KINETIC STUDY OF VITAMIN C DEGRADATION FROM PHARMACEUTICAL PRODUCTS*

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Two simple procedures for the determination of ascorbic acid (Vitamin C) content in a Vitamin C tablet are proposed: conductometry and titrimetric method with potassium bromat-bromide solution in the acid medium. The procedures have been applied to the analysis of locally commercial Vitamin C tablet samples. The variations of Vitamin C concentration were studied in formation of temperature. For the kinetic study was determinate the rate constant, the half-time and the activation energy for vitamin C.

Key words: conductometric and titrimetric methods, ascorbic acid, pharmaceutical products.

1. INTRODUCTION

Ascorbic acid is one of the important water soluble vitamins. It is essential for collagen, carnitine and neurotransmitters biosynthesis. [1] Most plants and animals synthesize ascorbic acid for their own requirement. However, apes and humans can not synthesize ascorbic acid due to lack of an enzyme gulonolactone oxidase. Hence, ascorbic acid has to be supplemented mainly through fruits, vegetables and tablets. [2]. The current US recommended daily allowance (RDA) for ascorbic acid ranges between 100–120 mg/ per day for adults. Many health benefits have been attributed to ascorbic acid such as antioxidant, anti-atherogenic, anti-carcinogenic, immunomodulator and prevents cold etc. Thus, though ascorbic acid was discovered in 17th century, the exact role of this vitamin/nutraceutical in human biology and health is still a mystery in view of many beneficial claims and controversies [3].

Ascorbic acid is a labile molecule; it may be lost from foods during cooking/processing even though it has the ability to preserve foods by virtue of

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its reducing property. Syntethis ascorbic acid is available in a wide variety of supplements, tablets, capsules, chewable tablets, crystalline powder, effervescent tablets and liquid form.

L-ascorbic acid ($C_6H_8O_6$) is the trivial name of Vitamin C. The chemical name is 2-oxo-L-threo-hexono-1, 4-lactone-2, 3-endiol, Fig. 1 [4].

Ascorbic acid being a water soluble compound is easily absorbed but it is not stored in the body. The major metabolites of ascorbic acid in human are dehydroascorbic acid, 2, 3-diketogluconic acid and oxalic acid, Fig. 2.

The main route of elimination of ascorbic acid and its metabolites is through urine. It is excreted unchanged when high doses of ascorbic acid are consumed. Ascorbic acid is generally non-toxic but at high doses (2-6g/day) it can cause gastrointestinal disturbances or diarrhea [5, 6].

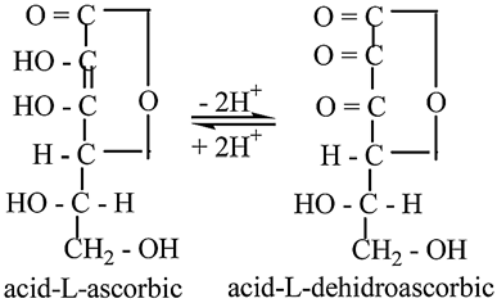


Fig. 1 – Vitamin C oxidation.

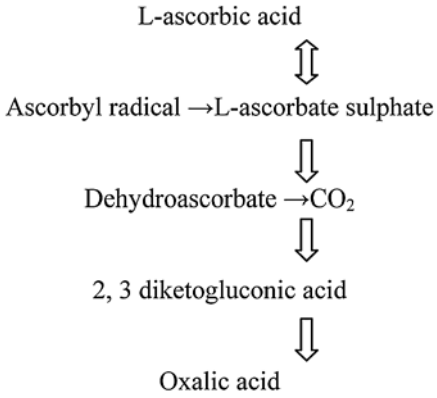


Fig. 2 – Catabolism of ascorbic acid.

Keeping in view its importance, the analysis of food products and pharmaceuticals containing this vitamin assumes significance.

Such attempts to quantify ascorbic acid in these samples have resulted in a large number of methods: titrimetry, voltametry, fluorometry, potentiometry, kinetic-based chemiluminiscence (CL), flow injection analyses and chromatography [7–9].

2. EXPERIMENTAL

For determination of ascorbic acid were used two methods: a titrimetric method with potassium brommat-bromide solution in the acid medium [2] and a conductometric method [1] based by the calibration curve which was plotted under the fallowing operative conditions: 4°C, 18°C, 30°C and 40°C, the linearity range is 0,008–0,1N ascorbic acid.

The methods have been applied to many samples to determine the Vitamin C quantity at different temperature [10].

2.1. REAGENTS

All reagents were of analytical-reagent grade and all solutions were prepared using distilled-deionized water.

A stock standard aqueous ascorbic acid solution (0,1N) was prepared from L-ascorbic acid (Merck). Other standard ascorbic acid solutions were obtained by appropriate dilutions of the stock solution.

For the titrimetric method, the reagents used have been: $Na_2S_2O_3$ 0,1N, $KBrO_3$-KBr 0,05N, $K_2Cr_2O_7$ 0,1N, H_2SO_4 1N, H_2SO_4 1:2, KI, starch indicator 1%.

2.2. APARATUS

For conductometric procedure was used a Conductivity Meter WTW, LF 340-A/SET, made in Germany.

2.3. CONDUCTOMETRY PROCEDURE

First was plotted the calibration graph (Fig. 3) of different ascorbic acid concentrations (0,008N; 0,01N; 0,03N; 0,05N; 0,08N respectively 0,1N) at the room temperature by reading it at the conductivity meter (ìS/cm).

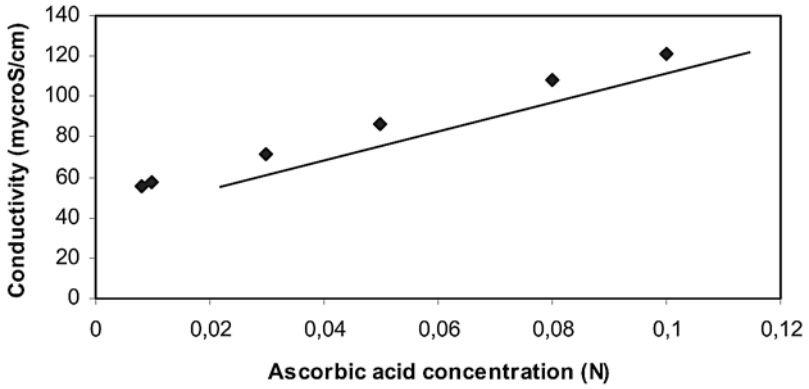
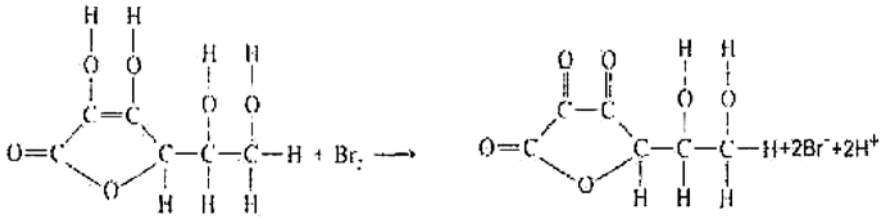


Fig. 3 – The calibration graph from ascorbic acid.

2.4. TITRIMETRY PROCEDURE

Ascorbic acid, $C_6H_8O_6$ is cleanly oxidized to dehydroascorbic acid by bromine:



An unmeasured excess of potassium bromide is added to an acidified solution of the sample. The solution is titrated with standard potassium bromate to the first permanent appearance of excess bromine: this excess is then determined iodometrically with standard sodium thiosulfate. The entire titration must be performed without delay to prevent air-oxidation of the ascorbic acid. [2, 10]

2.5. KINETIC STUDY

For the kinetic study was determinate the rate constant, the half-time and the activation energy for vitamin C.

For rate constant it was applied the formula:

$$k = \frac{2,303}{t} \log \frac{a}{a-x}$$

where: k = the rate constant;

t = the interval of time since the reaction has began;

a = the initial concentration at 18°C;

$a - x$ = the concentration at different temperatures (30°C and 40°C).

Arrhenius noted that the $k(T)$ data for many reactions fit the equation:

$$k = A \cdot e^{-\frac{Ea}{RT}} \qquad (*)$$

where A and E_a are constants characteristic of the reaction and R is the gas constant. E_a is the activation energy and A is the pre-exponential factor or the Arrhenius factor. The units of A are the same of those of k. E_a is usually expressed in kcal/mol or kJ/mol.

Taking logs of equation (*), we get:

$$\ln k = \ln A - \frac{E_a}{RT}$$

For two different temperatures (30°C and 40°C) it was determinate the values for activation energy.

If the Arrhenius equation is obeyed, a plot of log$k$ *versus* 1/T is a straight line with slope $-\frac{E_a}{2.303R}$ and intercept log$A$. This allows E_a and A to be found.

Also it was determinate the values of half-time using the equation:

$$t_{1/2} = \frac{0.693}{k}$$

The time required for concentration of the reactant to drop to half its value is called the reaction's half-time or half-life ($t_{1/2}$).

2.6. ANALYSIS OF SAMPLES

Various Vitamin C tablet samples, commercially available locally, were analyzed. The samples were: standard ascorbic acid solution (Merck), Vitamin C 200 mg tablets, Ascovit 100 mg tablets with orange taste and Vitamin C nose drops 10%.

Twenty tablets were weighed and an average weight of a tablet was calculated before being ground into fine powder. A portion of the powder, equivalent to the average weight of a tablet was dissolved in water and filtered before making a volume of 50 mL. Appropriate dilution may be required. The ascorbic acid liquid form was diluted. The samples were analyzed by both methods.

3. RESULTS AND DISCUSSION

Analyses of locally commercially available Vitamin C tablets are summarized in Tables 1 and 2. The results obtained from conductometry procedures agree with the titrimetric analysis. No significant change in the response was obtained from other ingredients in nominal amounts (reducing sugars (sucrose (30 mg) and lactose (30 mg)), and stearate salts (10 mg as calcium-or magnesium-salt) in a tablet).

Table 1

The results obtained from conductometry methods

Sample	Temperature [°C]	Conductometric procedure [g_{AA}/l]	Recovery [%]
Standard ascorbic acid (AA) by Merck	4	7.75	88
	18	8.55	97.1
	30	8.12	92.2
	40	7.34	83.4
Vitamin C tablet (200 mg)	4	0.77	96.2
	18	0.92	115.0
	30	0.62	77.5
	40	0.54	67.5

Table 1 (continued)

Sample	Temperature [°C]	Conductometric procedure [g_{AA}/l]	Recovery [%]
Ascovit tablet (100 mg) with orange flavor	4	0.36	90.0
	18	0.45	112.5
	30	0.34	85.0
	40	0.24	60.0
Vitamin C nose drops (10%)	4	4.88	97.6
	18	5.35	107
	30	4.50	90.0
	40	4.15	83.0

Table 2

The results obtained with volumetric method

Sample	Temperature [°C]	Titrimetric procedure [g_{AA}/L]	Recovery [%]
Standard ascorbic acid by Merck	4	7.74	87.9
	18	8.51	96.7
	30	8.13	92.3
	40	7.35	83.5
Vitamin C tablet (200 mg)	4	0.76	95.0
	18	0.95	118.7
	30	0.66	82.5
	40	0.57	71.25
Ascovit tablet (100 mg) with orange flavor	4	0.37	92.5
	18	0.47	117.5
	30	0.37	92.5
	40	0.28	70.0
Vitamin C nose drops (10%)	4	4.83	96.6
	18	5.22	104.4
	30	4.44	88.8
	40	4.24	84.8

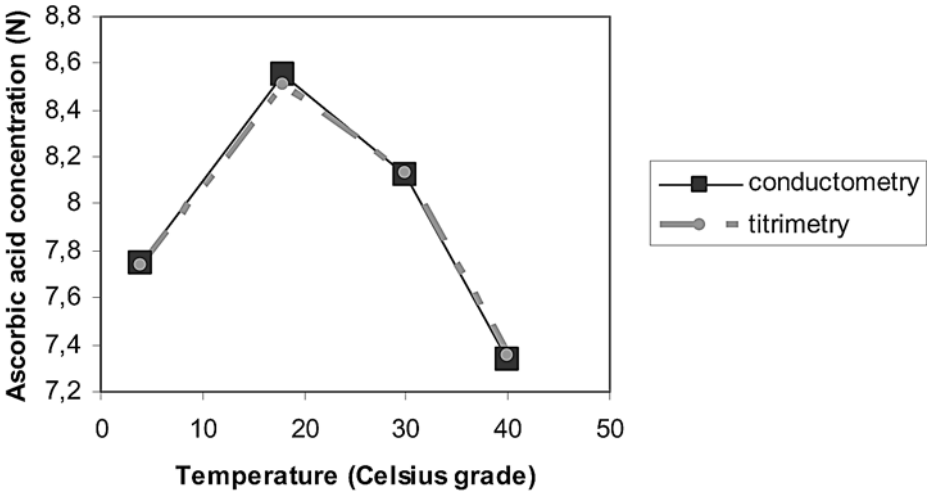


Fig. 4 – Ascorbic acid Merck.

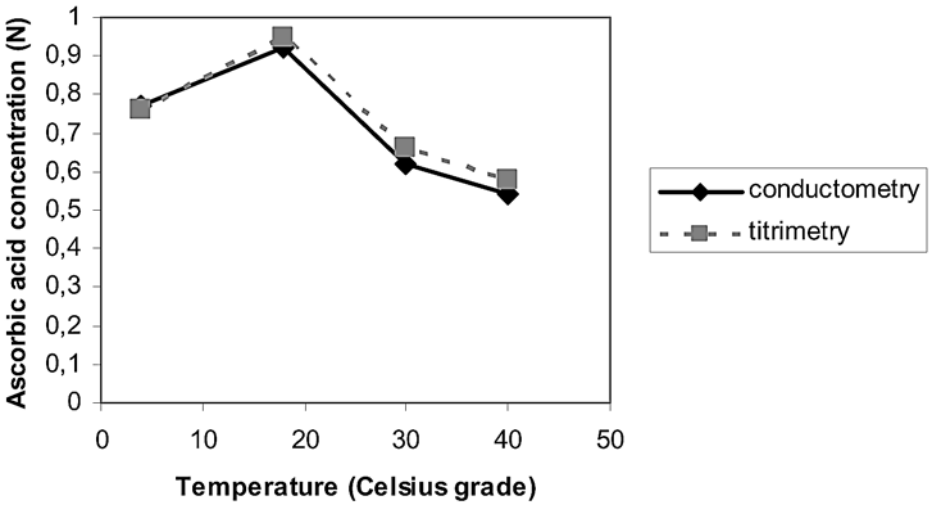


Fig. 5 – Vitamin C tablet (200 mg).

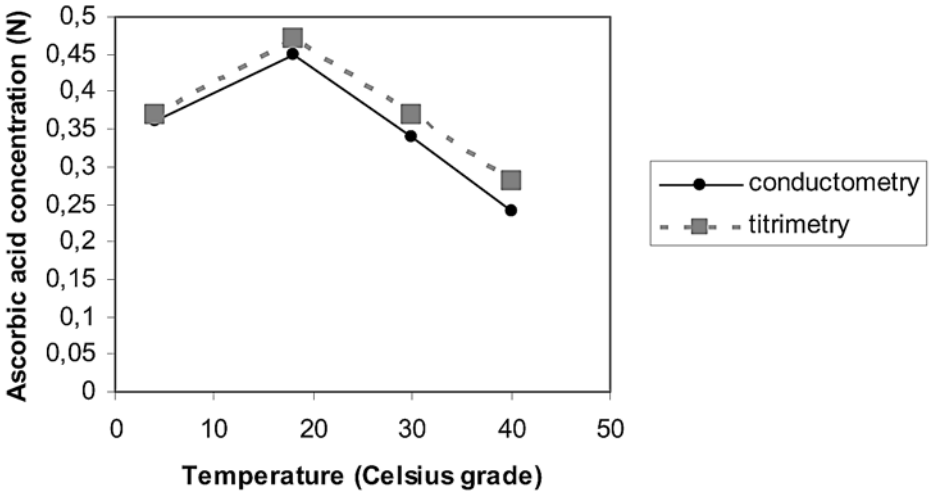


Fig. 6 – Ascovit tablet (100 mg) with orange taste.

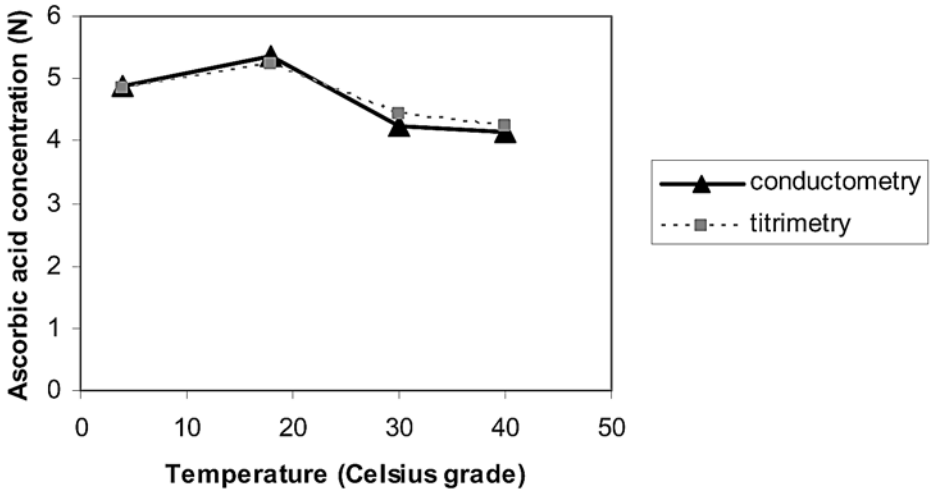


Fig. 7 – Vitamin C (10%) nose drops.

In Table 3 are presented the values for the rate constants determinate at 30°C and 40°C for all types of vitamin C.

It can observe that the rate constants depend strongly on temperature, typically increasing rapidly with increasing *T*.

In Table 4 are present the values of activation energy analytical and graphical determined.

Table 3

The values for the rate constants

Types of vitamin C	The rate constant k [s^{-1}]	
	At 30°C	At 40°C
Standard ascorbic acid solution (Merck)	$1.52 \cdot 10^{-4}$	$2.42 \cdot 10^{-4}$
Vitamin C 200 mg tablet	$8.38 \cdot 10^{-4}$	$1.19 \cdot 10^{-3}$
Ascovit 100 mg tablet	$7.53 \cdot 10^{-4}$	$8.66 \cdot 10^{-4}$
Vitamin C nose drops	$3.43 \cdot 10^{-4}$	$5.34 \cdot 10^{-4}$

Table 4

Activation energy by analytical and graphical

Types of vitamin C	Activation energy *Ea* [kcal/mol]	
	Analytical	Graphical
Standard ascorbic acid solution (Merck)	8.73	8.68
Vitamin C 200 mg tablet	6.65	6.61
Ascovit 100 mg tablet	2.62	2.61
Vitamin C nose drops	8.39	8.35

It can observe that the values of activation energy analytical and graphical determined are in good agreement.

In Table 5 are presented the average values of half-time for all types of vitamin C.

Table 5

The average values of half-time ($t_{1/2}$)

Types of vitamin C	Half-time's values $t_{1/2}$ [sec]
Standard ascorbic acid solution (Merck)	3699.7
Vitamin C 200 mg tablet	704.1
Ascovit 100 mg tablet	859.7
Vitamin C nose drops	1658.51

The value of half-time for standard ascorbic acid solution (Merck) is the highest and the values of half-time for vitamin C 200 mg tablet is the smallest.

4. CONCLUSION

Each conductometry analysis takes about 5 minute and titrimetry analysis about 20 minutes. No pre-treatments of the samples are requested. The variations of Vitamin C concentration were studied in function of light exposition and at different temperature.

The very simple and rapid procedures described in this paper can be an alternative to the more complex and expensive methods for assay of ascorbic acid content in Vitamin C tablets.

The conductometric method is very versatile and useful.

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