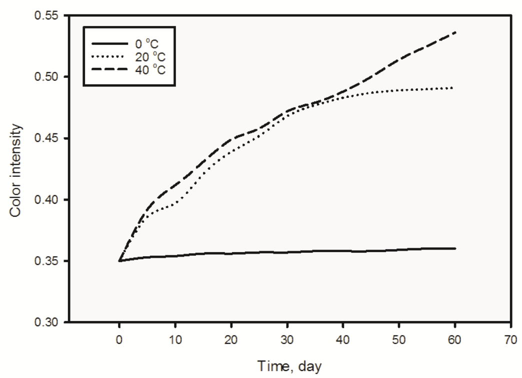

Fig. 2.a. Yellow color intensity change with time stored in different storage temperatures

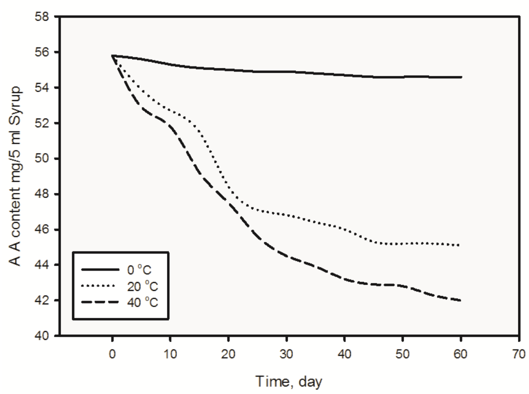

Fig. 2.b. Ascorbic acid concentration fall with time stored in different storage temperatures

3.4 Effects of Sodium Hydroxide Addition on Yellow No.5 Stability and Ascorbic Acid Loss

As mentioned earlier, in the literature, the studies point out that the solution pH is considered the most influential parameter on the degradation rate of ascorbic acid and the color change [13,15]. As an ascorbic acid is present in KndCold syrup with significant quantity, the solution has a high acidity. In order to increase the pH of the solution, varied amounts of sodium hydroxide were added and blended with the solution, which was 10 mg, 20 mg, and 40 mg NaOH per 5 ml of syrup. Once the NaOH powder was added, pH of the resultant solution has been determined. pH of the sample is 4.5 for 10 mg, 5.8 for 20 mg, and 7.4 for 40 mg NaOH content. These samples have been stored at SC in the stability chamber. Obviously, the rise in the color intensity is not proportional to pH of syrup. As pH of containing ascorbic acid solution above or equal 5.8, ascorbic acid undergoes a slow degradation reaction, as exhibited in Fig. 3.a and 3.b.

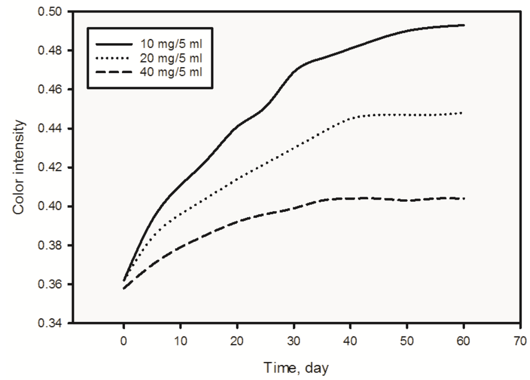

Fig. 3.a. effects of pH on color intensity of the syrup stored under standard storage conditions

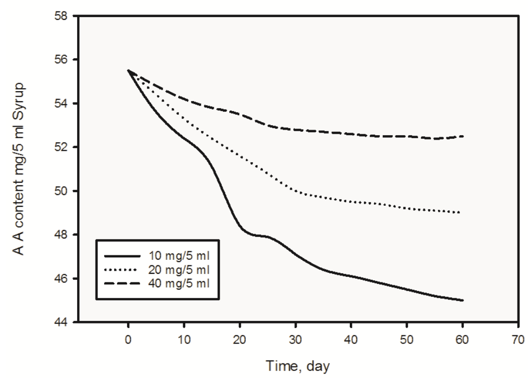

Fig. 3.b. effects of pH on Ascorbic acid content in the syrup stored under standard storage conditions

4. CONCLUSION

A link between ascorbic acid concentration and yellow colorant intensity is seen clearly in mentioned results under various conditions. As a consequence of AA degradation, the solution is colored with extremely faint yellow in a clear solution, as tested in the Lab. experiments. The higher the degradation rate of ascorbic acid, the greater color intensity. Along the lines of mentioned results, loss in of AA in KndCold Syrup can be predicted based on the severity of the storage conditions. Storage temperature highly motivates AA degradation reaction. After two months of storage at 40℃, nearly 25% of ascorbic acid was disappeared. Besides, solution pH plays a paramount role in control the reaction rate of AA. In the syrup pH of 7.4, the ascorbic acid loss is much lower than the initial pH of KndCold syrup. The last parameter that investigated in this study is the sunlight, same as temperature; sunlight slightly promotes the degradation of AA.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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