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Nano theoretical study of different solvents and temperatures effects on Beta Carotene anticancer properties by computational methods

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ABSTRACT: Cancer is described like a hocus pocus in our daily life, as growth, duplication and rarely unnatural proliferation of body cells. Free radicals are one of major factors that create cancer by oxidation. Nowadays, herbal materials are considered as one of anticancer drugs. This study is about anticancer properties of Beta carotene in carrot (Umbellifera Family) by Quantum Mechanic and Molecular Mechanic Calculation (QM/MM), NMR, Thermodynamic properties, vibration frequency, charge distribution and temperature effects are studied. It has the most negative Gibbs free energy. We can say that by increasing the molecule dipole moment, the interaction between molecules of solvent and solute will increase. Thus, interaction of solute molecules will decrease, which affects Gibbs free energy and entropy.

Keywords: *Anticancer; Beta Carotene; NMR; Quantum Mechanics; Thermodynamic*

INTRODUCTION

In the treatment of cancer patients, understanding of the pathophysiology of cancer and contact of anticancer compounds has the main role (Youngken, 1950). Many nutritional substances and medicinal plants are discovered with cancer precautionary properties. Nowadays such a large number of researches are about natural substances can affect cancer, but it remains like a main hocus pocus in modern medicine. Actually cancer is depicted as an unnatural growth, duplication and rarely proliferation of body cells. Human's body is consisting of million cells that built some tissues such as muscles, bones and cortex. Many of natural body cells, in response of stimulation from inside and outside of body, are grown, duplicated and finally dead. If this process happens in the perfect path, the body remains healthy and preserves its natural operation. Difficulties start when the cell transforms to the cancer cell. In other words, modified cell does not follow the intercellular order that other cells are in their control and acts headstrong instead of coordination with other cells. Such a large number of cancers are happened by reason of free radicals. Substantially free radicals are disastrous combinations that are formed because of oxidation, and

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cause destruction of body cells, hasty cell aging and cancer (Youngken, 1950, Szczepanska, *et al.*, 2007, EMEA Annual report, 2009, Gibson, *et al.*, 2007). One of the main researches in the world is identification of herbal substances in order to access to the new anticancer drugs (Gibson, *et al.*, 2007, Friedman, *et al.*, 2000). Iran, because of climate diversification, has a rich collection of plant species and there are unique samples in order to study of anticancer substances. Beta carotene is an important antioxidant that is abundant in carrot, can inactive free radicals and affective in prevention of different kind of cancers, especially pancreas cancer (Youngken, 1950), but there is not enough attention in thermodynamic and structure of these valuable substances. Because of this reason, research is limit in this context.

COMPUTATIONAL DETAILS

This research is about anticancer properties of Beta carotene in carrot (Umbelliferea family) by use of Mechanic Quantum Calculation and Molecular Mechanic. In this study, thermodynamic properties, vibrational frequencies, charges distribution, quantum mechanic equation, temperature affect, beta carotene properties, and anticancer properties are studied by use of combinational calculation methods QM/MM, NMR; that these conclusions can be used as usage models in pharmacy, medicine. Thermodynamic parameters of this structure in different solvent in comparison with water as natural solvent of live life's body are studied. Also, such parameters as asymmetric parameters, total charges of atoms are compared in order to assemble better condition for drug efficacy. The term of ab initio is given to calculations that are taking exactly from theoretical principles, without adding any testable data (Monajjemi, *et al.*, 2006, Young, 2001). The most common category of ab initio calculation is Hartree-Fock (HF), in which the initial estimation is named the mean field approximation. This means the coulombic electron-electron repulsion is not clearly contained, although its average effect is included in the computations (Nsangou, *et al.*, 2006, Khaleghian, *et al.*, 2011). In first step, this molecule structure is optimized by use of Hartree-Fock methods with basic series STO-3G that energy amounts and bipolar moments are studied. In the next step, NMR parameters that are a suitable analysis method for structure identification and different groups in molecule are used. Regarding to the NMR spectrometry that is very sensitive to the structure and environment of each atom and molecule and is one of the most important methods for checking and analyzing molecule structure and finding the factors and active sites of molecules, NMR study was done for this system (Furer, *et al.*, 2009, Dziembowska, *et al.*, 2009). Calculation was done by use of HF. On the other hand we know that atomic orbitals usually described by basic function that is consist of a large number of atomic functions and are the best description for electron basic state of a system (Karelson and Lomaka, 2001, Tsolakidis and Kaxiras, 2005, Monajjemi, *et al.*, 2008, Ramanathan, *et al.*, 2005). So, basic functions that mentioned above are used for describing of his system. System thermodynamic research was done via calculation of energy, Gibbs free energy and entropy in different phase such as different solutions like water, DMSO, methanol, ethanol and benzene in deference temperature (298 K, 310 K, 315 K), at HF theory and bye use of different basis sets (Lobert, *et al.*, 2007). Calculation of δiso, δaniso, η and Δδ was done according to the below equations (Monajjemi, *et al.*, 2008):

δiso is named privacy sigma and calculated by this equation (Eq. 1) :

$$\sigma_{iso} = \frac{\text{trace}\hat{\sigma}}{3} = \frac{\sigma_{11} + \sigma_{22} + \sigma_{33}}{3} \qquad (1)$$

Three main elements δ11, δ22 and δ33 show privacy interaction in three dimensions.

η: is the asymmetry parameter and is between zero and one.

$$0 \le \eta \le 1$$

If: $|\sigma_{11} - \sigma_{iso}| \ge |\sigma_{33} - \sigma_{iso}|$, then (Eq. 2) :

$$\eta = \frac{\sigma_{22} - \sigma_{33}}{\delta} \qquad (2)$$

And, if: $|\sigma_{11} - \sigma_{iso}| \le |\sigma_{33} - \sigma_{iso}|$, then (Eq. 3) :

$$\eta = \frac{\sigma_{22} - \sigma_{11}}{\sigma_{33} - \sigma_{iso}} \qquad (3)$$

Table 1. Solvent dielectric constant

Solvent dielectric Constant (ε)	Water	DMSO	Benzene	Ethanol	Methanol
	80	46.7	33	24.55	2.3

δ is an amount for chemical relocation anisotropy.

If: $|\sigma_{11}-\sigma_{iso}|\geq|\sigma_{33}-\sigma_{iso}|$, then (Eq. 4) :

$$\delta=\sigma_{11}-\sigma_{iso} \tag{4}$$

And, if: $|\sigma_{11}-\sigma_{iso}|\leq|\sigma_{33}-\sigma_{iso}|$, then (Eq. 5) :

$$\delta=\sigma_{33}-\sigma_{iso} \tag{5}$$

Δδ is chemical replacement anisotropy.

If: $|\sigma_{11}-\sigma_{iso}|\geq|\sigma_{33}-\sigma_{iso}|$, then (Eq. 6) :

$$\Delta\sigma=\sigma_{11}-\frac{\sigma_{22}+\sigma_{33}}{2} \tag{6}$$

And, if: $|\sigma_{11}-\sigma_{iso}|\leq|\sigma_{33}-\sigma_{iso}|$, then (Eq. 7):

$$\Delta\sigma=\sigma_{33}-\frac{\sigma_{22}+\sigma_{11}}{2} \tag{7}$$

The quantum mechanics (QM) calculations on the interactions of Beta carotene have been performed by GAUSSIAN 09 program (Frisch, *et al.*, 2009) applying the standard STO-3G basis set. In the Hartree-Fock (HF) level and in the Gaussian program, simple approximation is applied, and volume of the solute is utilized to calculate the radius of a cavity which forms the hypothetical surface of the molecule (Witanowski, *et al.*, 2002, Mora-Diez, *et al.*, 2006, Wong, *et al.*, 1992, Monajjemi, *et al.*, 2008). Solvent effects have been investigated on values of Gibbs free energy, entropy, energy, dipole moment of water, DMSO, methanol, ethanol and benzene surrounding in difference temperature.

RESULTS AND DISCUSSION

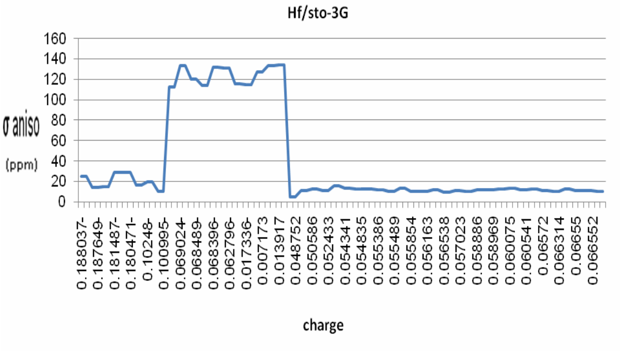

Fig. 1. Graph of σaniso on charge

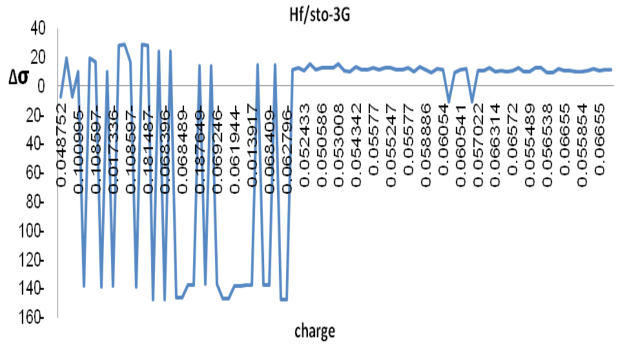

Fig. 2. Graph of Δσ on charge

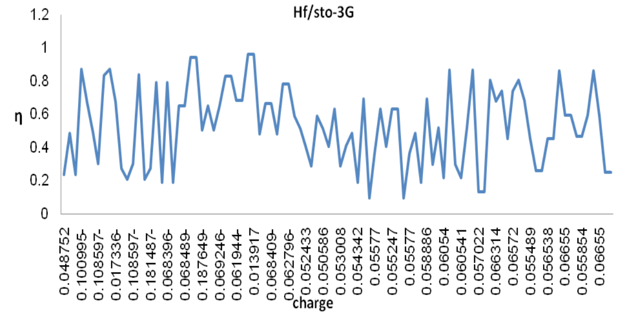

Fig. 3. Graph of η on charge

Perception of different molecular processes in chemistry and biochemistry is possible by the interaction between the solute and the solvent molecules. The graph δaniso is determined by charge Atomic number 38 is the minimum in both graphs (Fig. 1). The graph Δσ shows atomic number 20 is the maximum (Fig. 2). Also, graph η shows mentioned atom is the lowest (Fig. 3). Thermodynamic parameters for these systems are determined by calculating the energy (Fig. 4), Gibbs free energy and entropy in different solvents

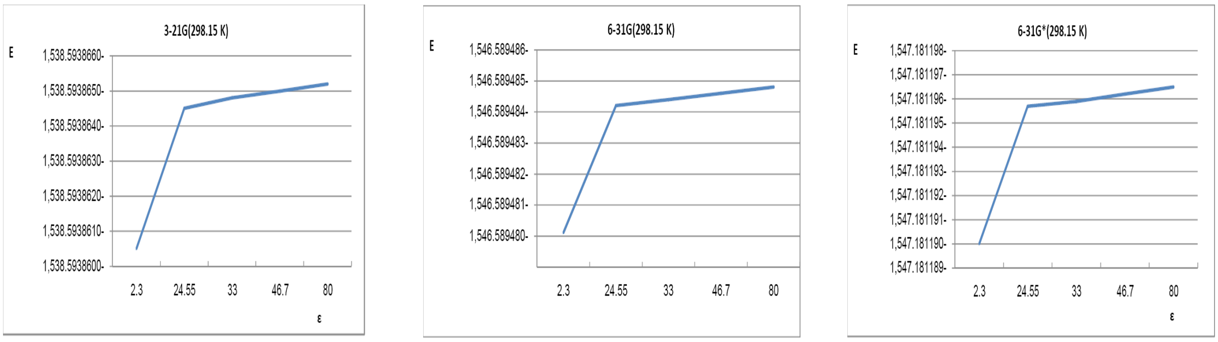

Fig. 4. The energy changes versus dielectric constant in different solvents and temperature

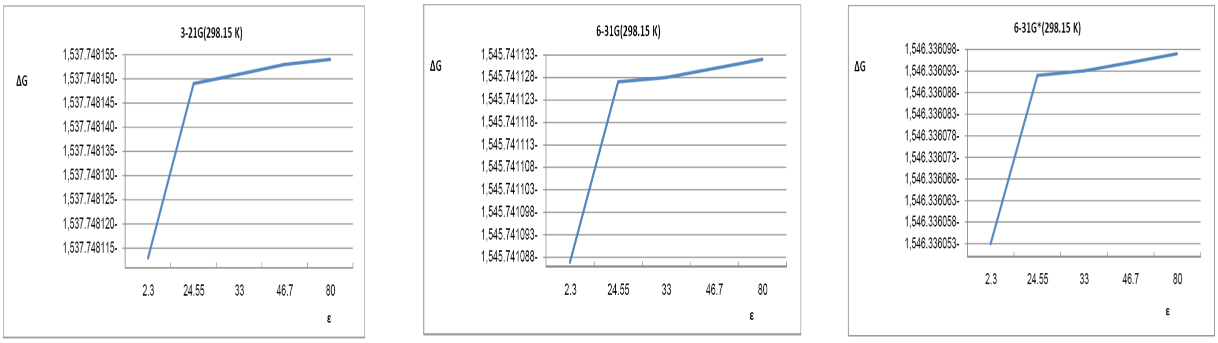

Fig. 5. Gibbs free energy changes versus dielectric constant in different solvents and temperature

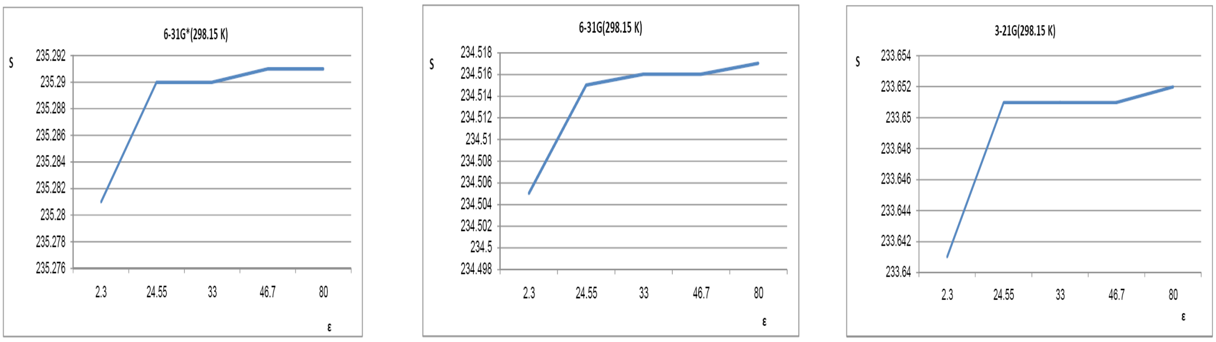

Fig. 6. Entropy changes versus dielectric constant in different solvents and temperature

such as water, DMSO, methanol, ethanol and benzene.

When solvent dielectric constant (Table 1) increases, the Gibbs free energy value of the interaction between solvent and solute molecules decreases. In fact, it moves toward negative values, and the system has more constancy. The Gibbs free energy with increasing temperature trends decreased energy levels, which contribute to the stability of the molecule. So we have the highest resistance for in 298 K (Fig. 5). System was more negative with increasing temperature and decreasing the amount of energy that reflects the stability of the molecule. The increase of solvent dielectric constant makes the entropy (Fig. 6) values of interaction between solvent and solute molecules move toward negative values. Other words, interaction between solvent and solute molecules is stronger, but interaction between solute molecules is weaker. As the temperature increases the entropy (disorder) is elevated as a result of irregularities are more atoms in a molecule.

Graph 6 shows that by increasing temperature, the value of reaction decreases. Then the most positive value of reaction is seen in 298 K, this is more stable. On the other hand, in Table 3, the change of ΔG reaction and reaction is considered in terms of solvent dielectric constant.

In Graph 5, increase of solvent dielectric constant will decrease the value of ΔG reaction, whereas the most negative value of ΔG reactions for water solvent. The water solvent is the best environment. In Graph 6, by increasing the solvent dielectric constant in temperatures between 298 K and 315 K, reaction values decrease. So Graph 6 proves that the value of reaction in 298 K has the most positive value. Then 298 K is best.

CONCLUSIONS

In this investigation, we have studied the effects of various solvents and temperatures on interaction of beta carotene. The calculations were performed by Hyperchem Program (Hyperchem, 2000), and then the ab initio computations were done with HF functional, using STO-3G basis set and the Gaussian 09. The attained result that water is the best solvent is completely logical if the anticancer substance. It has the most negative Gibbs free energy. We can say that by increasing the molecule dipole moment, the interaction between molecules of solvent and solute will increase. Thus, interaction of solute molecules will decrease, which affects Gibbs free energy and entropy.

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