

Temperature Effect of the Theobromine's Electronic and Antioxidant Properties

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Abstract: Theobromine exists in cocoa, which has an antioxidant ingredient. It is also affect our nervous system. For this reason, it's very important to know the properties of the theobromine. Theobromine is an experimentally studied molecule in the health and pharmaceutical fields. However, there are not many studies on theobromine properties in the theoretical field. Here, we show how theobromine electronic and antioxidant properties change with temperature theoretically. The calculations, were done by using Density Functional Theory (DFT), at B3LYP/6-31G(d,p) level. Six different temperature values (263.15 K, 273.15 K, 288.15 K, 298.15 K, 318.15 K, 328.15 K) were taken into account. Our results presented that the electronic structure of the theobromine didn't change while the antioxidant properties were changed. Theobromine indicated the most antioxidant property at 263.15 K. Therefore, this situation should be taken into consideration in order to benefit more from the antioxidant properties of theobromine in the field of health and pharmaceuticals.

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1. INTRODUCTION

Theobromine is a bitter and inhalant compound got from cacao seeds with the chemical formula $C_7H_8N_4O_2$. When someone see or hear word theobromine there is a bromine atom in the structure of it but there is no bromine atom. The root of the word theobromine is Greek, theo means 'God' and bromine means 'food', so *theobromine* means 'food of God'. In the sixteenth century the consumption of cocoa drink (chocolate) expanded in Europe especially in Spain which started in America. Because of the rich lasting aroma, chocolate was considered as a good nutrition. Conservatively, high antioxidant ingredient of theobromine found in cocoa beans, is being used in medicine and pharmacology. Especially, the methylxanthines in cocoa are remarkable because of their psychoactive effect. Theobromine and caffeine exist in cocoa, affect our psychology and our state of alertness. Theobromine has much more desirable effects than caffeine so that it is a remarkable molecule in cocoa. To understand the physiological effects of the theobromine in cocoa, characteristics of the ingredients need to be examined

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carefully. Besides, the high ingredients of carbohydrates in cocoa goods may take into account further [1].

The amount of adenosine effect on receptors in neurons is related to brain physiology. The impact of theobromine on adenosine in the brain by using blockers of its specific receptors is begin the daily activities quickly. The blockers of adenosine receptors are caffeine and theobromine. The studies in the recent years represented that theobromine has psychoactive actions in humans are much more effective than caffeine [2,3]. Also, the effect of theobromine on blood pressure distinctive than that of caffeine but the reasons for these differs are not retained [2,4].

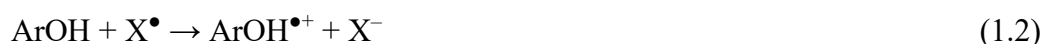
The basics of experimental and theoretical studies in the literature for the antioxidant activity of compounds are to give a hydrogen atom to free radicals. Especially, quantum chemical calculations for the quantitative structure-antioxidant activity relationship (QSAR) are more economical process than experimental studies [5–14].

The aim of this study was to investigate the electronic properties antioxidant effect of theobromine changing by temperature using quantum chemical calculations. There are five antioxidant mechanisms that explain antioxidant reactions we used are [15-23]:

1) HAT (Hydrogen Atom Transfer) mechanism:



2) SET (Single Electron Transfer) mechanism:



3) SET-PT (Single-Electron Transfer followed by Proton Transfer):



The SET-PT procedure has two steps. The initial step is an antioxidant molecule reacts with the free radical, and a cationic radical form of the antioxidant and an ionic form of the radical occur. In the continuing step the cationic radical form of the antioxidant separates into a radical and proton.

4) SPLET (Sequential Proton Loss Electron Transfer):



This procedure has also two steps. The initial step the antioxidant separates into an anionic form and proton, and then ions occurred in the first reaction react with the free radical. In this reaction a radical form of the antioxidant and a neutral molecule occur.

5) TMC (Transition Metals Chelation): Metals in their low oxidation state may generate free radicals according to the Fenton reaction:



In this procedure the ability of a molecule to produce the proton is taken into consideration. One of the significant elucidatory of the electronic and antioxidant properties are dispersion of HOMO and LUMO orbitals. The higher HOMO energy is responsible for the rich

abilities of a molecule to donate a proton. Therefore, the HOMO dispersion exposes which chemical groups in a molecule are freely attacked by free radicals. From the difference between LUMO and HOMO energy we can accomplish about chemical activity of the molecule. The higher ΔE (LUMO – HOMO) is bounded with higher activity of the molecule [24].

2. MATERIAL and METHODS

The electronic and thermal properties of the theobromine in gas phase are theoretically examined by means of Density Functional Theory (DFT) using B3LYP method with 6-31G(d,p) basis set. All the calculations (optimization of the geometry of mono- and dianions, optimization of the geometry of the radicals and cation radicals presented in Figure 1) were performed by using Gaussian 16. Revision B.01 program [25] and GaussView 6.0.16 [26] was used for the visualization of the structure and simulation.

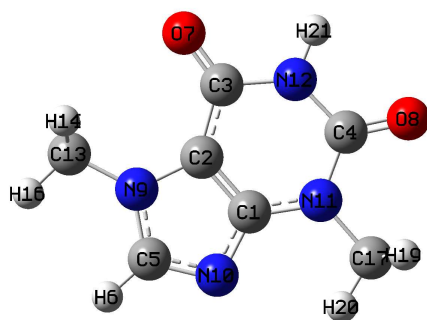


Figure 1. Optimize geometry of Theobromine

Numerical descriptors of the antioxidant mechanism such as Bond Dissociation Enthalpy (BDE), Adiabatic Ionization Potential (AIP), Proton Dissociation Enthalpy (PDE), Proton Affinity (PA), Electron Transfer Enthalpy (ETE), gas phase acidity ($\Delta H_{\text{acidity}}$) defined below have been calculated for the theobromine [15-23].

$$\text{BDE} = H_{\text{ArO}^\bullet} + H_{\text{H}^\bullet} - H_{\text{ArOH}} \quad (2.1)$$

in which H_{ArO^\bullet} is the enthalpy of the radical, H_{H^\bullet} is the enthalpy of the H atom, H_{ArOH} is the enthalpy of the compound.

$$\text{AIP} = H_{\text{ArOH}^{\bullet+}} - H_{\text{ArOH}} \quad (2.2)$$

here $H_{\text{ArOH}^{\bullet+}}$ is the enthalpy of cationic radical, H_{ArOH} is the enthalpy of the compound.

$$\text{PDE} = H_{\text{ArO}^\bullet} + H_{\text{H}^+} - H_{\text{ArOH}^{\bullet+}} \quad (2.3)$$

in which H_{ArO^\bullet} is the enthalpy of the radical, H_{H^+} is the enthalpy of the proton, $H_{\text{ArOH}^{\bullet+}}$ is the enthalpy of cationic radical.

$$\text{PA} = H_{\text{ArO}^-} + H_{\text{H}^+} - H_{\text{ArOH}} \quad (2.4)$$

here H_{ArO^-} is the enthalpy of the anion, H_{H^+} is the enthalpy of the proton, H_{ArOH} is the enthalpy of the compound.

$$\text{ETE} = H_{\text{ArO}^\bullet} - H_{\text{ArO}} \quad (2.5)$$

Here H_{ArO^\bullet} is the enthalpy of the radical, H_{ArO^-} is the enthalpy of the anion.

$$\Delta H_{\text{acidity}} = H_{ArO^-} - H_{ArOH} \quad (2.6)$$

in which H_{ArO^-} is the enthalpy of the anion, H_{ArOH} is the enthalpy of the compound.

3. RESULTS and DISCUSSION

3.1. Antioxidant Properties

For the HAT mechanism BDE is a significant numerical parameter so it presents the stability of the N-H bond in the theobromine. The lower BDE value identifies better antioxidant property. Our calculations presented in the [Table 1](#) indicated and exhibited [Figure 2](#) that theobromine in the 263.15 K we selected randomly is the better antioxidant activity selected.

Table 1. Antioxidant Parameters Changing by Temperature.

Temperature (K)	BDE (Hartree)	AIP (Hartree)	PDE (Hartree)	PA (Hartree.)	ETE (Hartree.)	ΔH (Hartree.)
263.15	0.176603	0.283914	0.392961	0.568707	0.108168	0.566624
273.15	0.176715	0.283920	0.393068	0.568805	0.108183	0.566642
288.15	0.176883	0.283929	0.393226	0.568949	0.108206	0.566668
298.15	0.176995	0.283936	0.393331	0.569441	0.107826	0.567081
318.15	0.177214	0.283950	0.393537	0.569236	0.108251	0.566717
328.15	0.177324	0.283958	0.393639	0.569330	0.108267	0.566732

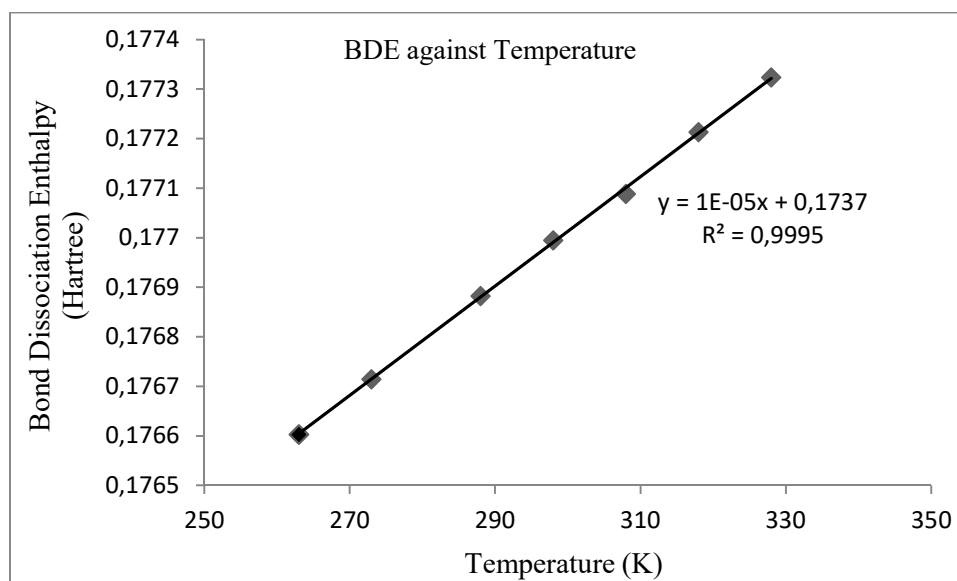


Figure 2. Bond dissociation enthalpy of the theobromine changing by the temperature.

For the SET-PT mechanism AIP is an important parameter because it defines electron forgiving by the antioxidant molecule. The molecule has low AIP parameter exhibited is more sufficient to ionization and shows strong antioxidant property. So from the [Table 1](#) and [Figure 3](#) that theobromine in the 263.15 K also better antioxidant activity.

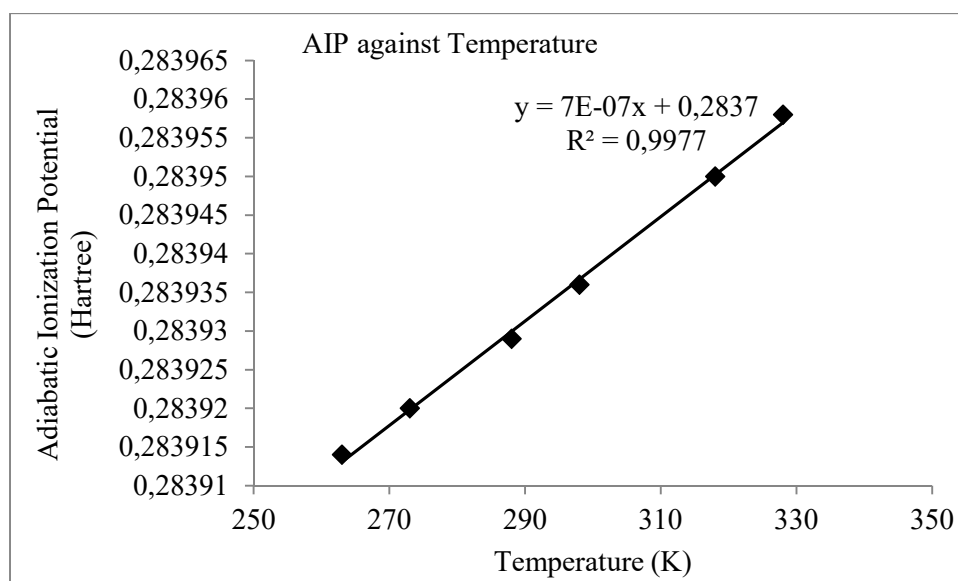


Figure 3. Adiabatic ionization potential theobromine changing by the temperature.

The second step of the SET-PT mechanism the PDE is a significant parameter. The low value of the PDE parameter indicates that SET-PT mechanism is energetically preferred. For the SPLET mechanism PA and ETE are very important parameters. Because of the PA values are higher than BDE and AIP, theobromine molecule doesn't favored SPLET mechanism.

3.2. Electronic Properties

For the electronic properties the energies of Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) are very important parameters. These parameters not explain the antioxidant property directly but describing the electron donating properties they can be connected to antioxidant activity. HOMO-LUMO energy difference represents the chemical reactivity of a molecule. The low HOMO-LUMO gap levels aren't beneficial to hole-injection [27] and evidence of the high probability of the charge transfer in the molecule [28].

In our calculations electronic parameters of the Theobromine didn't turn by the changing the selected randomly temperature. So, here in Figure 4, we use the only 298.15 K parameters for calculating the electronic parameters and presenting the HOMO-LUMO orbitals. E_{HOMO} is an energy of HOMO orbital, E_{LUMO} is an energy of LUMO orbitals, I represents ionization potential, A represents electron affinity, χ represents electronegativity, η represents global hardness, S represents global softness, ω represents global electrophilicity index and μ represents electronic chemical potential in the Table 2. The energy value between HOMO and LUMO orbitals is 5.13 eV (ΔE) as given Table 2. This value is high for the transition of the electron from the HOMO orbital to LUMO orbital. As seen from the Table 2 theobromine is a hard and electronegative molecule.

Table 2. Electronic Parameters of the Theobromine.

E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	I (eV)	A (eV)	X (eV)	H (eV)	s (eV)	M (eV)	Ω (eV)
-6.04	-0.91	5.13	6.04	0.91	3.48	2.57	0.39	-3.48	2.35

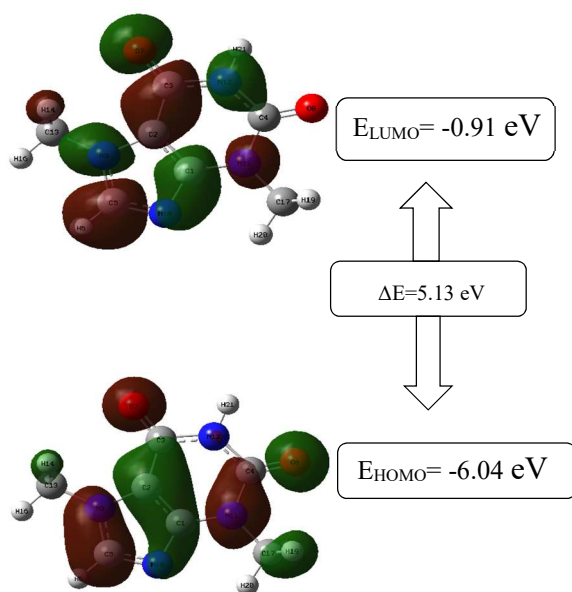


Figure 4. The atomic orbital compositions of the Theobromine.

4. CONCLUSION

In this paper, antioxidant and electronic properties of theobromine depending on the temperature were investigated theoretically using density functional theory calculations based on a B3LYP and 6-31G(d,p) basis set quality. Our calculations represented that theobromine showed best antioxidant activity in the 263 K since the bond dissociation enthalpy and adiabatic ionization potential values are lower in that temperature. However, the electronic properties of the theobromine didn't vary depending on temperature. Antioxidant parameters of the theobromine molecule presented that molecule prefer SET-PT reaction instead of SPLET. The energy difference between HOMO and LUMO orbitals of the theobromine is 5.13 eV. This large value is pointed out the proof of the poor probability of the charge transfer in the molecule and also the theobromine is a soft molecule. As a result, methods used in this article can applied to a variety of biomolecules and can enhance our understanding biomaterials nature and are shed light on how we will use such molecules.

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