

Explain to Interconnection Between Fe⁺² Ions and Vitamin C in Food By Density Functional Theory

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Abstract

As we know vitamin C is a both reducing agent and creating acid increases the absorption of non-heme iron from the iron source in food. In this study we explain to relation between ascorbic acid with ferric iron (Fe⁺³) by Density Functional Theory (DFT) method. Release to this effect firstly we optimized all molecules in this system than calculated to reaction mechanism energy.

Keywords: *Vitamin C, Iron metabolism, Gaussian, DFT*

Introduction

The first scientific studies on vitamin C that Holst and Frohlich is made in 1907, many foods, especially green vegetables and fruits began with the discovery of the inhibitory effects of the disease scurvy (1,2). Vitamin C, plays an important role in the water-soluble vitamins. There are two forms of structurally; D-ascorbic acid and L-ascorbic acid. D-ascorbic acid is inactive. The L isomer is biologically active form (3). Vitamin C is monosaccharide derivative which the chemical structure is C₆H₈O₆. In case of light red crystals, odorless and sour taste is a substance having (5). One of the most important function of Vitamin C, protecting the bodies against infection and bacterial toxin. Infections reduce the amount of vitamin C in the body. When these vitamins is taken a sufficient amount, prevented infection and vitamin C taken an amount increased, is seen that infections are reduction (6).

Dietary iron, there are heme iron (ferrous iron Fe⁺²) and non-heme iron (ferric iron Fe⁺³)

found two forms caused by hemoglobin and myoglobin. Acid environment and reducing agents, especially non-heme are positive factors for the absorption of iron (7). Ascorbic acid is a both reducing agent and creating acid environment increases the absorption of non-heme iron from the iron source and availability. Ferric iron Fe⁺³, ferrous iron Fe⁺² reductions by ascorbic acid as a result of non-heme iron absorption is known to increase (8). In a study performed; the meal added to 50-100 mg ascorbic acid has been reported that the absorption of non-heme increase 2-3 times. In another study; yet given with meals 3 times a day for 9 months for women who have entered menopause 100 mg of ascorbic acid, iron storage status of women has been found to significantly affect positive (9).

Theoretically there are similar studies in the literature (10). However, vitamin C does not have a study on the impact of the reduction of ferrous iron (Fe⁺²) to ferric iron (Fe⁺³) (11).

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Materials and Methods

In this study we tried to explain reaction mechanism of Ascorbic Acid with Ferric Iron (Fe^{+3}). The studied molecules are named as Cvit, Cvit1, Cvit2, Cvit3, Cvit4, Cvit5, Cvit6 and Cvit7 which are depicted in Figure 1. In Table 1 for studied molecules code of molecules, molecular formulas, name of molecules and molecular weights are given.

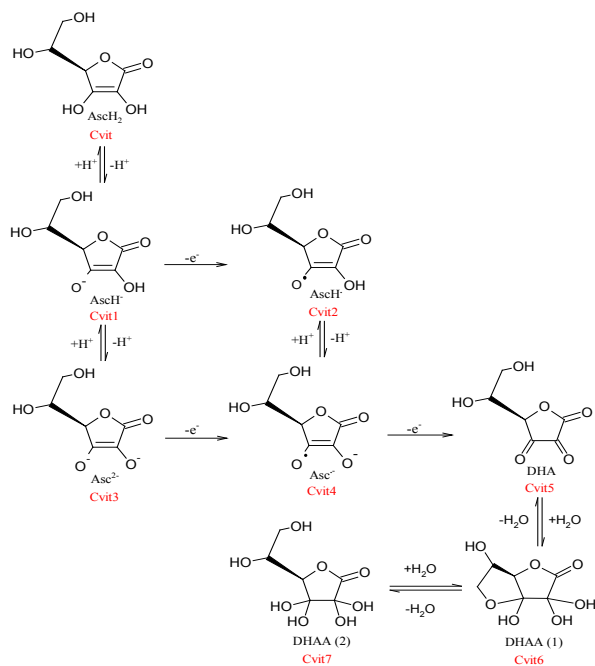


Figure 1. The Studied Molecules

Table 1. Code, structure formula, name and molecular weight for studying molecules

| Code | Structure formula | Name | Molecular weight (g) |
|-------|-------------------|---------------------|----------------------|
| Cvit | $C_6H_8O_6$ | Ascorbic acid (Asc) | 176 |
| Cvit1 | $C_6H_7O_6\cdot$ | AscH• | 175 |
| Cvit2 | $C_6H_7O_6$ | AscH | 175 |
| Cvit3 | $C_6H_6O_6^{-2}$ | AscH ²⁻ | 174 |

| | | | |
|-------|------------------|--------------|-------|
| Cvit4 | $C_6H_6O_6\cdot$ | Asc• | 174 |
| Cvit5 | $C_6H_6O_6$ | DHA | 174 |
| Cvit6 | $C_6H_8O_7$ | DHAA | 192 |
| Cvit7 | $C_6H_{10}O_8$ | DHAA | 210 |
| | Fe^{+2} | Ferrous iron | 55,84 |
| | Fe^{+3} | Ferric iron | 55,84 |
| | H^+ | Hydrogen ion | 1 |
| | H_2O | water | 18 |

We can divide our study in three parts. In the first part, these molecules are optimized by the density functional theory (DFT) (12,13) method, using the B3LYP hybrid functional (14) with the 6-31g(d) (15) basis set (basis set 1) implemented a DFT study on the structural and optical properties, in the Gaussian 03W software package (16) which are illustrated in Figure 1. After optimization, reaction energies are calculated using optimized molecule energies. In the second part, enlarged basis set 6-311G (d,p) (basis set 2) are used for reaction energy. Then the results of reaction energies which are calculated with 6-311G (d,p) and 6-31G (d) are compared. In the last part, Natural Bond Orbitals (NBO) charge distribution of molecules is calculated. In every stage of reaction mechanism we measured the charge transfers between molecules using calculated NBO charges.

Results and Discussion

Geometry optimizations of molecules are obtained using DFT methods B3LYP functional with basis sets 1 and 2 at gas phase and in water solution. Optimized molecular energies are given in Table 2.

Table 2. Molecular Energy for Studying Molecules in kcal/mol

| Molecule | 6-31G (d) Gas phase | | 6-311G (d,p) | |
|------------------|---------------------|--------------|--------------|--------------|
| | E (a.u.) | E (kcal/mol) | E (a.u.) | E (kcal/mol) |
| Cvit | -684,75 | -429.680,53 | -684,97 | -429.815,65 |
| Cvit1 | -684,23 | -429.352,82 | -684,41 | -429.467,68 |
| Cvit2 | -684,12 | -429.286,70 | -684,33 | -429.417,17 |
| Cvit3 | -683,50 | -428.894,65 | -683,72 | -429.031,63 |
| Cvit4 | -683,62 | -428.971,87 | -683,83 | -429.102,23 |
| Cvit5 | -683,52 | -428.909,05 | -683,72 | -429.035,57 |
| Cvit6 | -759,98 | -476.887,79 | -760,21 | -477.034,44 |
| Cvit7 | -836,41 | -524.844,45 | -836,68 | -525.015,71 |
| Fe ⁺² | -1261,50 | -792.216,93 | -1262,60 | -792.280,63 |
| Fe ⁺³ | -1261,27 | -791.446,50 | -1261,36 | -791.501,91 |
| H ₂ O | -76,01 | -476.96,19 | -76,45 | -479.70,77 |
| H ⁺ | 0 | 0 | -0,50 | -315,10 |

When Table 2 observed basis set 2 energies are higher than basis set 1. This change is between -0,2 to -0,27 kcal/ mol for Cvit, Cvit1, Cvit2, Cvit3, Cvit4, Cvit5, Cvit6 and Cvit7.

The energies of reactions which are given in Figure 1 are calculated using equation 1 for basis set 1 and basis set 2. The results are given in Table 3.

$$\Delta H = \Sigma_{\text{product}} - \Sigma_{\text{reactant}} \quad (\text{Eq 1})$$

Table 3. 6-31G (d) ve 6-311G (d,p) baz setleri ile hesaplanmış reaksiyon enerjileri

| ΔH | Reaction Mechanism | 6-31G (d) | 6-311G (d,p) |
|--------------|--------------------|--------------|--------------|
| | | E (kcal/mol) | E (kcal/mol) |
| ΔH_1 | Cvit → Cvit1 | 327,71 | 32,87 |
| ΔH_2 | Cvit1 → Cvit2 | 66,12 | 50,50 |
| ΔH_3 | Cvit2 → Cvit4 | 314,83 | -0,16 |

| | | | |
|-----------------|--|---------|---------|
| ΔH_4 | Cvit4 → Cvit5 | -62,83 | 66,67 |
| ΔH_5 | Cvit5 → Cvit6 | -282,55 | -28,10 |
| ΔH_6 | Cvit6 → Cvit7 | -260,47 | -10,50 |
| ΔH_7 | Cvit1 → Cvit3 | 458,17 | 120,94 |
| ΔH_8 | Cvit3 → Cvit4 | -77,22 | -70,60 |
| ΔH_9 | Fe ⁺³ + e ⁻ → Fe ⁺² | -770,43 | -778,72 |
| ΔH_{10} | Cvit1 + Fe ⁺³ → Cvit2 + Fe ⁺² | -704,32 | -728,22 |
| ΔH_{11} | Cvit3 + Fe ⁺³ → Cvit4 + Fe ⁺² | -847,66 | -849,32 |
| ΔH_{12} | Cvit4 + Fe ⁺³ → Cvit5 + Fe ⁺² | -707,61 | -711,70 |

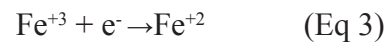
$$\Delta H_1 \quad \Delta H_2 \quad \Delta H_3 \quad \Delta H_4 \quad \Delta H_5 \quad \Delta H_6$$



$$\Delta H_{\text{Total}} = \Delta H_1 \quad \Delta H_2 \quad \Delta H_3 \quad \Delta H_4 \quad \Delta H_5 \quad \Delta H_6 \quad (\text{Eq 2})$$

$$\Delta H_{\text{Total}} = 102,80 \text{ kkal/mol}$$

Regarding to Equation 2 total reaction mechanism energy is calculated. As can be concluded from the results total reaction mechanism is endothermic. Using Ferric Iron used as source of electron (Equation 3) total reaction mechanism is recalculated.



As electron source when iron is used total reaction is exothermic.

$$\Delta H_{\text{Total}} = -1312,41 \text{ kkal/mol}$$

Same calculation carried out for basis 2 as done in basis 1.

$$\Delta H_{\text{Total}} = 111,28 \text{ kkal/mol without iron for basis set 2}$$

$$\Delta H_{\text{Total}} = -1445,81 \text{ kkal/mol with iron for basis set 2.}$$

For all molecules used in this study the giving atomic numbers show in Figure 2 for references molecule. In order to calculate NBO charges 'pop=(nbo,savenbos)' key word are used. Calculating NBO charges are given in Table 4.

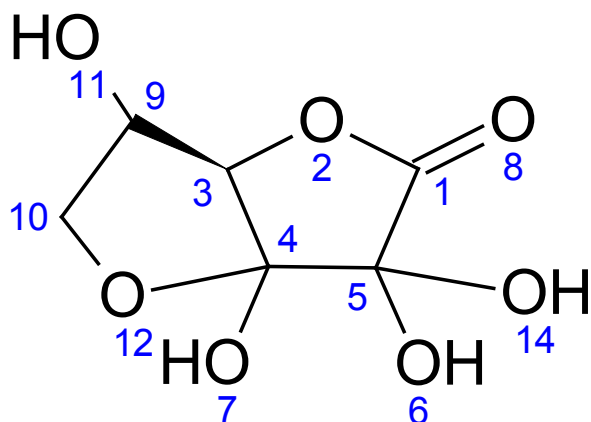


Figure 2. Referencemolecule with giving atomic numbers

In order to better observe the change of charges during reactions a graph is plotted as in Figure 3 using values in the Table 4.

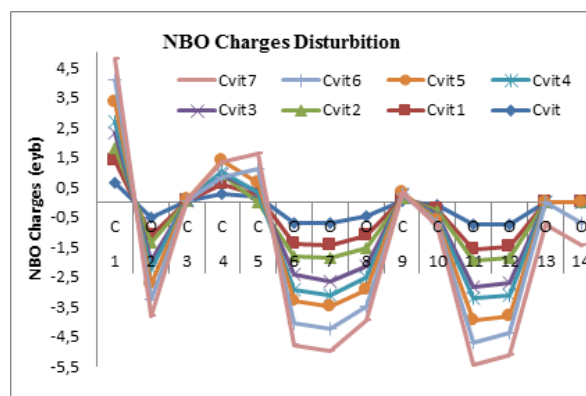


Figure 3. NBO charge transfer graph between molecules

When Figure 3 is investigated:

- In Cvit1 while charges of number 1 and 4 carbon atoms increase, the charge of the number 5 carbon atom decreases compared to Cvit. The reason for this behaviour can be attributed to removing of one H atom from hydroxyl group which is bounded to the number 1 C atom. When compared to Cvit, charges of all oxygens in Cvit1 are increased.
- Due to the removed electron in Cvit2 charges of the oxygens are decreased. Despite such decrease in Oxygens, the number 5 C atom in Cvit2 had different negative values.
- While in transition from Cvit2 to Cvit4, structure loses 1 hydrogen atom and the

Table 4. NBO charge distributions of the molecules (in eyb)

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|-------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | C | O | C | C | C | O | O | O | C | C | O | O | O | O |
| Cvit | 0.64 | -0.53 | 0.01 | 0.26 | 0.19 | -0.71 | -0.69 | -0.47 | 0.05 | -0.12 | -0.76 | -0.74 | - | - |
| Cvit1 | 0.72 | -0.60 | 0.01 | 0.33 | 0.02 | -0.72 | -0.76 | -0.65 | 0.05 | -0.12 | -0.81 | -0.78 | - | - |
| Cvit2 | 0.45 | -0.24 | 0.001 | 0.31 | -0.22 | -0.38 | -0.43 | -0.42 | 0.03 | -0.07 | -0.37 | -0.37 | - | - |
| Cvit3 | 0.52 | -0.59 | 0.02 | 0.04 | 0.33 | -0.64 | -0.80 | -0.64 | 0.08 | -0.12 | -0.92 | -0.84 | - | - |
| Cvit4 | 0.35 | -0.28 | 0.01 | 0.07 | 0.02 | -0.50 | -0.43 | -0.34 | 0.03 | -0.07 | -0.37 | -0.38 | - | - |
| Cvit5 | 0.65 | -0.51 | 0.003 | 0.36 | 0.30 | -0.37 | -0.38 | -0.43 | 0.05 | -0.12 | -0.74 | -0.72 | - | - |
| Cvit6 | 0.77 | -0.53 | -0.03 | -0.56 | 0.49 | -0.74 | -0.75 | -0.53 | -0.01 | -0.08 | -0.72 | -0.57 | - | -0.73 |
| Cvit7 | 0.69 | -0.53 | 0.03 | 0.53 | 0.47 | -0.74 | -0.76 | -0.47 | 0.05 | -0.13 | -0.77 | -0.74 | -0.75 | -0.72 |

number 4 and 1 C atom loses more charge compared to all other structure.

- It has been observed that since the structure lost an electron while forming Cvit5, It showed similar changes with Cvit2. While forming Cvit6 and Cvit7 a water joined in both structures.
- In Cvit6 number 4 C atom negatively charged however in transition to Cvit7 it changed back to earlier value

Conclusion

In this study we explain to relation between ascorbic acid with ferric iron (Fe⁺³) by Density Functional Theory (DFT) method.

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