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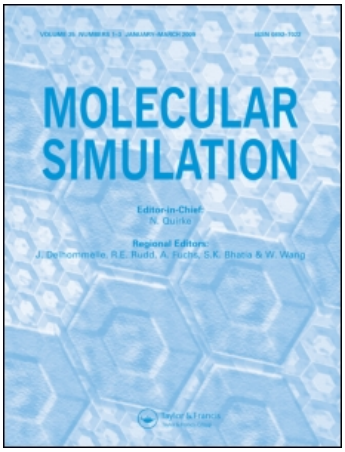

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Theoretical exploration of the ROS-photogenerating mechanisms of α-tocopherolquinone

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Vitamin E (VE) is one of the most popular bio-antioxidants, while meta-analysis indicates that high levels of supplementation with VE may increase all-cause mortality. In this study, the photosensitisation mechanisms of α-tocopherolquinone (α-TQ), one of the important oxidation products of VE, were explored by means of quantum chemical calculations. The results indicate that excited state α-TQ can photogenerate thermodynamically various reactive oxygen species (ROS), e.g. $^1O_2$ and $O_2^{\cdot-}$, and the corresponding ROS-photogenerating mechanisms in different solvents were illustrated. The present results are helpful to understand the paradoxical activities of VE.

Keywords: vitamin E; α-tocopherolquinone; photosensitisation mechanism; reactive oxygen species; density functional theory

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1. Introduction

In recent years, numerous natural antioxidants have been screened to alleviate or eliminate the free-radical induced impairments in the pathological processes of various diseases. Vitamin E (VE) is one of the most popular bio-antioxidants for its superb free-radical scavenging activities. However, meta-analysis indicates that high levels of supplementation with VE may increase all-cause morbidity [1,2]. Therefore, it is interesting to note a recent report that one of the important oxidation products of VE, α-tocopherolquinone (α-TQ, Figure 1), can photogenerate reactive oxygen species (ROS) [3], which may in part account for the enhanced levels of overall mortality caused by supplementation with high levels of VE. Thus, it is of significance to explore the photosensitive properties of α-TQ. Considering the successful applications of quantum chemical methods, especially time-dependent density functional theory (TD-DFT), in investigating the photophysicochemical properties of various photosensitive compounds [4–7], we attempt to illustrate the photosensitisation mechanisms of α-TQ by theoretical means.

2. Theoretical methods

The calculation details are as follows. Initial structure of α-TQ was fully optimised in solvents (benzene and water) by the hybrid B3LYP functional with 6-31G(d,p) Gaussian basis set and the nature of the stationary point was ascertained by performing harmonic frequency calculations. Then, the triplet excited state energy of α-TQ in benzene and water was calculated by TD-DFT formalism using the same basis set [8–10]. Although, the TD-DFT calculations neglected the geometry relaxation of the excited states, they can give reliable triplet state parameters used to study the photosensitisation mechanisms of various photosensitisers according to previous studies [4–7]. To ensure the accuracy of the calculation, the vertical electron affinities (VEAs) and vertical ionisation potentials (VIPs) of α-TQ were estimated by a combined method labelled as B3LYP/6-311 + G(2d,2p)//B3LYP/6-31G(d,p), which means that B3LYP/6-311 + G(2d,2p) was employed to perform a single-point calculation on the basis of B3LYP/6-31G(d,p)-optimised structures. During the calculations, the solvent effects were taken into consideration by employing the self-consistent reaction field (SCRF) method with polarisable continuum model (PCM) [11–13]. Considering the fact that the phytyl chain has little influence on the electronic properties of α-TQ, it was replaced by a methyl group during the calculation. All the calculations were completed using the Gaussian 03 package of programs [14].

3. Results and discussion

During the photosensitisation processes, photosensitiser is firstly excited from the ground (S_0) state to the first singlet excited (S_1) state upon irradiation and may then intersystem cross to the first triplet excited (T_1) state, which is mainly responsible for the photosensitive reactions owing to its relatively long life-time.

Firstly, T_1 state α-TQ may react with $^3O_2$ to generate $^1O_2$ through energy transfer (Equation (1)). Secondly, T_1 state α-TQ may directly pass one electron to $^3O_2$ to give

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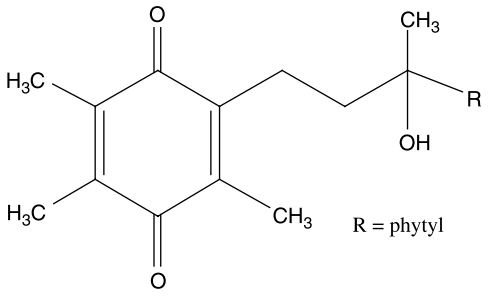

Figure 1. Chemical structure of α-tocopherolquinone.

Table 1. Lowest triplet excitation energy (E_{T_1}, in eV), VEA (in eV) and VIP (in eV) of α-tocopherolquinone in benzene and water.

	E_{T_1}	VEA_{S_0}	VEA_{T_1} [a]	VIP_{S_0}	VIP_{T_1} [b]
Benzene	2.09	−2.66	−4.75	7.86	5.77
Water	2.13	−3.52	−5.65	7.07	4.94

[a] $VEA_{T_1} = VEA_{S_0} - E_{T_1}$; [b] $VIP_{T_1} = VIP_{S_0} - E_{T_1}$.

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birth to $O_2^{\cdot-}$ (Equation 2). Moreover, α-$TQ^{\cdot-}$, which can be formed through autoionisation reactions between neighbouring T_1 and S_0 state (Equation 3) or both T_1 state α-TQ (Equation 4), may donate its extra electron to $^3O_2$ to generate $O_2^{\cdot-}$ (Equation 5).

$$\alpha\text{-TQ}(T_1) + {}^3O_2 \rightarrow \alpha\text{-TQ}(S_0) + {}^1O_2, \quad (1)$$

$$\alpha\text{-TQ}(T_1) + {}^3O_2 \rightarrow \alpha\text{-TQ}^{\cdot+} + O_2^{\cdot-}, \quad (2)$$

$$\alpha\text{-TQ}(T_1) + \alpha\text{-TQ} \rightarrow \alpha\text{-TQ}^{\cdot+} + \alpha\text{-TQ}^{\cdot-}, \quad (3)$$

$$\alpha\text{-TQ}(T_1) + \alpha\text{-TQ}(T_1) \rightarrow \alpha\text{-TQ}^{\cdot+} + \alpha\text{-TQ}^{\cdot-}, \quad (4)$$

$$\alpha\text{-TQ}^{\cdot-} + {}^3O_2 \rightarrow \alpha\text{-TQ} + O_2^{\cdot-}. \quad (5)$$

The lowest triplet excitation energy (E_{T_1}) of α-TQ, which is crucial to exploring the photosensitisation mechanisms, is firstly estimated (Table 1). It can be seen that the E_{T_1} of α-TQ in benzene and water are close to each other, indicating the solvent influences little on the E_{T_1}. As the effectiveness and accuracy of TD-DFT calculation in estimating the E_{T_1} of various photosensitisers have been demonstrated by previous studies [4–7], the theoretically predicted E_{T_1} of α-TQ is reliable, which will be employed for investigating the photosensitisation mechanisms of α-TQ.

For reaction (1), it was found that α-TQ can in principle photogenerate $^1O_2$ through direct energy transfer as the E_{T_1} of α-TQ is higher than the excited-state energy of $^1O_2$, 1.05 eV ($^3\sum_g^- \rightarrow \Delta_g^1$) or 1.65 eV ($^3\sum_g^- \rightarrow {}^1\sum_g^+$) [4], in consistent with the experimentally reported high $^1O_2$-yield of α-TQ [3].

Then, based on the related electronic parameters of α-TQ (Table 1) and O_2, the feasibility of reaction (2)–(5) is explored. As to reaction (2), the summation of VIP_{T_1} and electron affinity of O_2 is positive (3.44 eV in benzene and 1.05 eV in water), implying that this pathway is unfavourable in both solvents on thermodynamic grounds.

As to the autoionisation reactions, reaction (3) is not thermodynamically favourable both in benzene and water because of the positive value of the total reaction energy ($VEA_{T_1} + VIP_{S_0}$, 3.11 eV in benzene and 1.42 eV in water). Similar analysis indicates that reaction (4) is also forbidden in benzene, while permitted in water from the thermodynamic point of view based on the theoretical total reaction energy ($VEA_{T_1} + VIP_{T_1}$, 1.02 eV in benzene and −0.71 eV in aqueous solution). Once α-$TQ^{\cdot-}$ is formed, it may then donate one electron to $^3O_2$, subsequently resulting in the formation of $O_2^{\cdot-}$ (reaction (5)) for the negative value of total reaction energy (−0.37 eV). This accounts for the mechanism of $O_2^{\cdot-}$-generating by α-TQ in water [3]. Following the generation of $O_2^{\cdot-}$, other ROS, such as H_2O_2 and ·OH, can be produced through Fenton reaction [15] or Haber–Weiss reaction [16]. Moreover, even α-$TQ^{\cdot-}$ is generated in benzene under suitable conditions (e.g. electron transfer between T_1 state α-TQ

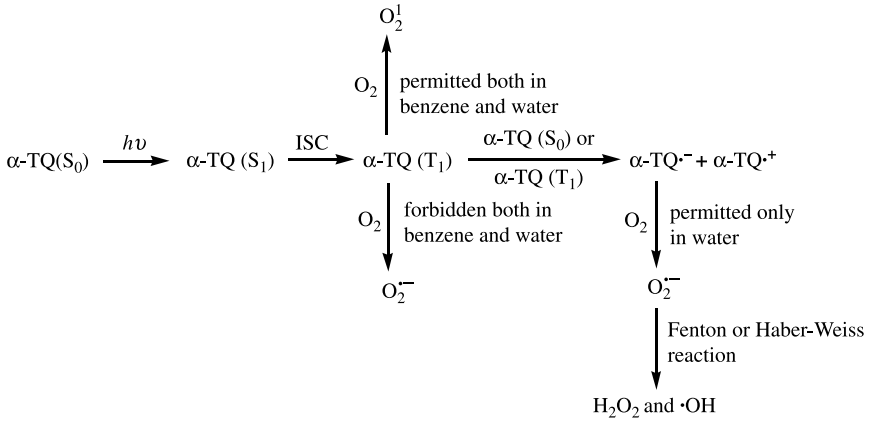

Figure 2. Theoretically proposed photosensitisation mechanisms of α-tocopherolquinone.

and ideal electron donors); it cannot give birth to $O_2^{\cdot-}$ theoretically based on the fact that reaction (5) is thermodynamically unfavourable. This implies that $^1O_2$ is the principal ROS during the photosensitisation of α-TQ in benzene. The difference of the photogeneration of $O_2^{\cdot-}$ by α-TQ in benzene and water mainly arises from the fact that polar solvent faciliates the electron transfer process compared with nonpolar medium.

In summary, based on the above analysis, the ROS-photogenerating mechanisms of α-TQ were provided and schemed in Figure 2, which gained some deeper insights into the paradoxical activities of VE.

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References

[1] E.R. Miller, R. Pastor-Barriuso, D. Dalal, R.A. Riemersma, L.J. Appel, and E. Guallar, *Meta-analysis: High-dosage vitamin E supplementation may increase all-cause mortality*, Ann. Intern. Med. 142 (2005), pp. 37–46.

[2] G. Bjelakovic, D. Nikolova, R.G. Simonetti, and C. Gluud, *Antioxidant supplements for prevention of gastrointestinal cancers: A systemic review and meta-analysis*, Lancet 364 (2004), pp. 1219–1228.

[3] A.G. Crisostomo, R.B. Moreno, S. Navaratnam, J.A. Wilkinson, and R.H. Bisby, *Generation of superoxide and singlet oxygen from alpha-tocopherolquinone and analogues*, Free Radic. Res. 41 (2007), pp. 730–737.

[4] J. Llano, J. Raber, and L.A. Eriksson, *Theoretical study of phototoxic reactions of psoralens*, J. Photochem. Photobiol. A Chem. 154 (2003), pp. 235–243.

[5] L. Shen, H.F. Ji, and H.Y. Zhang, *A theoretical elucidation on the solvent-dependent photosensitive behaviors of C_{60}*, Photochem. Photobiol. 82 (2006), pp. 798–800.

[6] ———, *A TD-DFT study on triplet excited-state properties of curcumin and its implications in elucidating the photosensitizing mechanisms of the pigment*, Chem. Phys. Lett. 409 (2005), pp. 300–303.

[7] ———, *Anion is crucial to elucidating the photosensitive features of hypericin*, Bioorg. Med. Chem. Lett. 16 (2006), pp. 1414–1417.

[8] R.E. Stratmann, G.E. Scuseria, and M.J. Frisch, *An efficient implementation of time-dependent density-functional theory for the calculation of excitation energies of large molecules*, J. Chem. Phys. 109 (1998), pp. 8218–8224.

[9] R. Bauernschmitt and R. Ahlrichs, *Treatment of electronic excitations within the adiabatic approximation of time dependent density functional theory*, Chem. Phys. Lett. 256 (1996), pp. 454–464.

[10] M.E. Casida, C. Jamorski, K.C. Casida, and D.R. Salahub, *Molecular excitation energies to high-lying bound states from time-dependent density-functional response theory: Characterization and correction of the time-dependent local density approximation ionization threshold*, J. Chem. Phys. 108 (1998), pp. 4439–4449.

[11] S. Miertus, E. Scrocco, and J. Tomasi, *Electrostatic interaction of a solute with a continuum. A direct utilization of* ab initio *molecular potentials for the prevision of solvent effects*, Chem. Phys. 55 (1981), pp. 117–129.

[12] S. Miertus and J. Tomasi, *Approximate evaluations of the electrostatic free energy and internal energy changes in solution processes*, Chem. Phys. 65 (1982), pp. 239–241.

[13] M. Cossi, V. Barone, and J. Cammi, Ab initio *study of solvated molecules: A new implementation of the polarizable continuum model*, Chem. Phys. Lett. 255 (1996), pp. 327–335.

[14] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, Jr., T. Vreven, K.N. Kudin, J.C. Burant et al., *Gaussian 03, Revision A.1*, Gaussian, Inc., Pittsburgh, 2003.

[15] H.J.H. Fenton, *Oxidation of tartaric acid in the presence of iron*, J. Chem. Soc. 65 (1894), pp. 899–910.

[16] F. Haber and J. Weiss, *The catalytic decomposition of hydrogen peroxide by iron salts*, Proc. R. Soc. Lond. Ser. A. 147 (1934), pp. 332–351.