INVESTIGATION OF REACTION OF GALLIC ACID WITH SUPEROXIDE RADICAL ANION, HYDROXYL RADICAL AND METHYL PEROXY RADICAL

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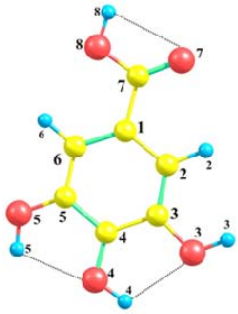
Abstract: In this paper are investigated the ΔH_{BDE}, ΔH_{IP}, and ΔH_{PA} values of the corresponding reactions in the solvents of different polarity (water and pentylethanoate). An approach based on the enthalpies of the reactions related to the HAT, SPLET, and SET-PT mechanisms of gallic acid with some radicals ($^{\bullet}OO^{-}$, $^{\bullet}OH$, and $CH3OO^{\bullet}$) is applied. The results show that thermodynamically favored mechanism depends on the polarity of reaction media and properties of free radical reactive species.

Key words: gallic acid, radicals, ΔH_{BDE}, ΔH_{PA}

Introduction

Gallic acid (trihydoxybenzoic acid, Figure 1) is broadly distributed in the plant world both free and as part of hydrolyzable tannins (Bianco et al., 1998). It can be found in gallnuts, witch hazel, tea leaves, oak bark, etc (Sakagami et al., 2001). Gallic acid is commonly used in pharmaceutical and chemical industry as well as foodstuff, and light industry. It also has great importance and application in medicine acting as an antioxidant and helping to protect human cells against oxidative damage.



Slika 1: Numeracija atoma galne kiseline
Figure 1: Atomic numbering for gallic acid

Due to its free radical scavenging activity, investigation of gallic acid has great practical and theoretical importance. Structually GA has phenolic groups which, as a

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source of readily available hydrogen atoms, enable the subsequently produced radicals to be delocalized over the whole phenolic structure (Figure 1).

Material and methods

The equilibrium geometries of gallic acid, radical cation of gallic acid and corresponding radicals and anions were fully optimized by the local density functional method (M05-2X), developed by the Truhlar group (Zhao and Truhlar, 2008) and 6-311++G(d,p) basis set, implemented in the Gaussian 09 package (Frisch et al., 2010). Another successful approach, originally developed by Grimme and called DFT-D, (Grimme, 2011) can be efficiently coupled with any existing DFT-based method. All B3LYP-D2 calculations have been carried out by using a Gaussian 09 program package (Frisch et al., 2010). The influence of water and pentylethanoate as solvents to mimic aqueous and lipid environments was approximated by a SMD solvation model.

Results and discussion

The scavenging mechanisms of different antioxidants are highly influenced by the properties of the scavenged radical species (Hussein, 2011). Reaction enthalpy is a quantity that can successfully contribute to the understanding of these processes. A direct approach to estimate the ΔH of a reaction is to apply the fundamental thermodynamic relationship, i.e., to subtract the enthalpy of reactants from the enthalpy of products.

If a reaction is exothermic, it means that the newly formed radical is more stable than the starting one, implying the reaction path is possible. Otherwise, if the reaction is endothermic, the reaction path is not favored, because the newly formed radical is less stable than the starting one.

In this paper this particle represents superoxide radical anion, hydroxyl radical, and methyl peroxyl radical.

In the HAT mechanism, the hydrogen atom is transferred from phenolic compound to the free radical $RO^{\bullet}$:

$$Ph{-}OH + RO^{\bullet} \rightarrow Ph{-}O^{\bullet} + ROH$$

ΔH_{BDE} for the HAT mechanism can be calculated using the following equation:

$$\Delta H_{BDE} = H(PhO^{\bullet}) + H(ROH) - H(Ph{-}OH) - H(RO^{\bullet})$$

where the $H(PhO^{\bullet})$, $H(ROH)$, $H(Ph{-}OH)$, and $H(RO^{\bullet})$ are the enthalpies of the phenolic radical, molecule obtained after hydrogen atom abstraction from the phenolic compound, starting phenolic compound, and free radical species, respectively. Lower ΔH_{BDE} values can be attributed to a greater ability of phenolic compound to donate a hydrogen atom to $RO^{\bullet}$ species.

The first step in the SET-PT mechanism is transfer of an electron from phenolic compound to free radical species, yielding the phenolic radical cation $Ph{-}OH^{\bullet+}$ and corresponding anion.

$$Ph{-}OH + RO^{\bullet} \rightarrow Ph{-}OH^{\bullet+} + RO^{-}$$

ΔHIP for the first step of the SET-PT mechanism can be calculated as follows:

$$\Delta H_{IP} = H(Ph{-}OH^{\bullet+}) + H(RO^{-}) - H(Ph{-}OH) - H(RO^{\bullet})$$

where the $H(Ph{-}OH^{\bullet+})$ and $H(RO^{-})$ are the enthalpies of the radical cation of initial phenolic compound and anion generated from the corresponding initial free radical.

The second step of this mechanism is deprotonation of $Ph{-}OH^{\bullet+}$ by RO^{-}:

$$Ph{-}OH^{\bullet+} + RO^{-} \rightarrow Ph{-}O^{\bullet} + ROH$$

ΔH_{PDE} can be calculated using the following equation:

$$\Delta H_{PDE} = H(Ph{-}O^{\bullet}) + H(ROH) - H(Ph{-}OH^{\bullet+}) - H(RO^{-})$$

The first step in the SPLET mechanism is deprotonation of phenolic compound by RO^{-} or other base. The outcome of this reaction is the formation of the phenoxide anion $Ph{-}O^{-}$:

$$Ph{-}OH + RO^{-} \rightarrow Ph{-}O^{-} + ROH$$

ΔHPA can be calculated as follows:

$$\Delta H_{PA} = H(Ph{-}O^{-}) + H(ROH) - H(Ph{-}OH) - H(RO^{-})$$

In the next step electron transfer from $Ph{-}O^{-}$ to $RO^{\bullet}$ takes place:

$$Ph{-}O^{-} + RO^{\bullet} \rightarrow Ph{-}O^{\bullet} + RO^{-}$$

ΔH_{ETE} can be determined by the equation:

$$\Delta H_{ETE} = H(Ph{-}O^{\bullet}) + H(RO^{-}) - H(Ph{-}O^{-}) - H(RO^{\bullet})$$

Reaction enthalpies of GA and three radicals: superoxide radical anion ($^{\bullet}O_2^{-}$), hydroxyl radical ($^{\bullet}OH$), and lipid peroxyl radical, here represented by $MeOO^{\bullet}$, related to three mechanisms of free radical scavenging activity (HAT, SET-PT and SPLET) are calculated by both DFT methods. These three radicals were selected because they are the most important radicals in food chemistry. The enthalpies of the reactions of these three radicals with position 4-OH of GA are presented in Table 1. Position 4-OH is the most stable and because of that fact the OH group from that position was used.

Tabela 1. Izračunate reakcione entalpije (kJ mol^{-1}) reakcija GA sa superoksid radikal anjonom, hidroksilnim radikalom, i metilperoksidnim radikalom

Table 1: Calculated reaction enthalpies (kJ mol^{-1}) for the reactions of GA with superoxide radical anion, hydroxyl radical, and methyl peroxy radical.

Gallic acid	*M05-2X*					*D2-B3LYP*				
	HAT	SET-PT		SPLET		HAT	SET-PT		SPLET	
	ΔH_{BDE}	ΔH_{IP}	ΔH_{PDE}	ΔH_{PA}	ΔH_{ETE}	ΔH_{BDE}	ΔH_{IP}	ΔH_{PDE}	ΔH_{PA}	ΔH_{ETE}
Water ε=78.35										
GAOH-4+•OH	-159	57	-216	-101	-58	-176	29	-206	-97	-80
GAOH-4+CH3OO•	-18	160	-178	-64	46	-31	139	-170	-61	30
GAOH-4+•OO^-	48	311	-263	9	39	32	284	-252	11	21
Pentylethanoate ε=4.73										
GAOH-4+•OH	-163	266	-429	-198	35	-180	231	-411	-190	9
GAOH-4+CH3OO•	-18	356	-374	-143	126	-32	328	-359	-138	106
GAOH-4+•OO^-	70	733	-663	-51	121	52	691	-639	-48	100

The preferred mechanism of antiradical activity of GA can be estimated from ΔH_{BDE}, ΔH_{IP}, and ΔH_{PA} values. Namely, the lowest of these values indicates which mechanism is favourable. The enthalpies for the reactions of •OH and CH3OO• with GA show that these reactions are exothermic in water and pentylethanoate. On the basis of the values in Table 1 it is clear that only the reaction of •OH with GA in water solution is considerably more exothermic when it obeys the HAT mechanism than when it that takes place via the SPLET mechanism. On the other hand, when CH3OO• reacts with GA in the aqueous medium ΔH_{PA} value is smaller by 45 kJ mol^{-1} than ΔH_{BDE}. The change of the solvent polarity considerably influences the enthalpy of these reactions: ΔH_{PA} values decrease with the decreasing solvent polarity, while ΔH_{BDE} values remain almost constant. All these facts indicate that SPLET is the prevailing mechanism in non-polar solvents, and HAT is favorable in water. In the case of the superoxide anion in water solution the reactions representing all three mechanisms are endothermic (Table 1). Thus, the newly formed radical is less stable than the starting one. As the dielectric constant of the solvent is getting smaller, the ΔH_{PA} values decrease and the corresponding reactions become more exothermic. The ΔH_{IP} values reveal that SET-PT is not operative antioxidative mechanism under any conditions.

Conclusion

In this paper we introduce a new approach based on the enthalpies of the reactions related to the HAT, SPLET, and SET-PT mechanisms of gallic acid with some radicals (•OO^-, •OH, and CH3OO•). Namely, the ΔH_{BDE}, ΔH_{IP}, and ΔH_{PA} values of the corresponding reactions in the solvents of different polarity are examined. In addition, the SET-PT mechanism is not suitable pathway for the reactions of GA with all three radicals. This procedure shows that the HAT mechanism is preferable reaction pathway only for the reaction of GA with •OH in water. In nonpolar solvents such as

pentylethanoate, the SPLET mechanism is more favorable. Obtained results also show that there is no mechanism suitable for the reaction of GA with $^{\bullet-}O_2$ in water.

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ISPITIVANJE REAKCIJE GALNE KISELINE SA SUPEROKSID RADIKALOM, HIDROKSILNIM RADIKALOM I METILPEROKSIDNIM RADIKALOM

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Izvod: U ovom radu su ispitivane ΔH_{BDE}, ΔH_{IP}, i ΔH_{PA} vrednosti odgovarajućih reakcija u rastvaračima različite (voda i pentiletanoat). Primenjen je pristup zasnovan na entalpijama reakcija povezanih sa HAT, SPLET, i SET-PT mehanizmima galne kiseline sa određenim radikalima ($^{\bullet}OO^{-}$, $^{\bullet}OH$, i $CH3OO^{\bullet}$). Rezultati pokazuju da termodinamički favorizovan mehanizam zavisi od polarnosti rastvarača u kome se reakcija odvija i osobina slobodno radikalske vrste koja reaguje.

Ključne reči: galna kiselina, radikali, ΔH_{BDE}, ΔH_{PA}

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