ORIGINAL ARTICLE

PHOTOLYSIS OF ASCORBIC ACID IN AQUEOUS SOLUTION: A KINETIC STUDY

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ABSTRACT:
The kinetics of photolysis of ascorbic acid in aqueous solution on UV irradiation has been studied in the pH range 1–11 and the apparent first–order rate constants for the degradation reactions have been determined. The *k*–pH profile for the photolysis in the acid range is represented by a sigmoid curve indicating the gradual ionization of the molecule (AH_2) to ascorbyl anion (AH^-). Ascorbic acid shows maximum stability around pH 5–6 due to the lowest rate of oxidation reduction of the mono–anion form. The rate of photolysis is increased up to sevenfold at pH 10.0, compared to that at pH 5.0, due to an increase in the redox potentials with pH leading to faster oxidation of the anionic species to dehydroascorbic acid in the alkaline range. The rate is very slow in the pH range 1–2 due to the existence of the non–ionized form. The apparent first–order rate constants for the photolysis of ascorbic acid at pH 1–11 range from $0.057–3.948\times10^{-2}$ min^{-1}. A scheme for the sequence of reactions involved in the photolysis of ascorbic acid is presented.

Keywords: Ascorbic acid, Ascorbyl anion, Rate–pH profile, Spectrometric assay.

INTRODUCTION:

Ascorbic acid (AH_2)(1) (Fig. 1) is an essential micronutrient and performs important metabolic functions in humans[1-5]. It is sensitive to air and light[6-8]and is degraded by chemical or Photooxidation. The stability of ascorbic acid has been studied in total parenteral nutrition (TPN) solutions[9-17], infusion solutions[18-42], plant material[43,44], biological fluids[45-48]and milk[49-51]. Attempts have been made to stabilize ascorbic acid by the use of various agents in aqueous solutions[52-55], vitamin preparations[56-60], cosmetic preparations[61-66], food products[63, 67], and [68] and by chemical derivatization[69, 70].An important consideration in the stability of AH_2 in TPN solutions is the generation of hydrogen peroxide in the presence of light[71-75]. This may result from the oxidation of ascorbyl anion by molecular oxygen[76-80]and may further be involved in the degradation of AH_2[81-83]. The kinetics and mechanism of oxidation reactions of AH_2 have been studied by several workers[44, 52, 77, 79, 84-95].

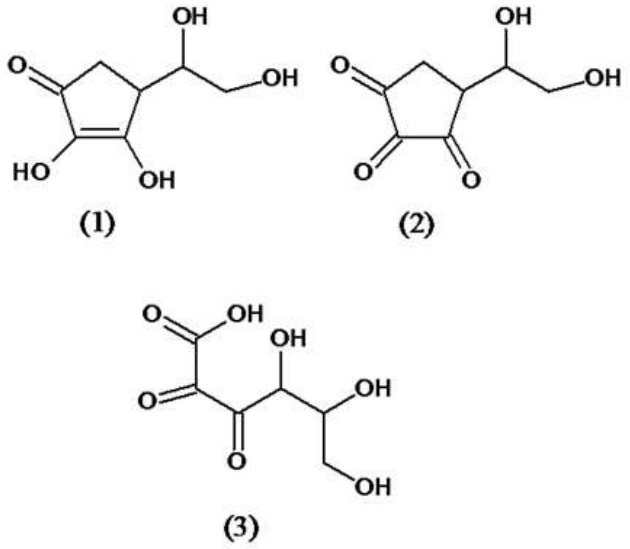

Fig. 1.
Chemical structures of ascorbic acid (1), dehydroascorbic acid (2) and 2, 3-diketogulonic acid (3).

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AH_2 is a well-known antioxidant and acts as an inhibitor of Photooxidation of a number of drugs and biological compounds by quenching the singlet oxygen[96-110]. The singlet oxygen ($^1O_2$) is highly reactive, electrophilic and non-radical specie. It can be produced from triplet oxygen ($^3O_2$) by photosensitization in the presence of light[111]. The oxidation reactions mediated by $^1O_2$ are very rapid due to the low activation energy required and the reaction rates are much greater than those causes by $^3O_2$[112]. AH_2also plays an important role in inhibiting the photosensitization processes and thus protects the substrates from degradation[80, 113-117].In view of the biochemical importance, photosensitivity and extensive use of AH_2 in liquid vitamin preparations / TPN solutions[7] and its high susceptibility to oxidation, the present work has been undertaken to study the photolysis of the vitamin over a wide range of pH and to determine the rate–pH profile to ascertain the range of optimum stability for liquid preparations. The *k*–pH profiles for the photolysis of cyanocobalamin[118-120], riboflavin[121,122], folic acid[123],AH_2 in the presence of nicotinamide[124] and for the hydrolysis of 7,8-dimethy 1,10-(formylmethyl) isoalloxazine (major intermediate in the photolysis of riboflavin)[125] have been reported. The object of this work is to conduct a detailed study of the photolysis of AH_2 in a wide pH range on UV irradiation, identification of the photoproducts formed, and determination of the rate constants, study of rate–pH profile and proposal of a mode of AH_2 photodegradation reactions.

MATERIALS AND METHODS:

AH_2 and dehydroascorbic acid (DHA) (2) (Fig. 1) were obtained from Sigma Chemical Co. 2, 3-diketogulonic acid (DKA) (3) (Fig. 1) was prepared by the method of Homann and Gaffron[76]. All reagents and solvents were of the purest form available from BDH/Merck. The following buffer systems were used throughout the study:

KCI–HCI, pH 1.0–2.0;
Citric acid–Na_2HPO_4, pH 2.5–8.0;
Na_2B_4O7–HCI, pH 8.5–9.0;
Na_2B_4O7–NaOH, pH 9.5–10.5;
Na_2HPO_4-NaOH, pH 11.0;
The ionic strength was 0.002 M in each case.

Photolysis:

$A10^{-4}$ M aqueous solution of AH_2 (200 ml) at an appropriate pH, contained in a 250 ml beaker (Pyrex), was placed in a water bath maintained at 251°C and irradiated with a Philips 15 W TUV tube (51.3% emission at 265nm, absorption maxima of AH_2 at pH 4–11) fixed horizontally at a distance of 25 cm from the center of the beaker. The solution was in free equilibrium with air and samples were withdrawn at appropriate intervals for thin-layer chromatographic examination and spectrometric assay.

Thin-Layer Chromatography (TLC):

The photolyzed solutions of AH_2 were subjected to TLC using 250-ìm silica gel GF_{254} plates using the following solvent systems:

A) Acetic acid–acetone–methanol–benzene (5:5:20:70, v/v/v/v)[126];
B) Ethanol–10% acetic acid (90:10, v/v)[127];
C) Acetonitrile–butyl nitrile–water (66:32:2,v/v/v)[128].

The spots were detected under UV light (254 nm) (AH_2) or by spraying with a 3% aqueous phenyl hydrazine hydrochloride solution (DHA, DKA).

Spectral Measurements:

All spectral measurements on freshly prepared AH_2 and the photolyzed solutions were carried out on a Shimadzu UV-240 spectrometer using quartz cells of 10mm pathlength.

Light Intensity Measurements:

The intensity of the Philips 15 W TUV tube was determined by potassium ferrioxalate actinometry[129] as $3.100.16\times10^{16}$ quanta s^{-1}.

Assay Method

A 5ml aliquot of the photolyzed solution was placed in a 20 ml beaker and the pH was adjusted to 2.0 with 0.1–1.0 M HCI or NaOH solution. The solution was quantitatively transferred to a 10 ml volumetric flask and made up to volume with 0.2 M KCI–HCI buffers (pH 2.0). The absorbance of the solution

was measured at the maximum at 243 nm and the concentration of AH_2 was determined using 9980 M^{-1} cm^{-1} as the value of molar absorptivity at the analytical wavelength.

RESULTS AND DISCUSSION:

Photoproducts of Ascorbic Acid

The photolysis of AH_2 in aqueous solution leads to the formation of degradation products which have been identified by TLC using solvent systems A, B and C. The following products were identified on comparison of their R_f values and spot color with those of the authentic compounds.

pH 1–8: DHA

pH 8–11: DHA, and DKA.

DHA is obtained by the Photooxidation of AH_2 and DKA by the hydrolysis of DHA. The formation of these products has been observed in the photooxidation[76, 130,131], chemical oxidation[132-138], and biotransformation[138, 139-142] of AH_2. In the presence of light, DHA is converted to the hydrated bi-cyclic hemiketal form at pH 2[143]. Ascorbate free radicals have been detected in the transition metal-dependent oxidation of AH_2 by ESR[144].

Assay of AH_2

AH_2 exhibits absorption maxima at 243 nm (pH 2) and 265 nm(pH 4–10)[7, 8,145].Spectrometric methods have been used for the assay of AH_2 in aqueous solutions at 244 nm (pH ~2)[85], 245 nm(pH 3.5)[52], 265 (pH 7)[146], 275 nm (pH 4.1 and 7.0)[147], 265 nm (pH 7)[148], 245 nm (pH ~2)[149], and 265 nm (pH ~7)[48]. DHA and DKA do not significantly absorb in this region[150-152] and, therefore, do not interfere with the assay of AH_2 in photolyzed solutions.

In the present study, the photolysis reactions of AH_2 have been carried out at 10^{-4} M concentration and the assays have been performed at 243 nm after suitable dilution of thedegraded solutions ($2.0–5.0\times10^{-5}$ M) at pH 2.0 (0.2 KCI–HCI buffer). The validity of Beer's law relation in the concentration range used was confirmed prior to the assay. The calibration data for AH_2 at the analytical wavelength are presented in Table 1. The correlation coefficient (R^2=0.999) indicates a good linear relationship over the concentration range employed. The value of molar absorptivity at 243 nm determined from the slope of the calibration curve is in good agreement with those reported by Davies et al.[151] and Sweetman[7]. The method has been found satisfactory for the assay of AH_2 in degraded solutions and has been applied to evaluate the kinetics of photolysis reactions.

Table 1. Calibration data for ascorbic acid showing linear regression analysis (n = 5)

Parameter	Value
λmax	243 nm
Concentration range ($M \times 10^{-5}$)	2.0–8.0
Slope	9980
SE of slope	1.502
Intercept	0.002
Correlation coefficient (R^2)	0.9999

3.3.Spectral Characteristics of Photolyzed Solutions

A typical set of absorption spectra of AH_2 solution photolyzed at pH 6.0 is shown in Fig. 2. There is a gradual loss of absorbance at 265nm, with time, due to oxidation of the molecule to DHA which does not absorb in this region. Similar spectral changes are observed on the photolysis of AH_2 throughout the pH range 1–11. However, the magnitude of these changes varies with pH and the loss of absorbance for a fixed interval of time increases with pH indicating the increase in the rate of photolysis.

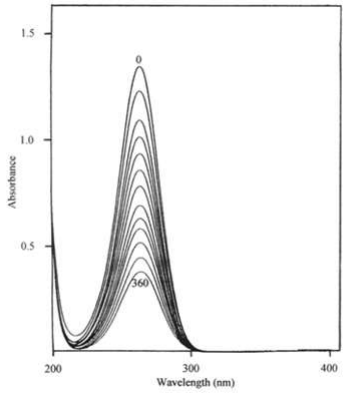

Fig. 2. Spectral changes during the photolysis of 8×10^{-5} M ascorbic acid at pH 6.0. Irradiation time: 0 to 360 min.

Redox and Acid–Based Equilibria of AH_2

The redox and acid-based equilibria of AH_2[91] are shown in Fig. 3.It is evident that a number of ionic and non-ionic species, depending upon the pH of the medium, are involved in the oxidation–reduction of AH_2 and may play an important role in the photolysis of the molecule. A reaction scheme showing the participation of some of these species

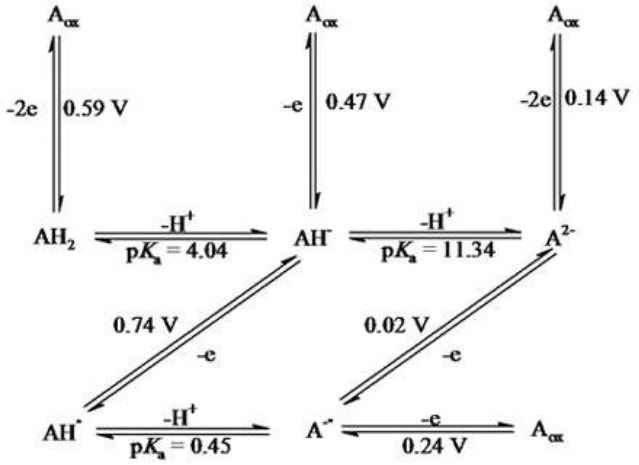

Fig. 3. Redox and acid-based equilibria of ascorbic acid.

Rate–pH Profile of AH_2

The philosophy and types of kinetic pH profiles have been discussed by Carstensen[153]. The major goals of a pH profile are to determine the optimal pH range and to select the best buffer system for a liquid formulation. Several workers have studied the rate–pH profiles of the oxidation of AH_2 in the pH range 2–7[22, 52, and 77,154–157]; however, the kinetics of Photooxidation of AH_2 in aqueous solution has not been reported. In view of the sensitivity of AH_2 to oxidation, it is necessary to study the photochemical behavior of the vitamin in aqueous solutions to determine the pH range of optimum stability.

The chemical oxidation of AH_2 in aqueous solution is pHdependent and proceeds by a first-order reaction[51, 75,121]. The maximum rate of oxidation has been observed at pH 4 near the pK_{a_1} (4.1)[7] of AH_2 and the minimum rate at pH 5–6 in the acid region[22, 156–159]. In this region, the molecule exists mostly in the mono-anion form and the delocalization of the electrons renders it relatively stable towards redox reactions[55].

The oxidation of AH_2 involves mainly the participation of ionized form and the rate of oxidation varies linearly with the concentration of the mono-anionic species[77]. The oxidation steps of AH_2 reaction have been studied by voltcoulmetry[160].

The *k*–pH profile for the photolysis of AH_2 at pH 1–11 is shown in Fig. 4 and the rates are reported in Table 2. The reaction in the pH range 1–6 is represented by a sigmoid curve indicating the gradual ionization of the molecule (pK_{a_1} 4.1)[7] with pH and the reactions of the fractions of un-dissociated AH_2 and monohydrate ascorbate anion (AH^-) present in the pH range. Thus the AH^- species appears to be more susceptible to Photooxidation than the AH_2 molecule. The behavior of AH_2 on Photooxidation in the acid region is similar to that observed for the chemical oxidation of AH_2 by molecular oxygen[22] and involves the interaction of AH_2 with singlet oxygen. The AH^-species (predominant in the pH range 4.2–7.0, 55.7–99.9%) is more reactive towardssinglet oxygen than its protonated form, the AH_2 molecule, as suggested by Bisby et al.[105] and, therefore, the rate of Photooxidation is higher in the pH range above pH 4.1 corresponding to the pK_{a_1} of AH_2. A seven-fold increase in the rate at pH 10.0 compared to that at pH 5.0 has been observed. The gradual further increase in the rate of Photooxidation in the pH range 7–10 is consistent with existence of AH^- species in the solution. Above pH 10, the rate of Photooxidation slows down due to gradual deprotonation of AH^-species to give A^{2-}(DHA) species (pK_{a_2} 11.6) which does not appear to undergo any photochemical change. Below pH 2, the rate of oxidation is very slow due to the existence of the molecule in the un-dissociated form (99.9%, pH 1.0).

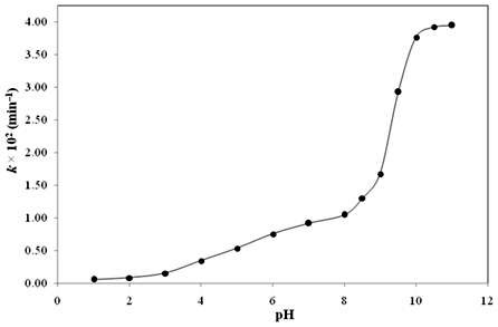

Fig. 4.*k*–pH profile for the photolysis of ascorbic acid in aqueous solution.

The Photooxidation of AH_2 is also influenced by its redox potentials which vary with ph. The greater photo stability of AH_2 at pH 5–6, compared to that at pH 10, is due to its lower rate of oxidation–reduction in the acid range (E pH 5.0 = +0.127 V). The increase in the rate of Photooxidation, with pH, is due to a corresponding increase in the redox potentials (E pH 7.0 = +0.058 V)[161] of AH_2 which is similar to the photolysis behavior of riboflavin at pH 5–6, compared to that at pH 10.0[121, 162]. Since the ionization as well as the redox potentials of $AH_2$is function ofpH, the rate of Photooxidation depends upon the species present and its redox behavior at particular pH.

Table 2. Apparent first-order rate constants for the photolysis of ascorbic acid at pH 1.0–11.0

pH	$k \times 10^2$ (min^{-1})	R^2
1.0	0.057	0.999
2.0	0.085	0.998
3.0	0.155	0.999
4.0	0.345	0.998
5.0	0.534	0.998
6.0	0.755	0.999
7.0	0.917	0.999
8.0	1.049	0.999
8.5	1.300	0.998
9.0	1.671	0.998
9.5	2.929	0.999
10.0	3.765	0.999
10.5	3.920	0.998
11.0	3.948	0.998

Primary Photochemical Reactions in the Oxidation of AH_2

Several schemes have been proposed for the chemical and Photooxidation of AH_2under different conditions. A reaction scheme based on general photochemical principles for the important reactions involved in the Photooxidation of AH_2 is presented below:

$$
\begin{aligned}
{}^0AH_2 &\xrightarrow{h\nu,\ k_1} {}^1AH_2\\
{}^1AH_2 &\xrightarrow{k_2} \text{Products}\\
{}^1AH_2 &\xrightarrow{\text{isc},\ k_3} {}^3AH_2\\
{}^3AH_2 &\xrightarrow{k_4} \text{Products}\\
{}^0AH^- &\xrightarrow{h\nu,\ k_5} {}^1AH^-\\
{}^1AH^- &\xrightarrow{k_6} \text{Products}\\
{}^1AH^- &\xrightarrow{k_7} {}^3AH^-\\
{}^3AH^- &\xrightarrow{k_8} \text{Products}\\
{}^3AH^- + {}^0AH_2 &\xrightarrow{k_9} AH^{\cdot -} + AH^{\cdot}\\
2\,AH^{\cdot} &\xrightarrow{k_{10}} A + AH_2\\
{}^3AH_2 + {}^3O_2 &\xrightarrow{k_{11}} {}^0AH_2 + {}^1O_2\\
AH^- + {}^1O_2 &\xrightarrow{k_{12}} {}^3AH^- + {}^3O_2\\
AH^{\cdot} + {}^1O_2 &\xrightarrow{k_{13}} AHOO^{\cdot}\\
AHOO^{\cdot} &\xrightarrow{k_{14}} A + HO_2^{\cdot}\\
AHOO^{\cdot} + {}^0AH_2 &\xrightarrow{k_{15}} AH^{\cdot} + AHOOH\\
AHOOH &\xrightarrow[\text{secondary reaction}]{k_{16}} A + H_2O_2
\end{aligned}
$$

According to this reaction scheme, the ground state AH_2 species ($^0AH_2$, ^0AH) are excited to the lowest singlet state ($^1AH_2$, ^1AH) by the absorption of a quantum of UV light [1,5]. These excited states may directly be converted to photoproducts [2,6] or may undergo intersystem crossing (isc) to form the excited triplet states [3,7]. The excited triplet may then degrade to photoproducts [4,8]. The triplet monoascorbate ion (^3AH) may react with the ground state AH_2 ($^0AH_2$) to form a monoascorbate anion radical (AH^-) and a monoascorbate radical (AH_s) [9]. The two AH_s species may lead to one oxidized and one reduced AH_2 species [10]. AH_2 triplet ($^3AH_2$) may react with molecular oxygen ($^3O_2$) to yield singlet oxygen ($^1O_2$) [11] which may be quenched by the monoascorbate anion (AH^-) to form the excited triplet state ($^3AH_2$) [12] or by the monovalent ascorbate radical to form an oxidized radical (AHOO) [13]. The oxidized radical (AHOO) may react with ground state $^0AH_2$ to form the monoascorbate radical (HA^-) and AHOOH [14]. AHOOH may be converted chemically to dehydroascorbic acid (A) and hydrogen peroxide [15]. Hydrogen peroxide may again react with the AH_2 triplet to form the oxidized species (A) [16].

CONCLUSION:

The photolysis of AH_2 in aqueous solution at pH 1–11 by UV radiation may be represented by a sigmoid curve. The main species involved in the

photolysis is the monohydrogen ascorbate anion and the optimum stability is exhibited in the pH range 5–6, the region most suitable for the formulation of pharmaceutical preparations. The increase in the rateof photolysis, with pH, is due to an increase in the redox potentials of AH_2 and the species involved. The monohydrogen ascorbate anion of AH_2 is much more susceptible to photolysis than the non–ionized molecule (pH 1–2) and the rate is slowed down in the pH range 10–11 due to the gradual formation of ascorbate anion. The photolysis of AH_2 in the pH range 1–11 is a function of the ionization and redox potentials of AH_2.

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CONFLICT OF INTEREST:
The authors declare no conflict of interest.

ETHICAL APPROVAL:
Not applicable

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