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Theoretical study of structure thermodynamic properties Caffeic acid as powerful antioxidants

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ABSTRACT: Analysis of caffeic acid a phenolic derived with well known antioxidant properties, was carried out by ab initio calculations, at the density functional theory (DFT) level. A complete geometry optimization was carried out for caffeic acid, in order to obtain the geometries and relative energies of the molecule.DFT calculations were performed at the B3LYP, B1LYP, B3P86, B3PW91, LSDA and HF methods With STO-3G, 3-21G* and 6-31G* basis set on the caffeic acid compound with Gaussian 09 program. The adsorption thermodynamic parameters (ΔG^0, ΔH^0, ΔE^0, Δzero-point energy and S^0) were calculated which showed an endothermic adsorption process. Calculated are accomplished at 298 K. The structures, energetic and thermodynamic properties will be discussed.

Keywords: Caffeic acid, Ab initio calculations, Density functional theory, Thermodynamic parameters

INTRODUCTION

Salvia officinalis (sage) dried leaves are frequently used as a culinary spice for flavoring and seasoning. The name Salvia comes from the Latin meaning 'to heal' and points to the popularity of this plant in traditional medicine (Kasimu *et al.,* 1998, Lenin, 1998). Helpful and several species, including 900 species in the world sage. Fifty-eight species of the genus Salvia (Lamiaceae) are found in Iran, which 17 are endemic (Beagi, 2007, Fatemeh, 2013).

The genus *Salvia* shows different biological activities manifested by the diverse components that allow for the many medicinal and pharmaceutical applications of the plant materials and/or extracts. In actual fact, many diterpenes, isolated from plants of some species of the genus Salvia, have been demonstrated attractive pharmacological properties, such as antioxidant, anti-microbial (González *et al.,* 1987) , antiinflammatory, analgesic (Hosseinzadeh *et al.,* 2003), antipyretic, hemostatic (Hernandez-Perez *et al.,*1995), hypoglycemic (Lima *et al.,* 2005) and antitumor (Liu *et al.,* 2000). Sage is reputed to be one of the richest sources of potent antioxidants (Nakatani, 1994), Cuvelier *et al.,* 1996, Luy, *et al.,* 2002), being rosmarinic acid, carnosic acid and their derivatives the best known examples (Cuvelier *et al.,* 1996, Luy, *et al.,* 2002, Wang *et al.,* 1998). Recent studies showed that different Salvia species including *Salvia officinalis* contain a surprisingly high number of various catechol compounds, most comprising oligomers of caffeic acid. Sage is reputed to be one of the richest sources of potent antioxidants (Lu and Foo 1999, Lu and Foo 2001, Ho *et al.,* 1994, Cuvelier *et al.,* 1996, Wang *et al.,* 1998), being rosmarinic acid, carnosic acid and their derivatives the bestknown examples (RW *et al.,* 2005). Caffeic acid, trans-3- (3, 4-dihydroxycinnamic acid) rophenic acid is one of the most common phenolic acids frequently occurred in fruits, vegetables, ereals, legumes and in beverage of plant such as wine, tea and coffee for human consumption as simple esters with quinic acid. Phenolic compounds are plant secondary metabolites, and they are usually found in herbs and fruits such as berries, apples, citrus fruit, cocoa, and grapes; vegetables like onions, olives, tomatoes, broccoli, lettuce, and soybeans; grains and cereals; green and black teas; coffee beans; propolis; and red and white wines. Phenolic compounds are synthesized in the secondary metabolism of plants from two major synthetic pathways: the shikimate and the acetate pathway. Plants have evolved to produce phenolic compounds compounds to protect against fungal parasites, 10 herbivores, pathogens, and oxidative cell injury. In addition, they produce stimuli to assist in pollination12 and guide insects to their food source. The term phenolic encompasses approximately 8000 obviously occurring compounds, all having a phenol ring. A further classification divides them in polyphenols and simple phenols, depending on the number of phenol subunits. Simple phenols include phenolic acids. Polyphenols possessing at least two phenol subunits contain the flavonoids and the stilbenes.

Those compounds with three or more phenol subunits are referred to as the tannins (Iglesias *et al.*, 2009, Hertog *et al.*, 1993, Kris-Etherton *et al.*, 2002, Bravo, 1988, Harbome, 1988, Swain, 1986, Robbins, 2003, King and Young 1999). The compound has attracted attention of researchers due to health promoting attributes, such as lowering the risks of cardiovascular disease, cancer, diabetes, and other conditions associated with aging. The biological mechanisms behind these effects are protection against free radicals, free radical mediated, inflammation and viral infection. Caffeic acid is a multifunctional obviously available organic acid substance which plays a significant role in binding metal ions from natural environment, food substances and beverage such as coca cola, mineral water etc. It completely blocks the production of reactive oxygen species (ROS). According to a current research, caffeic acid was a superior antioxidant compared with p-coumaric and ferulic acids in inhibiting LDL oxidation, but also in quenching radicals. In addition, the caffeic acid oligomers have been shown to be very efficient scavengers of 2,2-diphenyl-1-picryl hydrazyl (DPPH) and superoxide anion. And singlet oxygen. Caffeic acid had the strongest eliminating effects on intracellular active oxygen compared with protocatechuic acid and ferulic acid. Phenolic acid derivatives constitute a group of natural compounds present in human diet in significant amounts. They are involved in many metabolic reactions and are naturally occurring in many plant-derived food products, were they are chiefly responsible for the browning process (Jiang *et al.*, 2005, Vanbesiena and Marques 2003, Cornard and Lapouge 2004, Khvan *et al.*, 2001, Sudina and Mirzoeva 1993, Rao *et al.*, 1996, Meyer *et al.*, 1998, Cartron *et al.*, 2001, Kikuzaki *et al.*, 2002, Lu and Foo 2001, Del and Seguchi 2010, Singleton, 1987, Manuel, 1992).

This kind of compounds is becoming of increasing importance in applied science. In fact, apart from being commonly used as antioxidant food additives. The knowledge of the conformational preferences of this type of compounds is thus of the greatest importance as a starting point for future studies aiming at the understanding of the structure-activity relationships underlying their biological activity. All the same, the reported ab initio molecular orbital calculations on phenolic acid derivatives are very scarce, semiempirical quantum-chemical methods being generally used instead. In fact, apart from these only a few ab initio studies on phenolic antioxidants is to be found in the literature. One of them on several p-hydroxycinnamic acid derivatives, including caffeic acid. However, these studies aim completely at the explanation of the structural dependency of the antioxidant activity of this kind of phenolic analogues, focusing only on their most stable geometries. The goal of the present study, in turn, is to perform a thorough conformational analysis of caffeic acid (3, 4 -dihydroxy-trans-cinnamic acid, CA). Density functional methods-B3LYP,B1LYP,B3PW91,B3P86,LSDA,HF/6-31G*and 3-21G* and STO-3G-were used, in order to carry out a full geometry optimisation, along with rotational energy profile and harmonic vibrational frequency calculations, yielding all the minimum energy conformations of this molecule (Hosseinzadeh *et al.*, 2003, Silva *et al.*, 2001, Tanaka *et al.*, 1991, Bakalbassis *et al.*, 2001, Vanbesiena and Marques 2003).

COMPUTATIONAL DETAIL

In general, the hand-in-hand investigation of vibrational spectroscopy along with quantum mechanical calculations is a powerful tool for the thoughtful of undamental vibrational behavior of a molecule. Ab initio techniques provide detailed information that was unavailable experimentally. In this work, the density functional theory (DFT), calculations were done for geometry optimization of Caffeic acid structure and also thermodynamic parameters are used to predict the region selectivity in those. Geometry optimizations have been carried out for this compound. A molecular representation of this system can be found in Fig. 1 (Karthikeyan *et al.*, 2015, Pournamdari and Khaleghian 2010, Harbome, 1988, Kohn *et al.*, 1996, Chattaraj *et al.*, 2006).

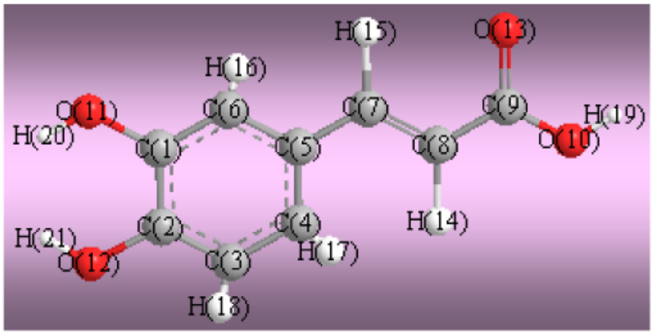

Fig. 1. Molecular structure of caffeic acid.

Herein, we report, structures, energetic, thermodynamic investigation of this system. Our calculations on ($C_9H_8O_4$) clusters are based on first-principles density functional theory (DFT) because electron correlation effects play an important role on this system. In the present work, The geometrics of all minimum energy structures for caffeic acid was optimized employing the Hartree-Fock (HF) and some of the hybrid methods; LSDA, B3LYP, B1LYP, B3P86 and B3PW91 are carried out using the basis sets of STO-3G, 3-21G* and 6-31G*. All these calculations are performed using GAUSSIAN 09 W program package on Pentium core i3 processor in personal computer. In DFT methods; Becke's three parameter hybrids function combined with the Lee-Yang-Parr correlation function (B3LYP), Becke's three parameter exact exchange-function (B3) combined with gradient-corrected correlational functional of Lee, Yang and Parr (LYP) and Perdew and Wang (PW91) predict the best results for molecular geometry for reasonably larger molecules Thermodynamic parameters were also calculated at 298 K and 1.0 atm (Lewis, 1993, Hartley *et al.,* 1985, Marchewka and Pietraszko 2008, Ivan, 2008, Ljupco *et al.,* 2009, Zhengyu *et al.,* 2000). In order to evaluate the thermodynamic parameters of the reactions, frequency calculations were carried out. The enthalpy for each species was calculated using the following equation:

$$H = E_{scf} + H_{corr} \quad (1)$$

where E_{scf} is the total energy from the quantum mechanical calculation, Hcorr is a correction term given by

$$H_{corr} = H_{corr} + K_bT \quad (2)$$

where Ecorr is the internal energy including the translational, rotational, and vibrational energies as well as zero point energy (ZPE), kB is the Boltzmann constant and T is the absolute temperature in Kelvin. Gibbs free energy of each compound was also calculated by using the following equation:

$$G = E_{scf} + G_{corr} \quad (3)$$

G_{corr} is a correction term given by

$$G_{corr} = E_{corr} + K_bT - T_s \quad (4)$$

where S is the entropy. The Gibbs free energy change of the reaction (ΔG) can be obtained in the same way as the enthalpy change (ΔH)(Hajmalek and Zare 2013).

RESULTS AND DISCUSSION

A. Thermodynamic parameters

As a matter of fact, the energies and thermo chemical parameters can give helpful information about structures and relative stabilities of these systems. The relative stability of structure of ($C_9H_8O_4$) compound are computed in DFT methods using B3LYP, B1LYP, B3P86, B3PW91, LSDA levels and HF with three basis set : STO-3G ,3-21G* and 6-31G* of theory which present thermodynamic properties of ($C_9H_8O_4$) and comparison of these diverse levels with each other's were shown in Fig. 2 .

Table1: Relative thermodynamic data for ($C_9H_8O_4$) system in kcal/mol entropy in cal/mol. kelvin by 6-31G* basis set.

Basis set	6-31G*				
Method	**ΔE**	**ΔH**	**ΔG**	**S**	**Δ zero-point Energies**
HF	0.00	0.00	0.00	107.75	0.00
LSDA	-193.35	-202.48	-202.58	108.09	-202.80
B1LYP	-2166.51	-2173.34	-2173.49	108.24	-2173.61
B3PW91	-2190.71	-2197.65	-2197.85	108.41	-2197.94
B3LYP	-2345.75	-2353.10	-2353.27	108.33	-2353.39
B3P86	-3401.57	-3408.38	-3408.53	108.25	-3408.65

Table 2. Relative thermodynamic data for ($C_9H_8O_4$) system in kcal/mol entropy in cal/mol.kelvin by 3-21G* basis set.

Basis set	3-21G*				
Method	**ΔE**	**ΔH**	**ΔG**	**S**	**Δ zero-point Energies**
HF	0.00	0.00	0.00	105.56	0.00
LSDA	-222.72	-231.92	-232.16	106.38	-232.21
B1LYP	-2171.68	-2178.61	-2178.95	106.71	-2178.89
B3PW91	-2201.59	-2208.61	-2209	106.89	-2208.91
B3LYP	-2353.41	-2360.85	-2361.22	106.81	-2361.16
B3P86	-3413.19	-3420.01	-3420.34	106.65	-3420.29

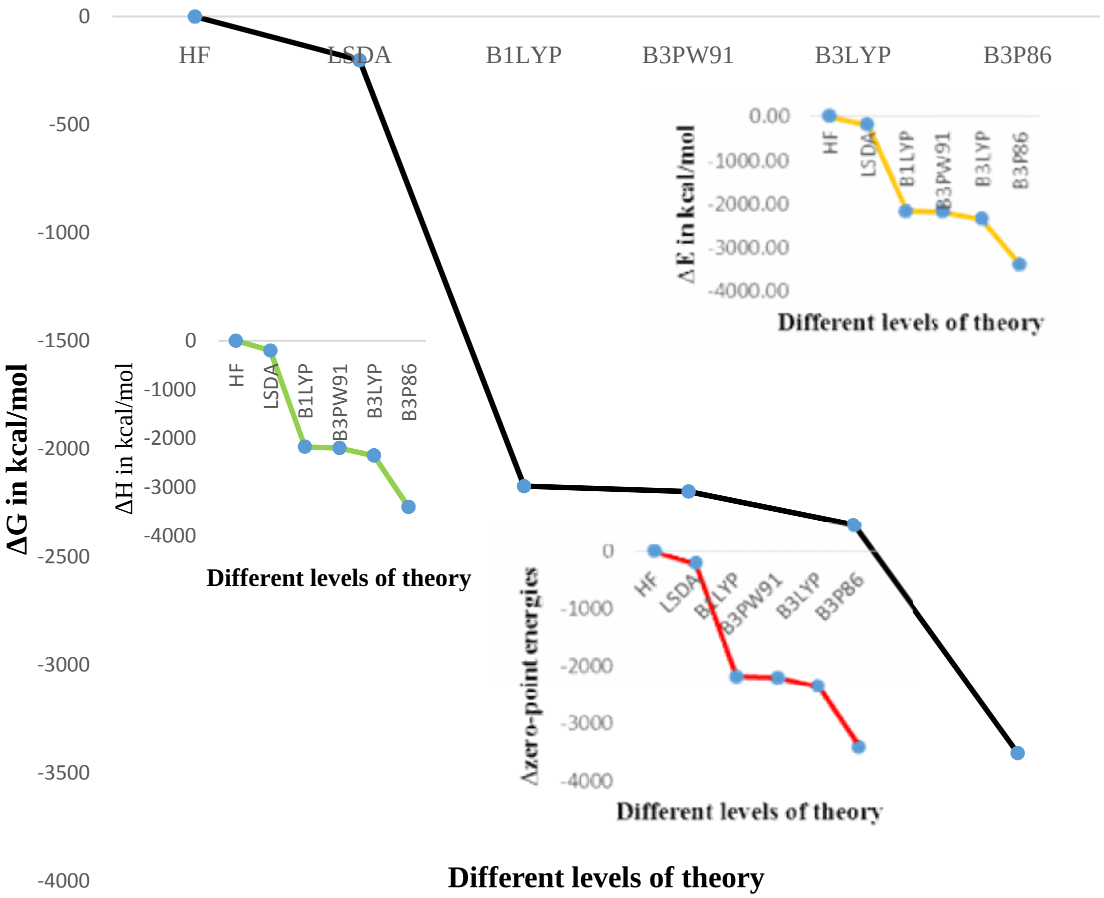

Fig .2. Different levels of theory as a function of ΔG, ΔH, ΔE, Δ zero-point energies kcal/mol and S cal/mol.kelvin.

Table 3. Relative thermodynamic data for ($C_9H_8O_4$) system in kcal/mol entropy in cal/mol. kelvin by STO-3G basis set.

	Basis set			**STO-3G**	
Method	**ΔE**	**ΔH**	**ΔG**	**S**	**Δ zero-point Energy**
HF	0.00	0.00	0.00	106.47	0.00
LSDA	-79.90	-90.56	-90.62	106.66	-90.69
B1LYP	-2054.48	-2064.18	-2064.92	108.94	-2064.61
B3PW91	-2132.95	-2142.41	-2143.16	108.99	-2142.84
B3LYP	-2232.07	-2242.42	-2243.24	109.23	-2242.90
B3P86	-3337.26	-3346.54	-3347.27	108.93	-3346.96

The thermodynamic parameters for the investigated reactions include: sum of electronic and thermal Gibbs free energies (G), sum of electronic and thermal enthalpies (H), and entropies (S). Also, the standard Gibbs free energy change (ΔG°), standard enthalpy change (ΔH°) and standard entropy (S°) of two pathways of reactions are obtained and reported in Table 1, 2, 3. Thermodynamic results show that all methods at diverse basis set are exothermic (ΔH°<0). It is found that the reaction with the largest exothermicity is related to method B3P86.

Computed standard Gibbs free energy change of reactions (Gibbs free energy difference, (ΔG°) show that all reactions are spontaneous processes (ΔG°<0) and indicate little differentiation between HF and LSDA methods at different basis sets. but it can be said that method B3P86 is thermodynamically more good and (ΔG°) at different basis set is among -3347.27_-3420.34 kcal/mol.

To confirm structural stability of our system we have optimized ($C_9H_8O_4$). As can be seen in Fig. 2, the ΔG value decreased from HF to B3P86, although the relative differences of the ΔG are almost the same as the ΔH and ΔE. So, in this paper, by using ab initio calculations, we analyze the Gibbs free energy of the formation. We found that between these methods, the results obtained at the B3P86 level are more negative than those of the other calculations though B3P86 shows the best results for ($C_9H_8O_4$) systems which are the most stable one with the minimum at -3347.27 kcal/mol for STO-3G, -3420.34 kcal/mol for 3-21G* and -3408.53 kcal/mol for 6-31G* basis set. As can be seen in Table 1, 2 and 3.

3-21G* among them was the best basis set because it has the most value equal by -3420.34 kcal/mol. Also the minimum amount is for STO-3G basis set and equat is by -3347.27 kcal/mol. As well as for ΔH, ΔE and Δzero point energies.

Zero-point energy is the energy that remains when all other energy is removed from a system. ?E^0 and ?ZPE correspond to the total energy difference and the zero-point energy diversity between basis sets and the greatest rate equal is by -3420.28 for B3P86 method 3-21G* basis set. That represents the most stable structure is the B3P86 method. Because it has the highest amount deta.

Entropy, which is included the measure of the level of disorder in a closed but changing system, a system in which energy can only be transferred in one direction from an ordered state to a disordered state .As you can see in the table the quantity of entropy in STO-3G basis set in various methods are among 106.46-108.92 cal/mol. kelvin , for 3-21G* basis set among 105.56-106.65 cal/mol.kelvin and for 6-31G* basis set among 107.74-108.25 cal/mol. kelvin. By comparing the data we can see that the basis set is the least quantity of entropy into 6-31G* and STO-3G basis set. It should be noted that there is a little difference between them, as shown in Fig. 3.

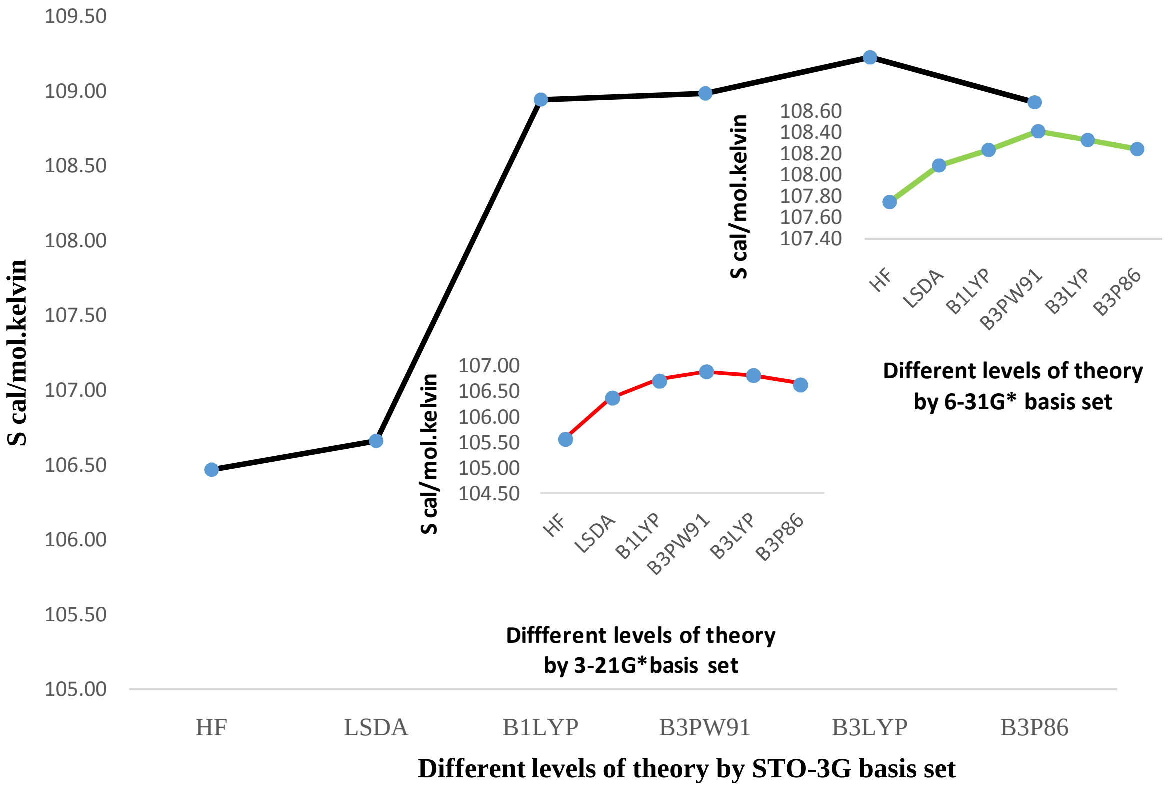

Fig. 3. Compare the amount of the data difference in the different basis sets.

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