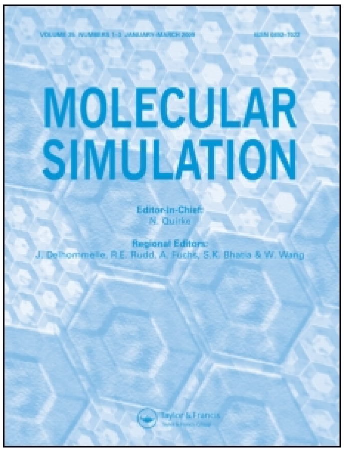

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Theoretical analysis of the deactivation reactions of triplet state riboflavin by hydroxycinnamic acid derivatives

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A thermodynamic analysis of the deactivation reactions of triplet state riboflavin (RF) by hydroxycinnamic acid derivatives has been performed on the basis of quantum chemical calculations. It was revealed that the H-atom transfer pathway is more thermodynamically feasible in comparison with the direct energy/electron transfer to be involved in the triplet state RF quenching by hydroxycinnamic acid derivatives. The results provide some deeper insights into the protective behaviours of hydroxycinnamic acid derivatives against the RF induced photooxidative damage.

Keywords: hydroxycinnamic acid derivatives; riboflavin; triplet state; quenching reaction; density functional theory

1. Introduction

In recent years, there is increasing interest in finding antioxidants to combat the photooxidative damages induced by various photosensitisers to biomolecules [1,2], including amino acids, protein and DNA, which have been implicated in various diseases. Hydroxycinnamic acid derivatives (HCA), including caffeic acid, ferulic acid and sinapic acid (Figure 1), are phenolic antioxidants with excellent free radical scavenging ability and possess great potential to be developed as medicines and food additives [3,4]. Previous studies demonstrated that HCA can inhibit the photosensitiser [e.g. riboflavin (RF)] induced oxidative damage under irradiation [5–7]. It has been demonstrated that triplet (T_1) state RF can photogenerate toxic reactive oxygen species (e.g. $^1O_2$ and $O_2^{\bullet -}$) [8–10] and obviously the protective effect of HCA can be ascribed to their free radical scavenging ability. Moreover, it was found that HCA can quench T_1 state RF [6]. As many antioxidants can inhibit RF's photooxidative damage through deactivating its T_1 state to a certain extent [2,11,12], it is of significance to investigate the T_1 state RF quenching reactions by HCA, which also contributes to their protective effect. In the present study, a thermodynamic analysis of the mechanisms of T_1 state RF quenching by HCA was performed on the basis of density functional theory (DFT) calculations, which have been successfully used to explore both the antioxidant and photosensitisation mechanisms of various bioactive compounds [9,13–16].

2. Methods

As HCA exist in anion form after proton dissociation from the carboxyl group, anions of HCA were used as the starting points of the calculations. Molecular geometries of HCA and RF were fully optimised by B3LYP functional with 6-31G(d,p) Gaussian basis set *in vacuo*. Then, the lowest triplet excitation energy (E_{T_1}) of HCA and RF was obtained by time-dependent-DFT [17–19] with the same functional and basis set in solvent (water). The vertical electron affinities (VEAs) and vertical ionisation potentials (VIPs), bond dissociation enthalpy (BDE) and H-atom affinity (HAA) of the molecules studied, here, were calculated by a combined method, labelled as (RO)B3LYP/6-311 + G(2d,2p)//B3LYP/6-31G(d,p). The combined method means B3LYP/6-31G(d,p) was used to optimise the molecular geometries and determine the vibrational frequencies *in vacuo* and then, single-point electronic energies were computed by (RO)B3LYP/6-311 + G (2d,2p) in an implicit water model. During the single point calculations, the self-consistent reaction field method with polarisable continuum model of Tomasi and coworkers was employed to include the solvent (water) effect [20–22]. All of the calculations were accomplished with Gaussian 03 suite of programs [23].

3. Results and discussion

Table 1 lists the theoretical parameters, including E_{T_1}, VEA, VIP, BDE and HAA, of HCA and RF, according to which, the mechanisms of T_1 state RF quenching by HCA were analysed on thermodynamic grounds.

Firstly, the excitation energy of T_1 state of RF may be transferred to HCA as represented in Equation (1).

$$\mathrm{RF(T_1) + HCA \rightarrow RF + HCA(T_1)}. \tag{1}$$

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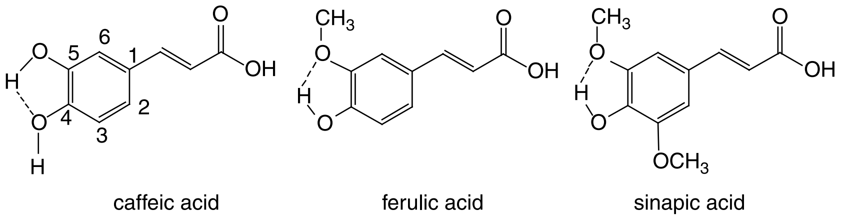

Figure 1. Chemical structures of caffeic acid, ferulic acid and sinapic acid.

Table 1. Theoretically estimated lowest E_{T_1}, VEA, VIP, BDE and HAA of hydroxycinnamic acid derivatives and RF in ground (S_0) and triplet (T_1) state (in kJ/mol).

	E_{T_1}	$\mathrm{VEA}_{\mathrm{T}_1}$[a]	$\mathrm{VIP}_{\mathrm{S}_0}$	BDE[b]	$\mathrm{HAA}_{\mathrm{T}_1}$[c]
Caffeic acid	256.48		544.21	324.09	
Ferulic acid	253.30		542.25	328.23	
Sinapic acid	251.92		547.52	323.47	
RF[d]	201.67	−532.20			−439.61

[a] $\mathrm{VEA}_{\mathrm{T}_1} = \mathrm{VEA}_{\mathrm{S}_0} - E_{\mathrm{T}_1}$. [b] H-atom abstraction from hydroxyl at position 4. [c] $\mathrm{HAA}_{\mathrm{T}_1} = \mathrm{HAA}_{\mathrm{S}_0} - E_{\mathrm{T}_1}$. [d] Data from Ref. [12].

The precondition for the occurrence of this reaction is that the E_{T_1} of RF should be larger than that of HCA. The theoretical E_{T_1} of the three HCA are very close to each other, indicating that the substitutes at positions 3 and 5 (Figure 1) exert little influence on the molecular E_{T_1}. According to the present results (Table 1), the E_{T_1} of RF is much lower in comparison with those of HCA, which makes the direct energy transfer-based quenching pathway thermodynamically unfavourable.

Secondly, T_1 state RF may be deactivated by HCA through direct electron transfer pathway (Equation (2)).

$$\mathrm{RF(T_1)} + \mathrm{HCA} \rightarrow \mathrm{RF}^{\bullet -} + \mathrm{HCA}^{\bullet +}. \tag{2}$$

The feasibility of this reaction relies on the $\mathrm{VEA}_{\mathrm{T}_1}$ of RF and VIP of HCA. It can be seen from Table 1 that the three HCA exhibit very similar VIP. As the summation of the $\mathrm{VEA}_{\mathrm{T}_1}$ of RF and VIP of HCA is positive, this pathway is unfavourable on thermodynamic grounds. However, in view of the small energy gap, which may be influenced by the solvent polarity as well as the reactant concentrations, the electron transfer pathway remains the possibility, while plays a minor role in the T_1 state RF quenching by HCA.

Moreover, as HCA are phenolic antioxidants with strong H-atom donating ability, T_1 state RF can be quenched by abstracting a H-atom from the phenolic hydroxyl of HCA. To explore the thermodynamic

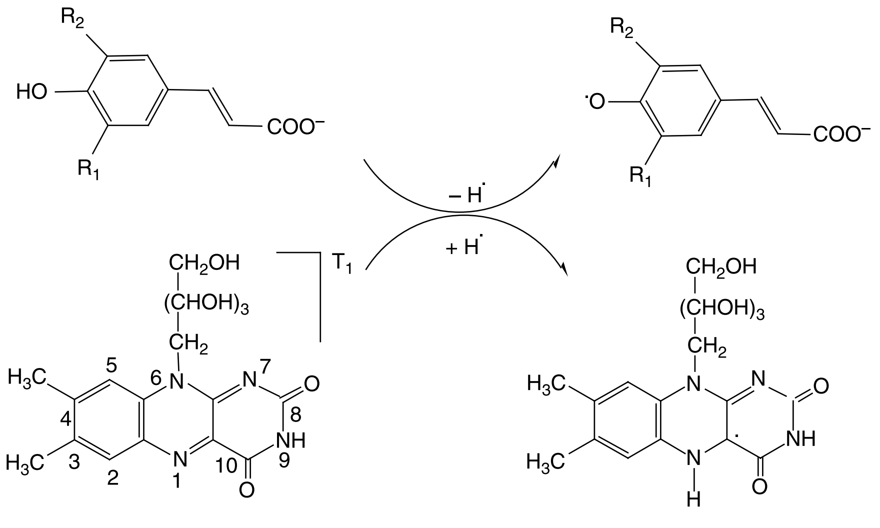

Figure 2. Postulated H-atom transfer-based quenching mechanisms of triplet state RF by hydroxycinnamic acid derivatives. Caffeic acid: $\mathrm{R}_1 = \mathrm{H}$, $\mathrm{R}_2 = \mathrm{OH}$; ferulic acid: $\mathrm{R}_1 = \mathrm{H}$, $\mathrm{R}_2 = \mathrm{OCH}_3$ and sinapic acid: $\mathrm{R}_1 = \mathrm{OCH}_3$, $\mathrm{R}_2 = \mathrm{OCH}_3$.

feasibility of this reaction, the O—H BDE of HCA (theoretical parameter to characterise the molecular H-atom-donating ability [13]) and the HAA of RF (theoretical parameter to measure the molecular H-atom-abstracting ability [13]) have been estimated (Table 1). According to the calculations, the summation of O—H BDE of the three HCA and the HAA_{T_1} of RF at position 1 (the most favourable position to accept a H-atom [11]) is negative, suggesting that this pathway is feasible from the thermodynamic point of view as schemed in Figure 2. Through H-atom transfer pathway, HCA radical can be formed, which is consistent with the experimental study that HCA radical is indeed observed during the T_1 state RF quenching by HCA [6].

In conclusion, the H-atom transfer should be the principle pathway during the T_1 state RF quenching by HCA based on the thermodynamic analysis. As HCA possess the catechin group with strong H-atom donating ability, they should be ideal quenchers of T_1 state RF.

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