

ANTIOXIDANT POTENTIAL OF EIGHT PHENOLIC ACIDS USING HIGH-PERFORMANCE DENSITY FUNCTIONAL THEORY

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Abstract. Phenolic acids are one of the major fractions identified in the extract of several vegetable seed oils which present interesting antioxidant properties. A density functional theory (DFT) study on the antioxidant potential of eight phenolic acids including gallic, vanillic, isovanillic, ferulic, caffeic, β -coumaric, cinnamic, and chlorogenic acids, is presented in this paper. The bond dissociation enthalpies (BDEs) of C–H and O–H bonds, the proton affinities (PA) and the ionization energies (IEs) were calculated in detail by using the LC- ω PBE functional coupled with the 6-311++G(d,p) basis set. The standard Gibbs free energies ($\Delta_r G^0$) for the scavenging reactions towards HOO^\bullet radical were calculated. In addition, the kinetics of H-atom transfer reaction was evaluated. As a result, the chosen long-range corrected DFT LC- ω PBE functional is shown as the highly reliable computational approaches in calculating geometrical properties as well as the thermochemical parameters by comparison with CCSD(T)/aug-cc-pVDZ results. The differences of bond length are about 0.1 Angstroms, while the ones of BDE are only from 0.1 to 0.6 kcal/mol. Furthermore, gallic, caffeic, ferulic and chlorogenic acids represent as the most reactive antioxidants in the reaction with HOO^\bullet radical in water occurring *via* H transfer process with the negative $\Delta_r G^0$ ranging from -3.3 kcal/mol for caffeic to -5.9 kcal/mol for ferulic compounds. Kinetic calculations in the gas phase based on transition state theory (TST) for the studied compound confirm that chlorogenic acid is shown as the most reactive antioxidant *via* HAT process with the lowest activation free energy (i.e. 17.9 kcal/mol) and the highest reaction rate (i.e. 4.20×10^{-19} cm³/molecule/s).

Keywords: phenolic acid, seed oils, antioxidant, HAT, PL, SET, RAF, DFT

Classification numbers: 1.4.4, 1.2.1, 1.2.6

1. INTRODUCTION

Phenolic acids are often included in phenolic compounds having one carboxylic function and two different carbon frameworks, consisting of the hydroxycinnamic (i.e., p-coumaric, caffeic, ferulic and sinapic acid) and hydroxybenzoic structures [1]. They are one of the main classes of the plant phenolic compounds and are found in different plant-based seeds, skins of fruits and leaves of vegetables [2]. Recently, several phenolic acids, including chlorogenic, gallic, caffeic, vanillic, isovanillic, β -coumaric, ferulic, and cinnamic acids with weight composition up to 14.5 wt.%, have been identified in the extract of the seed oils of five Fabaceae seeds: *Glycine soja*, *Vigna angularis*, *Phaseolus lunatus*, *Phaseolus vulgaris*, and *Phaseolus coccineus* [3].

Phenolic acids represent a majority of biological activities for human health such as antioxidant, anticancer, antimicrobial, skin care products, anti-inflammatory, anti-diabetic, food preservative, etc. [2], in which antioxidant properties have attracted interests. In fact, several works in the literature have focused on the antioxidant properties of different phenolic acids employing both experimental and computational approaches. Galano *et al.* reported that the bond dissociation enthalpy (BDE) values calculated at the M05-2X/6-311++G(d,p) level of theory in benzene solvent of caffeic and gallic acids were 78.8 and 78.1 kcal/mol, respectively [2]. Meanwhile, the ionization potential (IP) calculated under the same conditions is 157.0 and 163.0 kcal/mol, respectively. Tabrizi *et al.* [4] reported BDE values of 85.1 and 84.6 kcal/mol for caffeic and ferulic acids in water calculated at the M05-2X/6-311++G(d,p) level of theory, while the values in pentyl ethanoate solvent were 85.1 and 85.8 kcal/mol, respectively. The proton affinity (PA) values were also calculated as 26.8 and 26.1 kcal/mol in water for caffeic and ferulic acids, respectively, and their IP values in water are equal to 135.3 and 134.0 kcal/mol. In another study, de Souza and Peterson conducted a benchmark calculation on the O–H BDEs and IP for gallic acid in the gas phase and in water by employing density functional theory (DFT), second-order Møller-Plesset perturbation theory (MP2), coupled-cluster with single and double excitations (CCSD), and coupled-cluster with single and double excitations as well as perturbative inclusion of triples (CCSD(T)) [5]. The 6-311++G(df,p), cc-pVDZ, aug-cc-pVDZ, cc-pVTZ, and aug-cc-pVTZ basis sets were used. As a result, the M06-2X provided the best agreement for the BDEs when compared to the corresponding CCSD(T)/aug-cc-pVTZ results; M06-2X was also found to be the most suitable for probing the IP for the protonated forms of GA while LC- ω PBE was the most reliable in the case of deprotonated gallic acid [5]. Galano *et al.* have also recommended the use of LC- ω PBE and M06-2X as the most reliable DFT functionals for the calculation of potential energy surfaces of HAT reactions in addition to others including BMK, B2PLYP, M05-2X, and MN12SX [6]. However, it is surprisingly noted that the long range corrected Perdew–Ernzerhof (LC- ω PBE) functional has rarely been used in the antioxidant field in terms of thermochemistry [7].

Thus, the main goal of this study is to illustrate the performance of LC- ω PBE functional to predict the antioxidant potential of the 8 phenolic acids including gallic (GALA, 3,4,5-trihydroxybenzoic acid), caffeic (CAFA, (*E*)-3-(3,4-dihydroxyphenyl)prop-2-enoic acid), vanillic (VANA, 4-hydroxy-3-methoxybenzoic acid), isovanillic (ISOVA, 3-hydroxy-4-methoxybenzoic acid), β -coumaric (COUMA, (*E*)-3-(4-hydroxyphenyl)prop-2-enoic acid), ferulic (FERA, (*E*)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid), cinnamic (CINA, (*E*)-3-phenylprop-2-enoic acid) and chlorogenic (CHLA, (1*S*,3*R*,4*R*,5*R*)-3-[(*E*)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy-1,4,5-trihydroxycyclohexane-1-carboxylic acid) acids available in the extract of seed oils (Figure 1). First, dissociation energies (BDEs) and proton

affinities (PAs) of different C–H and O–H bonds along the molecules as well as their ionization potentials (IPs) are calculated. Second, Gibbs free energies ($\Delta_r G^0$) of H-atom transfer (HAT), radical adduct formation (RAF), proton loss (PL) and single electron transfer (SET) reactions towards HOO^\bullet radical are also investigated. Third, the kinetics of HAT and SET reactions are taken into account in the gas phase and in water. All of the calculations will be performed using the LC- ω PBE at the 6-311++G(d,p) basis set. The obtained results are then compared with other results in the literature to provide more information about the reliability of the functional used.

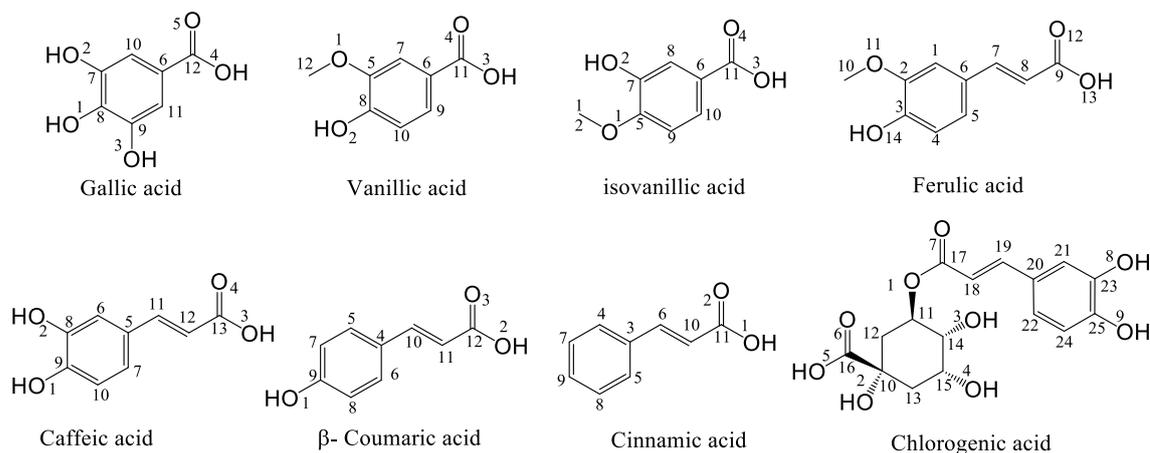


Figure 1. Structure of 8 phenolic acids with the numbered atoms for Gaussian calculations.

2. COMPUTATIONAL METHODS

All calculations were performed using the Gaussian 16 Rev.A.03 package [8]. The optimized geometries of molecules and the vibrational frequencies of the studied acids were calculated with the basis set of 6-311++G(d,p) using the long range corrected LC- ω PBE functional [7]. Three common antioxidant mechanisms were investigated in this study including H-atom transfer (HAT), proton loss (PL) and single electron transfer (SET). Intrinsic reactivity parameters characterizing the three studied mechanisms in the gas phase and in water at 298.15 K and 1 atm were calculated as follows [11]:

$$\text{BDE}(A-H) = H(A^\bullet) + H(H^\bullet) - H(AH) \quad (1)$$

$$\text{PA} = H(A^-) + H(H^+) - H(AH) \quad (2)$$

$$\text{IE} = H(AH^{\bullet+}) + H(e^-) - H(AH) \quad (3)$$

where H is the sum of electronic and thermal enthalpies including zero-point energy (ZPE) of the species studied at a temperature of 298.15 K and usually estimated from the expression below:

$$H = \text{ZPE} + \varepsilon_0 + (E_{\text{trans}} + E_{\text{rot}} + E_{\text{vib}} + E_e) + k_B \cdot T \quad (4)$$

where E_{trans} , E_{rot} , E_{vib} and E_e are the translational, rotational, vibrational and electronic contributions to the enthalpy, respectively; ε_0 is the total electronic energy at 0 K, and ZPE is the zero-point energy. $E_{\text{tot}} = (E_{\text{trans}} + E_{\text{rot}} + E_{\text{vib}} + E_e)$ corresponds to thermal correction to energy, and $H_{\text{corr}} = E_{\text{tot}} + k_B \cdot T$ is thermal correction to enthalpy. k_B is the Boltzmann constant of 1.380662×10^{-23} J/K. The enthalpy value for the hydrogen atom in the gas phase is calculated at

the same level of theory. The enthalpy values in the gas phase of proton (H^+) are taken to be 1.4811 kcal/mol ($5/2RT$, the value of the ideal gas) and the one for electron (e^-) to be 0.7519 kcal/mol [9].

The influence of water solvent was also evaluated using the Polarizable Continuum Model (PCM) combined with SMD variation [10] of the integral equation formalism variant (IEFPCM) which is available as the default SCRF method [11]. The method used creates the solute cavity *via* a set of overlapping spheres. Solvation enthalpies of the electron and proton in water solvent were calculated as recommended in the literature [12]. In principle, a proton or an electron binds to a solvent molecule (S_{sol}) to produce charged particles, $[(S-H)^+_{sol}$ and $(S-e)^-_{sol}$, respectively]. The particles formed were embedded in the dielectric continuum. As a result, the $H(e^-)$ and $H(H^+)$ calculated at the LC- ω PBE/6-311++G(d,p) level of theory in water are equal to -13.8 and -252.5 kcal/mol, respectively.

Finally, to provide more insight into the antioxidant activities of the studied phenolic acids, their reactions towards HOO^\bullet radical were considered. The Gibbs free energies of reaction ($\Delta_r G^0$) and the reaction barriers, in terms of Gibbs free energies ($\Delta_r G^\ddagger$) have been calculated as the relative energies of the products and transition states, respectively, with respect to the isolated reactants. The kinetics of reactions in the gas phase and the solvents were also calculated on the basis of the quantum mechanics-based test for overall free radical scavenging activity (QM-ORSA) protocol [13]. It is noteworthy that all kinetic calculations were performed using 1M standard state. The results from computational codes like Gaussian normally correspond to a standard state of 1 atm. However, the QM-ORSA methodology calculated bimolecular rate constants in units of $M^{-1} s^{-1}$. For that reason, the standard state was changed to 1M. Details of this methodology can be found elsewhere and in ref [13]. All rate constant calculations were performed using *Eyringpy* code [14].

3. RESULTS AND DISCUSSION

3.1. Geometrical and electronic properties

Figure 2 represents the optimized structures of all eight phenolic acids evaluated at the LC- ω PBE/6-311++G(d,p) level of theory in the gas phase. Generally, the geometrical properties calculated by the LC- ω PBE/6-311++G(d,p) level of theory are highly reliable with a small deviation as compared to those obtained by the CCSD(T)/cc-pVDZ method. For example, for the gallic acid (GALA, Figure 2A) the length of the C6-C12 bond is equal to 1.48 and 1.49 Å, the C8-O2 1.37 and 1.38 Å, the C7-O1 1.36 and 1.37 Å, the C9-O3 1.35 and 1.37 Å obtained by the LC- ω PBE/6-311++G(d,p) level method and the CCSD(T)/cc-pVDZ method investigated by de Sousa *et al.* (2021) [5], respectively.

Furthermore, the electronic properties such as the highest occupied molecular orbital (HOMO), the lowest unoccupied molecular orbital (LUMO) and the electrostatic potential (ESP) maps are displayed in Figure S1 of the SI file. In general, both the frontier orbitals are mainly localized at the phenyl ring and at the O-atom on the molecules. Similarly, these positions also correspond to the most negatively charged molecular regions. Thus, these regions could be the active sites in the reaction of electron transfer with the external free radicals.

The frontier orbitals (LUMO and HOMO) play an important role in the reactivity of a molecule. The lower the LUMO energy, the easier the LUMO orbital is to accept an electron and reversely, the higher the HOMO energy, the higher the electron donating ability of the molecule.

Thus, the narrower the LUMO – HOMO energy gap, the better the electron transfer reaction of the molecule. Figure 3 represents the LUMO, HOMO energies and the band gap of eight phenolic acids studied in this work.

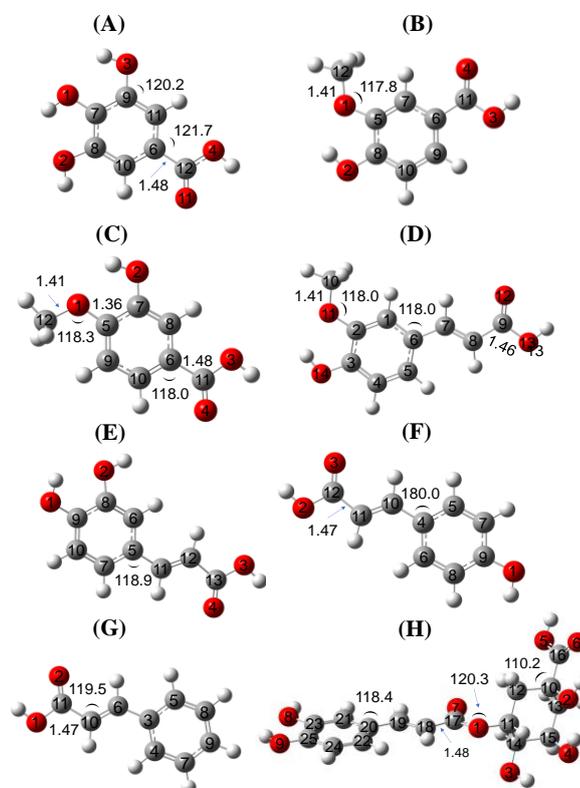


Figure 2. Optimized structures of the studied phenolic acids calculated in the gas phase at the LC- ω PBE/6-311++G(d,p) level of theory: (A) gallic (GALA), (B) vanillic (VANA), (C) isovanillic (ISOVA), (D) ferulic (FERA), (E) caffeic (CAFA), (F) β -coumaric (COUMA), (G) cinnamic (CINA) and (H) chlorogenic (CHLA) acids.

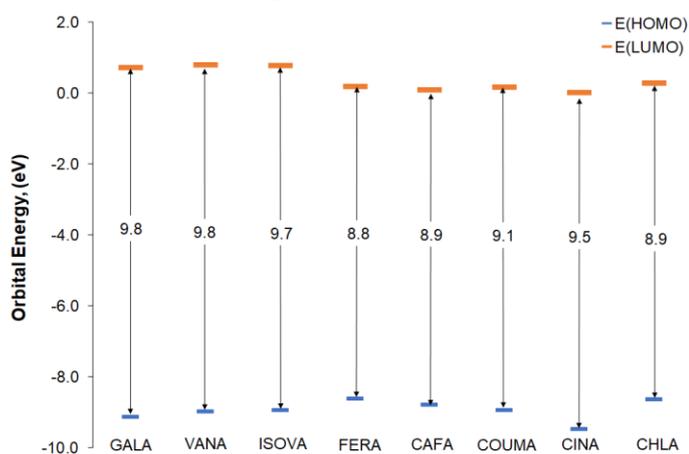


Figure 3. Frontier orbital energies (E_L and E_H) and band gap ($\Delta E_{L-H} = E_L - E_H$) of the studied phenolic acids calculated in the gas phase at the LC- ω PBE/6-311++G(d,p) level of theory.

It is revealed that the LUMO energies vary from 0.02 eV for CINA to 0.80 eV for VANA, whereas the HOMO ones vary from -9.46 eV for CINA to -8.60 eV for FERA. And the lowest band gap values are recognized for FERA (8.8 eV), CAFA (8.9 eV) and CHLA (8.9 eV). This observation suggests that FERA, CAFA and CHLA may have better antioxidant activity via electron transfer process.

3.2. Intrinsic reactivity parameters characterizing for antioxidant mechanisms

Three antioxidant processes including H-atom transfer (HAT), proton loss (PL) and single electron transfer (SET) are firstly considered in this section. The PL and SET are corresponding to the first step of the two-step processes, namely sequential proton loss - electron transfer (SPL-ET) and sequential electron transfer - proton transfer (SET-PT). These three processes could be primarily evaluated by three intrinsic thermochemical properties including bond dissociation enthalpies (BDEs), proton affinities (PAs) and ionization potential (IPs), respectively (Table 1).

The BDEs represent the feasibility of a hydrogen-containing bond which is dissociated and donates H-atom to a free radical. Thus, the lower the BDE value, the easier it is for the H-atom to be donated, and the higher the antioxidant potential of the compound *via* HAT process. In the gas phase, all the phenolic acids present potential antioxidant reactivity with BDE values varying from 75.3 (for CHLA) to 85.0 kcal/mol (for VANA), except for cinnamic acid (CINA) with a BDE value of 108.3 kcal/mol. All the compounds studied have lower reactivity than the standard antioxidants, i.e. ascorbic acid (73.8 kcal/mol) and trolox (72.7 kcal/mol). Similarly, the BDE values in aqueous phase are not changed as compared to the ones obtained in the gas phase, since the HAT is included in a neutral particle (an atom) transition. The BDEs in water vary from 79.0 (for GALA) to 84.2 kcal/mol (for COUMA) which are also higher than the BDEs of ascorbic acid (75.7 kcal/mol) and of trolox (74.7 kcal/mol) calculated at the same level of theory. It is noteworthy that all the easiest H-donating sites are located at the hydroxyl group of the phenyl rings. The easiest H-donating position on the hydroxyl groups of benzyl ring can be explained by the lowest spin densities of the H-donors, i.e. the O-atoms (see Tables S1 and S2 of the SI file). Furthermore, the long range corrected LC- ω PBE functional combined with the 6-311++G(d,p) basis set proves to be a very high performing DFT functional for BDE calculations. In fact, the BDE values obtained for GALA differ only by 0.1 to 0.3 kcal/mol from those obtained by the RO-CCSD(T)/aug-cc-pVDZ method [5]. And BDE(O1-H) of CAFA obtained in the gas phase at the RO-CCSD(T)/aug-cc-pVDZ/LC- ω PBE/6-311++G(d,p) level is 0.6 kcal/mol higher than that at the LC- ω PBE/6-311++G(d,p), i.e. 76.8 compared with 76.2 kcal/mol, respectively. Whereas, the BDEs obtained M05-2X/6-311+G(d,p) level of theory are underestimated from 4.9 (for CAFA) to 5.7 kcal/mol (for FERA) compared to the ones in this study. However, it is noteworthy that the results calculated at the CCSD(T)/cc-pVDZ level of theory are not a standard for criticizing or praising a method.

Based on the proton affinities (PAs), it is possible to predict the ability of a compound to donate a proton to a free radical. The lower the PA value, the higher the proton-donating ability of the compound studied, and thus the higher the antioxidant potential *via* the PL process. As can be seen from Table 1, the PA values in the gas phase vary from 320.7 (for CHLA) to 342.3 kcal/mol (for ISOVA). While the PAs in the aqueous phase drop significantly compared to the corresponding ones in the gas phase, since the PL is included in a charged particle transfer, so the solvent media, especially the polar solvent, favor this type of process. In fact, the PAs in water change from 22.0 (for CHLA) to 45.8 kcal/mol (for COUMA).

Table 1. Intrinsic reactivity including zero-point correction (ZPC) of the studied phenolic acids calculated at the LC- ω PBE/6-311++G(d,p) level of theory in the gas phase and in water. Unit is in kcal/mol. BDE: bond dissociation enthalpy, IP: ionization potential, PA: proton affinity. Numbered atomic sites are based on Figures 1 and 2. Ascorb. is ascorbic acid.

Cpd. /bonds	BDE		PA		IP		Cpd. /bonds	BDE		PA		IP	
	Gas	Wat.	Gas	Wat.	Gas	Wat.		Gas	Wat.	Gas	Wat.	Gas	Wat.
GALA					192.2 (189.1 ^a) (189.1 ^d)	126.2 (150.1 ^a) (138.7 ^d)	CAFA					184.8 (181.2 ^d)	121.1 (136.4 ^d)
O1H	77.9 (78.2 ^a)	79.0 (82.3 ^d)	333.3	31.0			O1H	76.2 (81.1 ^b) (76.8 ^c)	80.7 (86.0 ^d)	330.1	33.8		
O2H	78.5 (78.8 ^a)	82.7	332.1	33.0			O2H	82.0 (87.2 ^b)	80.1	337.6	35.1		
O3H	85.4 (85.3 ^a)	84.1	346.8	36.5			O3H	-	-	342.2	28.0		
O4H	-	-	339.5	26.5			C11H	101.0	102.2	383.8	78.6		
VANA					188.9	125.0	C12H	-	-	375.3	71.7		
O2H	85.0	83.8	341.7	34.3			COUMA					188.6	125.1
O3H	-	-	340.9	26.9			O1H	80.9	84.2	333.1	53.1		
C12H	94.2	97.1	395.7	89.8			O2H	-	-	343.6	45.8		
ISOVA					187.9	124.8	C10H	101.2	103.8	385.7	96.7		
O2H	84.3	83.0	349.3	37.5			C11H	-	-	377.9	89.9		
O3H	108.0	96.4	342.3	26.7			CINA					200.5	136.3
C12H	94.1	97.4	392.1	89.3			O1H	116.5	112.9	342.6	27.5		
FERA					180.3	119.0	C6H	108.3	102.2	382.8	76.9		
O14H	81.2 (86.9 ^b)	79.2 (84.6 ^b)	338.9	33.8			C10H	115.5	110.7	376.7	70.9		
O13H	-	-	343.4	28.0			CHLA					179.9	120.2
C8H	-	-	378.2	71.8			O3H	104.1	120.9	361.6	47.6		
C10H	100.6	96.8	411.5	150.3			O4H	75.3	120.5	345.0	42.4		
Trolox							O5H	87.3	95.2	320.7	22.0		
O2H	72.7	74.7					O8H	75.3	79.8	331.8	34.2		
Ascorb.							O9H	-	-	339.0	35.6		
O3H	73.8	75.7					C19H	87.3	102.4	383.7	78.8		
							O2H	108.3	112.3	345.4	41.2		

^aValues were calculated at the RO-CCSD(T)/aug-cc-pVDZ [5]; ^bValues were obtained at the M05-2X/6-311+G(d,p) [4];
^cValues were calculated in this work at the RO-CCSD(T)/aug-cc-pVDZ/LC- ω PBE/6-311++G(d,p) level of theory;
^dValues were calculated at the B3LYP/6-311++G(3df,2p) level of theory [15].

Finally, the ionization potential (IP) represents the possibility of a compound to mitigate an electron to a free radical. Thus, the lower the IP value, the higher the donating ability of the electron, and then the higher the antioxidant activity *via* SET action. Similarly, in the PL process, the polar solvent like water remarkably reduces the IP value as compared to the one in the gas phase. The IPs obtained from the LC- ω PBE/6-311++G(d,p) level is quite comparable with the one obtained at the B3LYP/6-311++G(3df,2p) level of theory [15]. For example, the IP

for CAFA in the gas phase is 184.8 and 181.2 kcal/mol, respectively. Similarly, the ones for GALA in the gas phase is 192.2 and 189.1 kcal/mol, respectively. The PAs in the gas phase change from 179.9 (for CHLA) to 200.5 kcal/mol (for CINA), while the values in water vary from 119.0 (for FERA) to 136.3 kcal/mol (for COUMA).

On the basis of the BDEs, PAs and IPs of the compounds studied, it can be seen that in the gas phase the HAT process is more dominant than the PL and SET. Conversely, in the aqueous phase the PL is more preponderant than the HAT and SET.

The most important advantage of the intrinsic reactivity approach consists in the rapid screening of the antioxidant potential. Its limitation, however, is related to the failure to consider the chemical nature of the reactive free radical in the reaction with a potential antioxidant compound. For that reason, in the next section we will calculate the standard Gibbs free energy of the reaction between the phenolic acids with the HOO^\bullet radical in the gas phase and in water.

3.3. Thermochemical properties and kinetics of the HOO^\bullet scavenging reactions

The hydroperoxyl radical HOO^\bullet is chosen as the reference free radical in the calculation of antioxidant properties [13]. The standard Gibbs free energies of the reaction ($\Delta_r G^0$) were calculated as the differences between the ones of the products and reactants. Basically, a reaction is considered spontaneous and exothermic with a negative $\Delta_r G^0$ value. As a result, Table 2 resumes $\Delta_r G^0$ of HAT, PL and SET reactions of the studied phenolic acids with HOO^\bullet radical in the gas phase and in water. It can be seen that almost all of the HAT reactions between the phenolic acid compound and HOO^\bullet radical are spontaneous and favorable with the negative $\Delta_r G^0$ in water varying from -5.9 (for FERA) to -0.7 kcal/mol (for VANA), except for CINA compound (15.1 kcal/mol in water). In the gas phase, only GALA, CAFA and CHLA are favorably reactive with HOO^\bullet via HAT reaction. Furthermore, all the proton loss (PL) and single electron transfer (SET) reactions with HOO^\bullet are not favorable in both the gas phase and in water with highly positive value of free energies. Thus, it is logically noted that the antioxidant properties of the phenolic acids are based solely on the H atom transfer action.

Table 2. Standard Gibbs free energies ($\Delta_r G^0$) including zero-point correction (ZPE) of the HAT, PL, and SET reactions of the studied phenolic acids towards HOO^\bullet radical calculated at the LC- ω PBE/6-311++G(d,p) level of theory in the gas phase and in water. Unit is in kcal/mol.

Compound	HAT		PL		SET	
	Gas	Wat.	Gas	Wat.	Gas	Wat.
GALA	-2.1	-4.4	186.6	23.1	169.8	35.8
VANA	3.7	-0.7	194.5	41.7	166.1	33.7
ISOVA	4.0	-1.7	196.4	41.3	166.0	34.7
FERA	0.2	-5.9	196.7	42.5	157.9	27.5
CAFA	-3.4	-3.3	184.9	25.6	162.8	31.8
COUMA	0.4	-1.2	187.9	28.4	166.7	33.1
CINA	48.6	15.1	196.4	42.0	177.6	45.2
CHLA	-4.3	-3.8	187.1	5.1	158.2	31.3

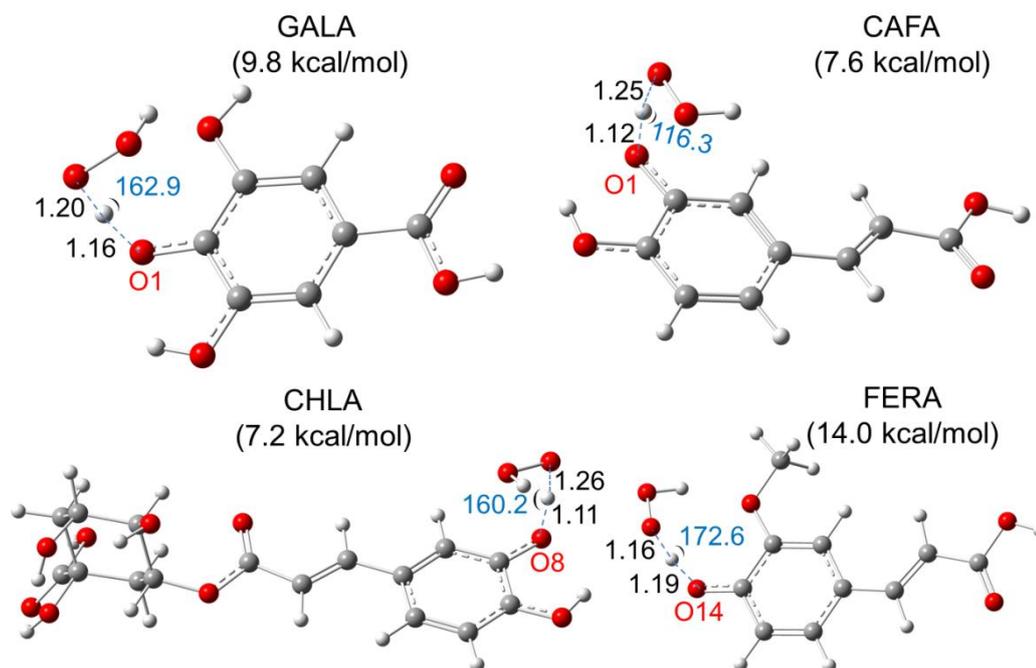


Figure 4. Transition state (TS) of the HAT reaction between GALA, CAFA, CHLA and FERA with HOO^\bullet radical in the gas phase calculated at the LC- ω PBE/6-311++G(d,p) level of theory. Bonds are in Angstroms, angles are in degree. Values in parentheses are relative enthalpies of TS in kcal/mol.

In the next section, the kinetics of HAT reaction of the most potential antioxidants including GALA, FERA, CAFA and CHLA are evaluated in both the gas phase and in water. Figure 4 displays the transition states (TSs) of the HAT reaction between HOO^\bullet radical and GALA, CAFA, FERA and CHLA which are the most reactive phenolic acids observed in this study. It has widely been accepted that the H-atom transfer process occurs via three states including reactant complex (RC), transition state (TS) and product complex (PC). The reaction process is initiated by the formation of complex between the phenolic acid with HOO^\bullet radical at the reactive position to form the RC state with a lower energy than the ones of separated reactants. Then, at a specific structure named TS state, the H atom is elongated and then O–H bond is broken. The H atom forms a new sigma bond with the O-atom in HOO^\bullet radical (Fig. 3). The relative enthalpies of TS are 9.8, 7.6, 7.2 and 14.0 kcal/mol higher than the initial reactants for GALA, CAFA, CHLA and FERA, respectively. Finally, H_2O_2 establishes the PC complexes with the resulted radicals of the phenolic acids with lower relative energies than the final separated products.

The Gibb free energies of activation at the standard concentration (1 M) and the rate constant calculated *via* transition state theory (TST) (k_{TST}) at a temperature of 298.15 K for the four HAT reactions studied are presented in Table 3. Other thermochemical and kinetic data calculated from these reactions using *Eyringpy* code are all shown in Table S3 of the SI file. As can be found in Table 3, CHLA represents the lowest activation free energy (i.e. 17.9 kcal/mol) and the highest reaction rate (i.e. $4.20 \times 10^{-19} \text{ cm}^3/\text{molecule/s}$). These results once again confirm the highest antioxidant activity of chlorogenic acid (CHLA) towards HOO^\bullet radical under reaction conditions of the study.

Table 3. The activation Gibbs free energy ($\Delta G^{\ddagger,1M}$, in kcal/mol) at the standard concentration (1 M) and the TST rate constant (k_{TST} , in $\text{cm}^3/\text{molecule/s}$) including the Eckart tunneling correction at 298.15 K calculated in the gas phase for HAT reactions of GALA, CAFA, CHLA and FERA towards HOO^\bullet radical. All electronic properties are calculated at the LC- ω PBE/6-311++G(d,p) level of theory.

Reactions	$\Delta G^{\ddagger,1M}$, (kcal/mol)	k_{TST} (298.15 K), ($\text{cm}^3/\text{molecule/s}$)
CAFA-O1H + OOH	18.9	8.90×10^{-20}
CHLA-O8H + OOH	17.9	4.20×10^{-19}
FERA-O2H + OOH	25.6	2.40×10^{-20}
GALA-O1H + OOH	21.1	2.30×10^{-20}

Thus, among the eight phenolic acids studied in this work, GALA, CAFA, CHLA and FERA represent as the most reactive antioxidants occurring *via* the HAT process with negative $\Delta_r G^0$ values, whereas other antioxidant processes like PL or SET are not favored with high free energies of reactions. Especially, chlorogenic acid represents as the most reactive antioxidant *via* the HAT process with the lowest activation free energy and the highest reaction rate.

4. CONCLUSIONS

A theoretical study on the antioxidant properties of eight phenolic acids including gallic (GALA), caffeic (CAFA), vanillic (VANA), isovanillic (ISOVA), β -coumaric (COUMA), ferulic (FERA), cinnamic (CINA) and chlorogenic (CHLA) acids available in the extract of seed oils was carried out. The long-range corrected LC- ω PBE functional combined with the 6-311++G(d,p) basis set were employed in the gas phase and in water. The main conclusions are as follows:

- The chosen computational approaches using LC- ω PBE/6-311++G(d,p) level of theory are highly reliable with the geometrical properties that agree well with those obtained by the coupled-cluster CCSD(T)/aug-cc-pVDZ. In addition, the differences of the BDE results calculated by these two approaches are only in a small range of 0.1 to 0.3 kcal/mol. So the LC- ω PBE functional combined with the basis set 6-311++G(d,p) or higher is recommended for the calculation of antioxidant properties.

- GALA, CAFA, CHLA and FERA represent as the most reactive antioxidants occurring *via* HAT process with a negative $\Delta_r G^0$ of -3.3 kcal/mol for CAFA and -5.9 kcal/mol for FERA compounds in the reaction with HOO^\bullet radical in water.

- Relative enthalpies of HAT reactions are 9.8, 7.6, 7.2 and 14.0 kcal/mol for GALA, CAFA, CHLA and FERA, respectively. Meanwhile, the kinetic calculations based on the TST confirm that CHLA represents as the most reactive antioxidant *via* HAT reaction with the lowest activation free energy (i.e. 17.9 kcal/mol) and the highest reaction rate (i.e. $4.20 \times 10^{-19} \text{ cm}^3/\text{molecule/s}$).

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Declaration of competing interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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