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ORIGINAL PAPER

Theoretical study of the pH-dependent antioxidant properties of vitamin C

Jon I. Mujika · Jon M. Matxain

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Abstract Molecules acting as antioxidants capable of scavenging reactive oxygen species (ROS) are of utmost importance in the living cell. Vitamin C is known to be one of these molecules. In this study we have analyzed the reactivity of vitamin C toward the $\cdot OH$ and $\cdot OOH$ ROS species, in all acidic, neutral and basic media. In order to do so, density functional theory (DFT) have been used. More concretely, the meta-GGA functional MPW1B95 have been used. Two reaction types have been studied in each case: addition to the ring atoms, and hydrogen/proton abstraction. Our results show that $\cdot OH$ is the most reactive species, while $\cdot OOH$ displays low reactivity. In all three media, vitamin C reactions with two hydroxyl radicals show a wide variety of possible products.

Keywords Antioxidant properties · OH and OOH · Reactive oxygen species · Vitamin C

Introduction

Radicals are necessary intermediates in a variety of normal biochemical reactions. A prominent feature of radicals is that they have extremely high chemical reactivity, due to the presence of unpaired electrons. This fact explains not only their normal biological activities, but also how they inflict damage on cells. Some of the radicals that are most abundantly produced in biochemical reactions are the so-called reactive oxygen species (ROS). These species are highly reactive and produced in a variety of biochemical processes. For instance, oxygen-derived radicals are continuously generated as part of normal aerobic life; in mitochondria as oxygen is reduced along the electron transport chain, and as necessary intermediates in a variety of enzymatic reactions. However, there are situations in which oxygen radicals are overproduced in cells. White blood cells such as neutrophiles specialize in producing oxygen radicals, which are used in host defense against invading pathogens. Cells exposed to abnormal environments such as hypoxia or hyperoxia generate high and often damaging levels of reactive oxygen species. A number of drugs have oxidizing effects on cells and lead to production of oxygen radicals. Ionizing radiation is well known to generate oxygen radicals within biological systems. Due to the overproduction or poor control of these species, they can cause severe damage to a broad range of macromolecules, being the origin of many free-radical mediated pathologies [1–3]. They are believed to be involved in causing cancer, in the aging process and other diseases [4–7]. One of the best known toxic effects of oxygen radicals is damage to cellular membranes, in the form of lipid peroxidation [8]. Vitamins are some of the molecules that prevent the oxidation of the cell biomolecules. Concretely, lipid peroxidation is prevented by lipid soluble molecules, such as vitamin E. Oxidation of water soluble biomolecules, like proteins, DNA and RNA, is prevented by water-soluble vitamins, namely, vitamin B_6 (pyridoxine), vitamin B_9 (folic acid) and vitamin C (ascorbic acid) [9, 10].

Vitamin C (see Fig. 1a), the L-enantiomer of ascorbate, was first isolated independently by the Hungarian research team of Joseph L Svirbely and Albert Szent-Györgyi, and the American Charles Glen King. For this, Szent-Györgyi was awarded the 1937 Nobel Prize in Medicine. In pure form it exists as a white crystal [11]. The presence of

J. I. Mujika · J. M. Matxain (✉)
Kimika Fakultatea, Euskal Herriko Unibertsitatea (UPV/EHU) and Donostia International Physics Center,
PK 1072, 20080 Donostia, Euskadi, Spain
e-mail: jonmattin.matxain@ehu.es

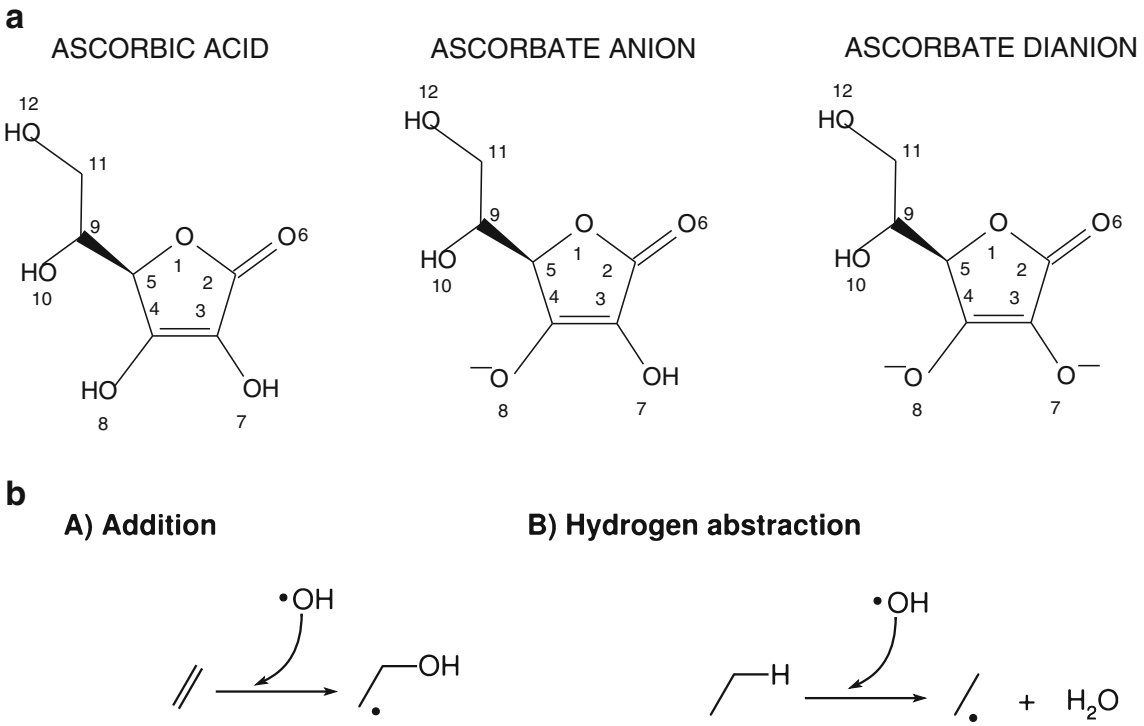

Fig. 1 Above, the most stable vitamin C structures as a function of pH, including atomic labeling. Below, the two mechanisms of the ·OH attack considered in this work: addition and hydrogen abstraction

ascorbate is required for a range of essential metabolic reactions in all animals and in plants. While almost all organisms produce the molecule by their own, humans must intake it in food. Its deficiency is the cause of scurvy [12]. In addition to this, vitamin C is a cofactor in several vital enzymatic reactions. Moreover, it is an antioxidant, as it protects the body against oxidative stress [10, 13, 14]. When L-ascorbate, which is a strong reducing agent, carries out its reducing function, it is converted to its oxidized form, L-dehydroascorbate. This process takes place by the donation of the two electrons from a double bond between two carbons of the ring. This process occurs sequentially. After the loss of the first electron, a fairly unreactive radical, ascorbyl radical, is formed, which is less reactive than the attacking radical. This property explains the antioxidant properties of ascorbate. Further electron loss leads to L-dehydroascorbate, which can then be reduced back to the active L-ascorbate form in the body by enzymes and glutathione [15]. L-dehydroascorbate may exist in more than one different structural form [16]. Vitamin C can be oxidized by a number of species involved in human diseases, [17, 18] such as molecular oxygen, superoxide, hydroxyl radical, hydroperoxyl radical, hypochlorous acid, reactive nitrogen species and some transition metals such as copper and iron.

In this work we present a theoretical study of the capacity of vitamin C as a quencher of hydroxyl and hydroperoxyl radicals, within the density functional theory framework. In aqueous solution, vitamin C may exist in three different forms, ascorbic acid, the monoanionic and dianionic ascorbate (see Fig. 1a). At physiological pH the vitamin C is present in the monoanionic form, [19] which was found to be one of the most effective aqueous phase antioxidants in

Table 1 ΔH_{aq}^{298}, in kcal/mol, for the formation of ascorbic radical intermediate by the addition to or H abstraction from ascorbic acid atoms (indicated as "ad" or "ab", respectively in brackets) by the first $\cdot OH$ and $\cdot OOH$ radicals. The transition state (TS) barriers for the most exothermic radical intermediates (INT) are also included

	$\cdot OH$		$\cdot OOH$	
	TS	INT	TS	INT
$\cdot C3(ad)_{cis}$	13.47	-22.51	-	8.92
$\cdot C3(ad)_{trans}$	17.44	-22.51	-	9.57
$\cdot C4(ad)_{cis}$	12.47	-33.82	-	-3.37
$\cdot C4(ad)_{trans}$	12.99	-33.82	-	-6.61
$\cdot C5(ab)$	2.94	-35.59	17.95	-5.26
$\cdot O7(ab)$	5.33	-34.02	16.42	-3.28
$\cdot O8(ab)$	4.80	-35.65	18.40	-5.46
$\cdot C9(ab)$	2.59	-21.32	-	8.91
$\cdot O10(ab)$	21.44	18.57	-	48.76
$\cdot C11(ab)$	0.50	-23.61	-	6.28
$\cdot O12(ab)$	30.86	-11.45	-	19.54

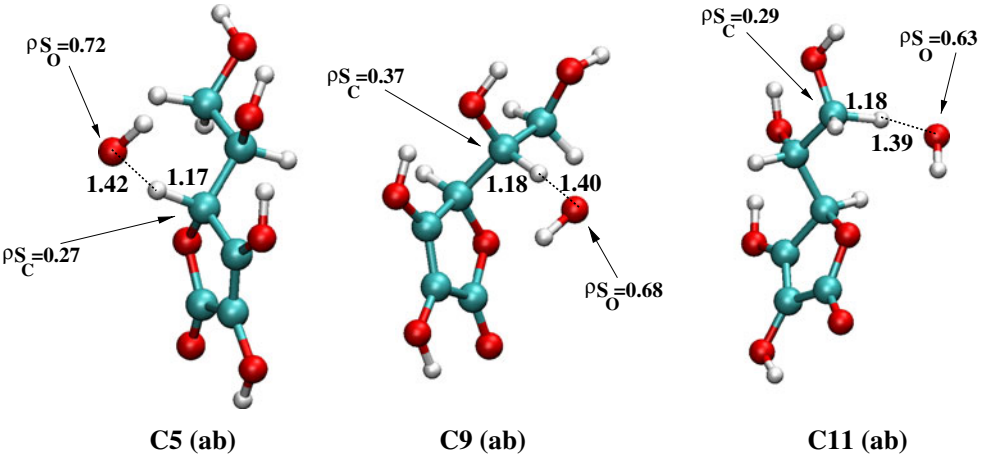

Fig. 2 Transition state structures that lead to the formation of the three most stable radical intermediates of ascorbic acid. The spin density (ρ_S) at the oxygen atom of the radical and at the C atom are illustrated, along with the cleaving C-H and forming O-H bond distances, in Å

human blood plasma [20–23]. The ascorbic acid may be found in extremely acidic media [24]. The dianionic form is found for pH larger than 11.6 [25]. The most stable tautomeric form of ascorbic acid and the most stable monoanionic and dianionic forms of ascorbate have already been characterized in the literature, [26–28] and are taken as reference for this study. The most stable monoanionic and dianionic ascorbate structures come from the deprotonation of O8, and further deprotonation of O7, according to the labeling used throughout this work and shown in Fig. 1a. In all cases, a two-step mechanism, with an ascorbyl radical as intermediate, has been assumed, considering different possibilities for each step, namely, addition to the double-bonded ring carbon atoms and hydrogen abstraction (dehydrogenation) (see Fig. 1b). For the monoanionic and dianionic cases, electron transfer to iron and copper complexes may also occur, but these processes need to be studied very carefully and deserve a specific and systematic study. Therefore, in this study we focus on the H abstraction and addition processes, and study the antioxidant properties of vitamin C in different pH, without the presence of any transition metal complex.

Table 2 ΔH^{298}_{aq}, in kcal/mol, for the addition to or H abstraction from ascorbic acid atoms (ad or ab, respectively in brackets) by the second $\cdot OH$ radical, leading to the oxidized products

	$\cdot OH$ (ad)		$\cdot OH$ (ab)
C5(ab)-C3(ad)	-97.32	C5(ab)-O7(ab)	-92.42
C5(ab)-C4(ad)	-66.22	C5(ab)-O8(ab)	-66.87
C5(ab)-C5(ad)	-110.65	C5(ab)-C9(ab)	-105.15
C9(ab)-C9(ad)	-116.82	C5(ab)-O10(ab)	-69.62
C11(ab)-C11(ad)	-117.02	O7(ab)-C9(ab)	-80.28
		C9(ab)-O10(ab)	-107.40
		C9(ab)-C11(ab)	-103.25
		C11(ab)-O12(ab)	-106.40

Method

The study is carried out using the meta-GGA functional MPWB1K, developed by Truhlar and coworkers [29–32], within density functional theory [33, 34]. Structure optimizations are carried out in gas phase, using the 6-31 + G(d,p) basis set. Harmonic vibrational frequencies are obtained by analytical differentiation of gradients, in order to determine whether the structures found are minima or transition states and to extract zero-point energies and Gibbs free energy contributions. Intrinsic reaction coordinate (IRC) calculations [35, 36] are performed to assess that the calculated transition states connect the appropriate reactants and products. Single point calculations using the 6-311 + G(2df,p) basis set and the integral equation formalism of the polarized continuum model (IEFPCM) of Tomasi and coworkers [37, 38] were performed on the optimized structures to

Table 3 ΔH^{298}_{aq}, in kcal/mol, for the addition to or H abstraction from ascorbate monoanion atoms (ad or ab, respectively in brackets) by the first $\cdot OH$ and $\cdot OOH$ radicals. The transition state (TS) barriers for the most exothermic radical intermediates (INT) are also included

	$\cdot OH$		$\cdot OOH$	
	TS	INT	TS	INT
$C3_{cis}(ad)$	-9.19	-18.38	-	9.94
$C3_{trans}(ad)$	-10.91	-	-	9.16
$C4_{cis}(ad)$	-7.30	-18.42	-	7.30
$C4_{trans}(ad)$	-9.30	-18.05	-	5.50
C5(ab)	11.39	-29.27	-	1.56
O7(ab)	-8.99	-48.80	2.23	-17.97
C9(ab)	25.80	-24.01	-	6.82
O10(ab)	-	-1.42	-	29.41
C11(ab)	-1.47	-23.15	-	7.68
C12(ab)	-	-0.14	-	30.70

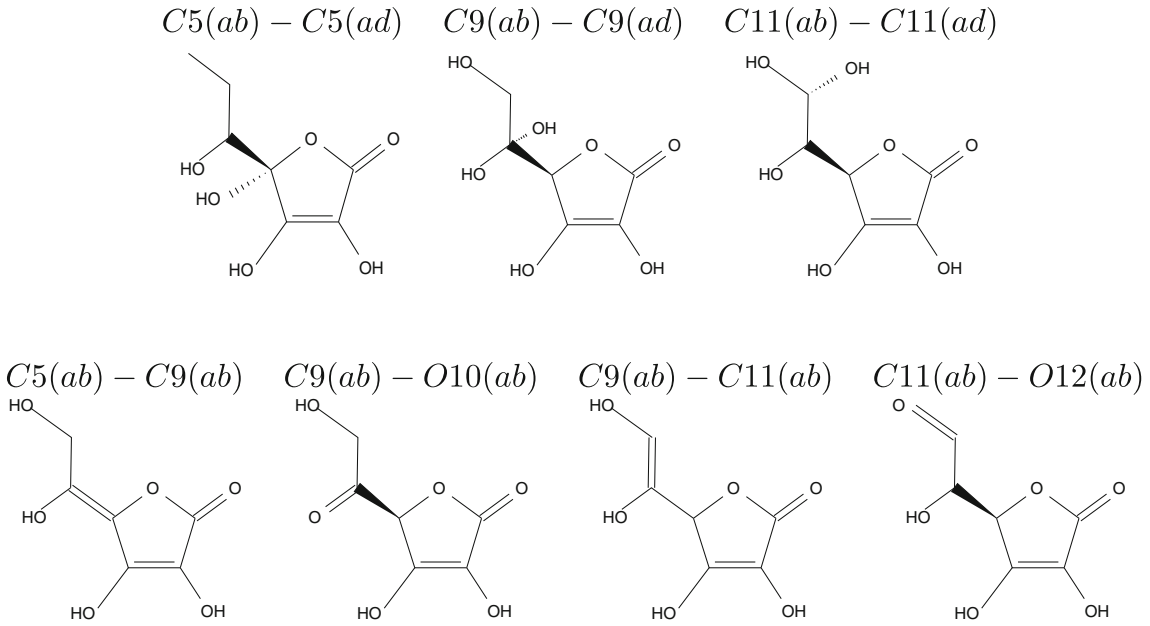

Fig. 3 Possible products of the reaction of ascorbic acid with 2 · *OH* radicals

estimate the effects of bulk solvation. In order to take into account the influence of enthalpy and entrophy, the enthalpic and Gibbs free energy contributions from the gas phase were added to give the final enthalpies, ΔH_{aq}^{298}, and free energies, ΔG_{aq}^{298}. It has been demonstrated elsewhere that this methodology is appropriate to study these type of reactions [39–41]. It should be noted that the reactions studied in this work consider infinitely separated reactants and products, which leads to the overstimation of the entrophic effects in ΔG_{aq}^{298}. In these cases ΔH_{aq}^{298} is more significant and therefore the ΔH_{aq}^{298} values have been considered for discussion along the paper. The GAUSSIAN03 [42] package was used throughout the study.

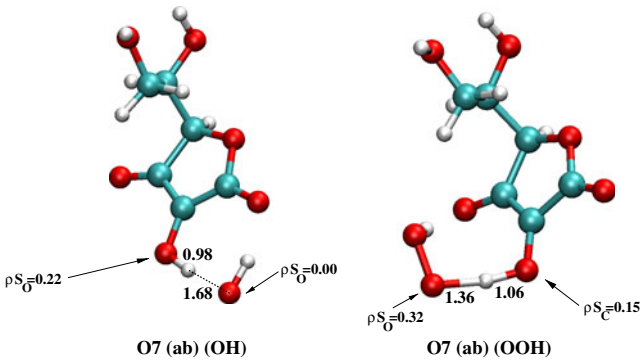

Fig. 4 Transition state structures for the abstraction of H from O7, by · *OH* and · *OOH*, that lead to the formation of the two most stable radical intermediates of ascorbate monoanion. The spin density (ρ_S) at the oxygen atom of the radical and at the C atom are illustrated, along with the cleaving C-H and forming O-H bond distances, in Å

Results and discussion

The capacity of vitamin C, in both neutral and anionic forms, as hydroxyl and hydroperoxyl radical scavenger has been studied, and the obtained results are given and discussed below. Concretely, the reaction of the neutral ascorbic acid, ascorbate anion and dianion with hydroxyl and hydroperoxyl radicals are studied in subsections 1, 2 and 3, respectively. In all cases, the well accepted two-step mechanism, with an intermediate radical, has been assumed, considering different possibilities in each step, namely, addition to the double-bonded ring carbon atoms and hydrogen abstraction (dehydrogenation). It has to be pointed out that transition states have only been characterized for the exothermic steps.

1. Ascorbic acid reaction with · *OH* and · *OOH*

Reaction paths for the attack by · *OH* and · *OOH* radicals to the double-bonded ring carbon atoms and hydrogen abstractions have been characterized, leading to adduct

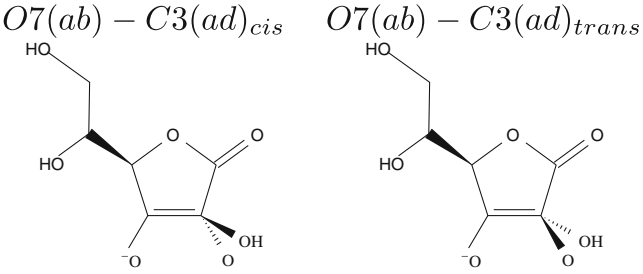

Fig. 5 Most probable products of the reaction of ascorbate monoanion with 2 · *OH* radicals without the presence of metals. Similar structures would be obtained for the attack of 2 · *OOH* radicals

Table 4 ΔH_{aq}^{298}, in kcal/mol, for the addition to or H abstraction from ascorbate monoanion atoms (ad or ab, respectively in brackets) by the second $\cdot OH$ and $\cdot OOH$ radicals, leading to the oxidized products

	$\cdot OH$ (ad)	$\cdot OOH$ (ad)		$\cdot OH$ (ab)	$\cdot OOH$ (ab)
$O7(ab)-C3(ad)_{cis}$	-94.50	-33.87	O7(ab)-C5(ab)	-87.05	-25.39
$O7(ab)-C3(ad)_{trans}$	-93.50	-32.82	O7(ab)-C9(ab)	-73.75	-12.10
$O7(ab)-C4(ad)_{cis}$	-91.03	-26.79	O7(ab)-O10(ab)	-65.81	-4.15
$O7(ab)-C4(ad)_{trans}$	-89.96	-29.31	O7(ab)-C11(ab)	-89.56	-31.86
			O7(ab)-O12(ab)	-63.12	-1.46

radicals, and semidehydro ascorbic radicals and H_2O or H_2O_2 molecules, respectively. In Table 1 geometric, electronic and energetic values for the addition and H abstraction reactions, respectively, along the reaction path are given. Addition on a given atom is denoted as (ad), and abstractions as (ab). For instance, C3(ad) denotes the addition on atom C3. Notice that the addition of $\cdot OH$ and $\cdot OOH$ radicals to both C3 and C4 may occur in both *cis*- or *trans*- orientation with respect to the $CHOH-CH_2OH$ group, the first leading to the same radical intermediate, since hydroxyl groups are linked to both C3 and C4 atoms. Thus, in Table 1 the same values are given for the *cis* and *trans* radical intermediates.

First of all, we study the attack of a first radical to ascorbic acid. The ΔH_{aq}^{298} collected in Table 1 reveal that hydroperoxyl radical is much less reactive with ascorbic acid than hydroxyl radical, as expected. The formation of few intermediate radicals are calculated to be slightly exothermic for $\cdot OOH$ attack, but the calculated barriers are quite high. Therefore, for further details we only focus on the reaction of ascorbic acid toward hydroxyl radical. In the hydroxyl radical attack, both addition and H abstraction are exothermic, with similar energetics for both processes, in a range $\sim$ -20 to -35 kcal/mol, with the exception of H abstraction from O10 and O12, which are the least exothermic process by far. However, barriers are about 10 kcal/mol lower for H-abstraction processes. Specially low barriers have been calculated for H-abstraction from the carbons of the side chain, namely, C5, C9 and C11, being lower than 3 kcal/mol. According to the energetics, we propose that the reaction of ascorbic acid with hydroxyl radical would lead to the formation of the above mentioned three radical intermediates. In the TS structures that lead to the formation of the above mentioned intermediates (depicted in Fig. 2) the distance between the abstracted H and the ascorbic acid carbon atom is elongated from 1.09 Å to $\sim$ 1.18 Å, and the distance between the radical oxygen and the abstracted H is reduced to $\sim$ 1.40 Å, which are characteristic for an early TS. The spin density (ρ_S), initially located totally at the oxygen atom of the radical, is partially transferred to the ascorbic acid atom linked to the abstracted H. Thus, for O ρ_S values are $\sim$ 0.7, while for ascorbic acid atoms are $\sim$ 0.3. In the intermediate radicals the spin density is located at the ascorbic radical, but while for C9 and C11 is mainly located at those carbon atoms, with $\rho_S \geq 0.9$, for the C5 case the spin density is delocalized at the ring atoms, which is shown by the ρ_S of 0.5 located at C5.

The reaction of the ascorbic acid radical toward a second hydroxyl radical has been studied considering the above mentioned three radicals as the most probable intermediates. Hydroperoxyl radical is not considered due to its smaller reactivity seen in the first step. As for the first attack, both addition and H-abstractions have been considered. In this case addition to the double-bonded ring carbon atoms is only considered for the C5(ab) intermediate radical, while additions to C5, C9 and C11 are considered for the cases where the H-abstraction occurred from the same atoms. The obtained energetics are collected in Tables 2. For all cases the second step is highly exothermic, as could be expected for two radical reaction, with ΔH_{aq}^{298} larger than -100 kcal/mol. No barriers are expected due to this two radicals reaction character. The most exothermic products are those coming from an addition to the C whose H was abstracted in the first step, mainly those from the chain, i.e., C9 and C11. Thus, similar ΔH_{aq}^{298} of $\sim$ -117 kcal/mol are calculated for C9(ab)-C9(ad) and C11(ab)-C11(ad) cases. C5(ab)-C5(ad) is less exothermic by $\sim$ 6 kcal/mol. The abstraction of a second H is less

Table 5 ΔH_{aq}^{298}, in kcal/mol, for the addition to or H abstraction from ascorbate dianion atoms (ad and ab, respectively in brackets) by the first $\cdot OH$ and $\cdot OOH$ radicals. The transition state (TS) barriers for the most exothermic radical intermediates (INT) are also included

	$\cdot OH$		$\cdot OOH$	
	TS	INT	TS	INT
$C3(ad)_{cis}$	-	-5.32	-	20.83
$C3(ad)_{trans}$	-	-5.80	-	14.08
$C4(ad)_{cis}$	-34.75	-37.75	-8.88	-15.85
$C4(ad)_{trans}$	-31.01	-38.54	-10.09	-18.17
C5(ab)	-37.60	-42.30	-	-11.47
C9(ab)	-	-15.01	-	15.82
O10(ab)	-	-50.34	-	-19.51
C11(ab)	-	-7.85	-	22.98
O12(ab)	-	-48.09	-	-17.26

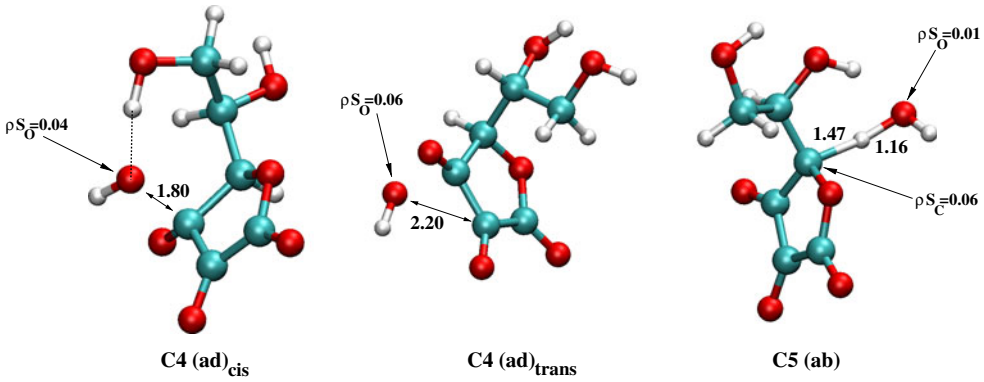

Fig. 6 Transition state structures that lead to the formation of the three most stable radical intermediates of ascorbate dianion. The spin density (ρ_S) at the oxygen atom of the radical and at the C atom are illustrated, along with the bond distances, in Å involved in the reactions

favored. In this case the most exothermic abstractions are those involving C9 and C11 with their neighbor in the chain, namely, C5, O10 and O12. The four products formed in this way have ΔH_{aq}^{298} ranging -100 to -110 kcal/mol. For abstractions involving ring atoms, ΔH_{aq}^{298} is much smaller. We observe, therefore, that chain atoms are more reactive toward hydroxyl radical than ring atoms. Summarizing, H-abstraction seems to be the most probable step for the formation of the ascorbic radical, while addition is seen to be favored against H-abstraction for the reaction with a second hydroxyl radical. Similar ΔH_{aq}^{298} are calculated for several cases, which predicts a mixture of different final products. The most exothermic ones are depicted in Fig. 3.

2. Ascorbate monoanion reaction with $\cdot OH$ and $\cdot OOH$

For the reaction of ascorbate anion with both hydroxyl and hydroperoxyl radicals, besides the addition to double-bonded carbon atoms and H-abstractions, electron transfer to an oxidizing agent should be considered. As mentioned in the introduction, the metabolism of ascorbate follows an electron transfer and then H-abstraction from O8. For electron transfer, a metal is needed. However the metal availability in a cell is rather small, since they are mainly found forming complexes. Therefore, what happens when ascorbate is attacked by these radicals without the presence of a metal? In this work we focus on the addition and H-abstraction processes, and, consequently, we will not study the electron transfer process.

First of all the attack of a first radical to ascorbate anion is analyzed. The obtained results are given in Table 3. Focusing on addition, $\cdot OH$ addition to C3 and C4, in both cis and trans conformations, are exothermic processes with negative barriers, which means that these are spontaneous reactions. $\cdot OOH$ is less reactive, and positive ΔH have been calculated for addition reactions. Therefore, while $\cdot OH$ could undergo addition to C3 or C4, $\cdot OOH$ would not add to them. H abstraction processes are more exothermic than addition, but energy barriers are, in general, larger, with the exception of H abstraction from O7, which has similar barriers, and is much more exothermic, ~ 30 kcal/mol. Even more, $\cdot OOH$ could, in principle, abstract that H. Notice that it is the only exothermic process with a small barrier of 2 kcal/mol involving $\cdot OOH$ radical. We hence predict that the most probable intermediate would be that of H abstraction from O7, due mainly to thermodynamic reasons rather than kinetic. In the TSs (see Figs. 4, 5), we observe that $\cdot OH$ forms the TS earlier than $\cdot OOH$ (larger R(X-H) and smaller R(O-H)), which means that $\cdot OOH$ must approach closer to form the TS. Spin density is more transferred in the $\cdot OH$ case. Both statements are in concordance with the calculated smaller barrier for $\cdot OH$ attack.

The reaction of the O7 (ab) intermediate toward a second $\cdot OH$ and $\cdot OOH$ radical has been studied, and the thermodynamics of the obtained possible adduct and H abstraction products are given in Table 4. All these processes are exothermic, but addition to the C3 carbon, is the most likely product, either in cis or trans configurations (see Fig. 5).

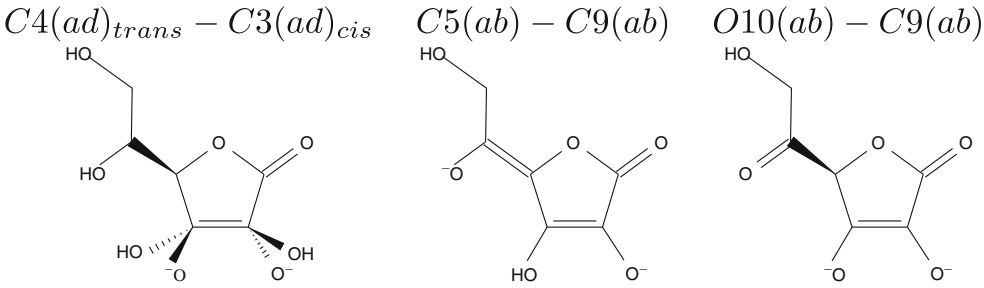

Fig. 7 Most probable products of the reaction of ascorbate dianion with 2 $\cdot OH$ radicals without the presence of metals. Similar structures would be obtained for the attack of 2 $\cdot OOH$ radicals

Table 6 ΔH_{aq}^{298}, in kcal/mol, for the addition to or H abstraction from ascorbate dianion atoms (ad and ab, respectively in brackets) by the second $\cdot OH$ and $\cdot OOH$ radicals, leading to the oxidized products

	$\cdot OH$ (ad)	$\cdot OOH$ (ad)		$\cdot OH$ (ab)	$\cdot OOH$ (ab)
$C4(ad)_{cis} - C3(ad)_{cis}$	-94.68	-49.62	C5(ab)-C9(ab)	-114.83	-53.17
$C4_{cis}(ad) - C3_{trans}(ad)$	-95.47	-43.97	C5(ab)-O10(ab)	-88.82	-27.16
$C4_{trans}(ad) - C3_{cis}(ad)$	-106.93	-51.16	C5(ab)-C11(ab)	-50.71	10.95
$C4_{trans}(ad) - C3_{trans}(ad)$	-99.53	-46.24	C5(ab)-O12(ab)	-81.19	-20.16
			O10(ab)-C9(ab)	-112.97	-51.31
			O10(ab)-C11(ab)	-109.24	-47.58
			O10(ab)-O12(ab)	-89.12	-27.46
			O12(ab)-C11(ab)	-109.24	-47.58

Therefore, we conclude that ascorbate anion may quench both $\cdot OH$ and $\cdot OOH$, without the presence of any metal, via H abstraction from C4 in a first step followed by addition to C3 either in cis or trans conformations.

3. Ascorbate dianion reaction with $\cdot OH$ and $\cdot OOH$

For the reaction of ascorbate dianion with both hydroxyl and hydroperoxyl radicals, besides the addition to double-bonded carbon atoms and H-abstractions, electron transfer to an oxidizing agent should also be considered. However, as mentioned for the ascorbate monoanion, we are interested mainly on the addition and H abstraction processes, and therefore, the electron transfer processes will not be studied in this work.

The attack of a first radical to ascorbate dianion is analyzed. The obtained results are collected in Table 5. Focusing first on addition, $\cdot OH$ addition to C3 and C4, in both cis and trans conformations, are exothermic processes with negative barriers, which means that these are spontaneous reactions. $\cdot OOH$ is less reactive, and positive ΔH have been calculated for addition to C3. However, negative values have been calculated for addition to C4, in both cis or trans conformations (TS given in Figs. 6). Therefore, while $\cdot OH$ could undergo addition to C3 or C4, $\cdot OOH$ would only add to C4. Notice that dianion is more reactive than monoanion for this type of reactions. H abstraction processes are also exothermic processes. Compared to addition, abstraction from C5, O10 and O12 are more exothermic for the attack of hydroxyl radical, while similar values are obtained for hydroperoxyl radical. Therefore, according to these results, $\cdot OH$ radical would prefer H abstraction from the three mentioned atoms, while for $\cdot OOH$ both addition and abstraction might happen. Notice the negative values for the TS involved in these reactions. For abstraction reactions, different attempts to locate the TS did not succeed. We think that this is due to the huge reactivity of these species.

The reaction of the dianion radical intermediates toward a second $\cdot OH$ and $\cdot OOH$ radical has been studied, and the thermodynamics of the obtained possible adduct and H abstraction products are given in Table 6. A number of products are possible according to the calculated reaction enthalpies, since all these processes are exothermic. However, unlike with the neutral and monoanionic vitamin C molecule, the most favored process would be a second H abstraction on the radical intermediate (illustrated in Fig. 7). Namely, the abstractions on the C9 atom at the C5(ab) and O10(ab) intermediates show the most exothermic ΔH_{aq}^{298} values (-112-114 kcal/mol), and the ΔH_{aq}^{298} of O10(ab)-C11 (ab) and O12(ab)C11(ab) products are -109 kcal/mol. On the other hand, only one of the addition of a second radical ($C4_{trans}(ad) - C3_{cis}$ (ad)) presents a comparable ΔH_{aq}^{298}, with a value of -107 kcal/mol.

Conclusions

The reactions between vitamin C in its three neutral, anionic and dianionic forms and several oxygen radicals ($\cdot OH$, $\cdot OOH$) have been investigated in this work without the presence of a metal. The results clarify that the $\cdot OH$ radical is significantly more reactive than $\cdot OOH$. Two alternative reaction pathways have been explored, addition of the radical to the ring carbons, and hydrogen abstraction. The reaction enthalpies indicate that for all protonation states of vitamin C the attack of the first $\cdot OH$ radical onto the vitamin C involves a hydrogen abstraction. The radical intermediate formed is very reactive, and the attack of a second radical is very favorable in all cases. However, while a second hydrogen abstraction is favorable for the neutral and monoanionic species, the addition of the $\cdot OH$ radical is more favored in the dianionic form.

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