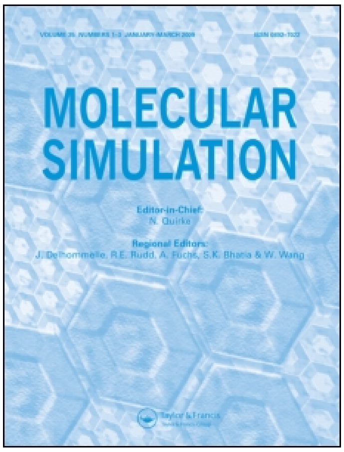

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Deactivation mechanisms of triplet excited state hypericin by β-carotene

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Deactivation mechanisms of triplet excited state hypericin by β-carotene

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The deactivation mechanisms of the triplet excited state hypericin (HYP) by β-carotene (CAR) were studied employing quantum chemical calculations in the present study. The results suggest that CAR may deactivate the triplet excited state HYP through the following two pathways on thermodynamic grounds: (1) direct energy transfer from the triplet excited state HYP to CAR; (2) electron transfer from the triplet excited state CAR, which was formed through direct energy transfer pathway, to the triplet excited state HYP.

Keywords: hypericin; β-carotene; triplet excited state; deactivation; quantum chemical calculation

1. Introduction

As a naturally occurring phenanthroperylene quinine pigment, hypericin (HYP, Figure 1) has attracted increasing attentions owing to its multiple pharmacological effects, such as antiviral, antiretroviral and particularly photosensitising activities [1–4]. Upon irradiation, HYP is initially raised from the ground (S_0) state to the singlet excited (S_1) state and then may intersystem cross to the triplet excited (T_1) state with high quantum yield [5], which is mainly responsible for the photosensitising reactions owing to its relatively long lifetime. The T_1 state HYP can photogenerate reactive oxygen species, e.g. $^1O_2$ and $O_2^{\cdot-}$ [1,2,5,6]. Moreover, it has been demonstrated that the T_1 state HYP can be deactivated by various quenchers [7,8]. β-Carotene (CAR) is one of the most important naturally occurring antioxidants, and thus it is interesting to explore the T_1 state HYP quenching behaviours of CAR. In the present study, the mechanisms of the T_1 state HYP deactivation by CAR were explored by taking the advantage of the density function theory (DFT) and time-dependent (TD)–DFT calculations, which have been widely used to elucidate numerous pigments' photosensitisation characters [6,9–11].

2. Calculation methods

The Gaussian 03 suite of programs was employed to perform the calculations [12]. The vicinal hydroxyls in the bay region of HYP (Figure 1) tend to dissociate one proton in polar solvents to give birth to an anion of HYP, which has been proved to be crucial to understand the photosensitive features of the pigment [6]. Thus, the anion of HYP was taken as the starting point of the calculation. Initial structures of CAR and HYP were fully optimised in dimethyl sulfoxide (DMSO) by the hybrid B3LYP functional with 6-31G(d) Gaussian basis set. The lowest triplet excitation energy (E_{T_1}) of CAR and HYP was obtained by using the TD-B3LYP/6-31G(d) method [13–15]. The self-consistent reaction field method with a polarisable continuum model [16–18] was used to take the solvent (DMSO) effect into consideration during the calculations.

3. Results and discussion

Theoretically, the T_1 state HYP may be quenched by CAR through direct energy transfer and electron transfer processes, whose feasibilities were explored from the thermodynamic point of view.

Primarily, the T_1 state excitation energy of HYP can be transferred to CAR resulting in the deactivation of the T_1 state HYP as well as the formation of the T_1 state CAR (Equation 1).

$$\mathrm{HYP}(T_1) + \mathrm{CAR} \rightarrow \mathrm{HYP} + \mathrm{CAR}(T_1). \qquad (1)$$

The TD–DFT-estimated E_{T_1} of HYP and CAR was listed in Table 1. It can be seen that the theoretical E_{T_1} of CAR (0.81 eV) and HYP (1.52 eV) is close to the experimental values (0.88 eV for CAR [19] and 1.64 eV for HYP [20]), which verifies the present methodology. Obviously, the E_{T_1} of HYP is much larger than that of CAR, which implies that the direct energy transfer-based quenching pathway is thermodynamically feasible.

Secondly, the deactivation may occur through electron transfer from CAR to the T_1 state HYP (Equation 2)

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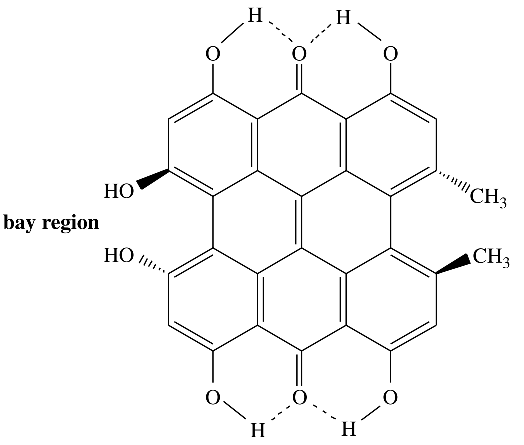

Figure 1. Chemical structure of hypericin.

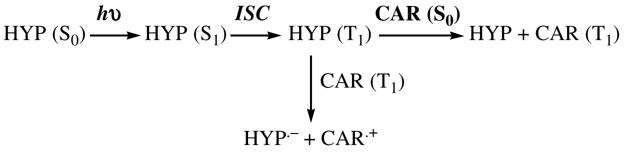

Figure 2. Theoretically postulated deactivating mechanisms of the triplet excited state hypericin (HYP) by β-carotene (CAR).

or from the T_1 state HYP to CAR (Equation 3).

$$\mathrm{HYP}(T_1) + \mathrm{CAR} \rightarrow \mathrm{HYP}^{\cdot -} + \mathrm{CAR}^{\cdot +}, \qquad (2)$$

$$\mathrm{HYP}(T_1) + \mathrm{CAR} \rightarrow \mathrm{HYP}^{\cdot +} + \mathrm{CAR}^{\cdot -}. \qquad (3)$$

According to the electronic parameters of CAR and HYP (Table 1), the feasibilities of the two possible electron transfer processes were analysed. As to reaction (2), the summation of the vertical electron affinity of the T_1 state HYP (VEA_{T_1}) and vertical ionisation potential of CAR (VIP) is positive (0.13 eV), implying that the electron transfer from CAR to the T_1 state HYP is thermodynamically unfeasible. Similar analysis indicates that reaction (3) is also not permitted because of the positive total reaction energy (summation of the VIP_{T_1} of HYP and VEA of CAR). However, in view of the facts that the conformational flexibility of CAR will influence the total reaction energy and the TD–DFT calculations neglected the structural relaxations of the excited state HYP, the electron transfer processes from CAR to the T_1 state HYP (Equation 2) remain probable owing to the relatively small energy gap, while should play a minor role.

Table 1. Lowest triplet excitation energies (E_{T_1}, in eV), vertical electron affinities (VEAs, in eV) and vertical ionisation potentials (VIPs, in eV) of β-carotene and hypericin in DMSO.

	E_{T_1}	VEA_{S_0}	VEA_{T_1} [a]	VIP_{S_0}	VIP_{T_1} [b]
CAR	0.81	−2.34	−3.15	4.33	3.52
HYP[c]	1.52	−2.68	−4.20	4.88	3.36

[a] $\mathrm{VEA}_{T_1} = \mathrm{VEA}_{S_0} - E_{T_1}$. [b] $\mathrm{VIP}_{T_1} = \mathrm{VIP}_{S_0} - E_{T_1}$. [c] Data from [6].

Moreover, as discussed above, through energy transfer from the T_1 state HYP to CAR (Equation 1), the T_1 state CAR may be formed in solution, which may then pass one electron to the T_1 state HYP according to Equation 4.

$$\mathrm{HYP}(T_1) + \mathrm{CAR}(T_1) \rightarrow \mathrm{HYP}^{\cdot -} + \mathrm{CAR}^{\cdot +}. \qquad (4)$$

The feasibility of this process depends on the summation of the VIP_{T_1} of CAR and the VEA_{T_1} of HYP. Based on the present results, this electron transfer-based quenching pathway is favourable on thermodynamic grounds because of the negative total reaction energy (−0.68 eV).

To summarise, based on the quantum chemical calculations, two possible pathways have been proposed to be involved in the T_1 state HYP deactivation by CAR, i.e. direct energy transfer from the T_1 state HYP to CAR and electron transfer from the T_1 state CAR to the T_1 state HYP (Figure 2). As electron transfer pathway relies on the concentrations of CAR and HYP both in their T_1 state, direct energy transfer process should play a predominant role during the deactivation of the T_1 state HYP by CAR. Moreover, electron transfer pathway may get more thermodynamically disadvantageous compared with direct energy transfer in non-polar solvents, which are unfavourable for electron transfer reaction.

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References

[1] H. Falk, *From the photosensitizer hypericin to the photoreceptor stentorian-the chemistry of phenanthroperylene quinones*, Angew. Chem. Int. Ed. 38 (1999), pp. 3116–3136.

[2] N. Duran and P.S. Song, *Hypericin and its photodynamic action*, Photochem. Photobiol. 43 (1986), pp. 677–680.

[3] G. Lavie, D. Mazur, D. Lavie, and D. Meruelo, *The chemical and biological properties of hypericin-A compound with a broad spectrum of biological activities*, Med. Res. Rev. 15 (1995), pp. 111–119.

[4] Z. Diwu, *Novel therapeutic and diagnostic applications of hypocrellins and hypericins*, Photochem. Photobiol. 61 (1995), pp. 529–539.

[5] S. Dumas, J.-C. Lepretre, A. Lepellec, A. Lepellec, A. Darmanyan, and P. Jardon, *Reactivity of the photo excited forms of hypericin, hypocrellin A, hypocrellin B and methylated hypericin towards molecular oxygen: The role of charge transfer interaction*, J. Photochem. Photobiol. A: Chem. 163 (2004), pp. 297–306.

[6] L. Shen, H.F. Ji, and H.Y. Zhang, *Anion is crucial to elucidating the photosensitive features of hypericin*, Bioorg. Med. Chem. Lett. 16 (2006), pp. 1414–1417.

[7] A. Michaeli, A. Regev, Y. Mazur, J. Feitelson, and H. Levanon, *Triplet-state reactions of hypericin. Time-resolved laser photolysis and electron paramagnetic resonance spectroscopy*, J. Phys. Chem. 97 (1993), pp. 9154–9160.

[8] G. Xia, X. He, Y. Zhou, M. Zhang, and T. Shen, *A study of photoinduced electron transfer and redox properties of hypericin*, J. Photochem. Photobiol. A: Chem. 114 (1998), pp. 31–35.

[9] L. Shen and H.F. Ji, *Theoretical exploration on the photosensitive properties of xanthurenic acid, a tryptophan metabolite in cataractous human lens*, Dyes Pigment. 76 (2008), pp. 646–649.

[10] L. Shen, H.F. Ji, and H.Y. Zhang, *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.

[11] L. Shen and H.F. Ji, *How α-tocopherol quenches triplet state riboflavin? Insights from theory*, J. Photochem. Photobiol. A: Chem. 199 (2008), pp. 119–121.

[12] 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*, Gaussian, Inc., Pittsburgh PA, 2003.

[13] 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.

[14] 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.

[15] 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.

[16] 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.

[17] 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.

[18] 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.

[19] J.L. Haley, A.N. Fitch, R. Goyal, C. Lambert, T.G. Truscott, J.N. Chacon, D. Stirling, and W. Schalch, *The* S_1 *and* T_1 *energy levels of all-trans β-carotene*, J. Chem. Soc., Chem. Commun. (1992), pp. 1175–1176.

[20] A. Angerhofer, H. Falk, J. Meyer, and G. Schoppel, *Lowest excited state of hypericin and isohypericin*, J. Photochem. Photobiol. B: Biol. 20 (1993), pp. 133–137.