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Computational study of chemical properties of Captopril drug and the connected form to Fullerene (C_{60}) as a medicine nano carrier

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ABSTRACT

In this research at the first, captopril drug (CA) and its fullerene connected form (FCA) were optimized. Natural Bond Orbital (NBO) calculations for these compounds were carried out at the B3LYP/6-31G quantum chemistry level, in the gas phase and the liquid phase. These calculations can be performed at different accuracy levels depending on the aim of the theoretical study [1]. For instance, Density Functional Theory (DFT) can be used to calculate an accurate electronic structure, HOMO and LUMO energies, Mulliken charge of atoms, energetic_orbital levels, chemical hardness, chemical potential and electrophilicity of systems, and finally chemical, physical, biological, pharmacological and industrial of fullerene and fullerene derivatives [4–7]. Theoretical calculations such as NBO are very important to understand the pathways of electron transfer in assemblies. Consequently, the obtained results showed that energy orbital levels decreased considerably by linking structure of Captopril to structure of fullerene C_{60}. In the study some other characteristics such as chemical potential, chemical hardness, electrophilicity in these structures; it was found that they changed considerably. These changes show dependency of the results, on power of electron affinity of C_{60}. In another part, the valence electrons populations for carbons, nitrogen, oxygens and hydrogens atoms in similar position for FCA and CA were compared. Finally the data were compared and discussed.

Keywords: DFT; Electrophilicity; Chemical hardness; Chemical potential; Captopril

INTRODUCTION

In the recent years, many studies have been done on the structure of fullerene and their derivatives form to drug as medicine nano-carrier compounds. The theoretical study of the electronic structure has used to predict physic-chemical properties of donor -acceptor systems. Captopril is an oral drug and a member of a class of drugs called angiotensin converting enzyme (ACE) inhibitors. ACE inhibitors are used for treating high blood pressure, heart failure, and for preventing kidney failure due to high blood pressure and diabetes. Other ACE inhibitors include enalapril (Vasotec), quinapril (Accupril), ramipril (Altace), fosinopril (Monopril), benazepril (Lotensin), lisinopril (Zestril, Prinivil), moexipril (Univasc) and trandolapril (Mavik). Angiotensin II is a very potent chemical that causes the muscles surrounding blood vessels to contract, thereby narrowing the vessels. The

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narrowing of the vessels increases the pressure within the vessels causing high blood pressure (hypertension). Angiotensin II is formed from angiotensin I in the blood by the enzyme angiotensin converting enzyme or ACE. ACE inhibitors are medications that slow (inhibit) the activity of the enzyme ACE and decrease the production of angiotensin II. As a result, blood vessels enlarge or dilate, and blood pressure is reduced. The lower blood pressure makes it easier for the heart to pump blood and can improve the function of a failing heart. In addition, progression of the blood vessel disease within the kidney caused by high blood pressure or diabetes is slowed. The FDA approved captopril in April 1981. Captopril is used alone or in combination with other drugs for the treatment of high blood pressure and heart failure [1-20]. Fullerene is one of the other artificial forms of carbon element which is made by heating graphite. Due to its similarity to ball, it is called buckyball. Fullerene has different types and can be as spherical, elliptical and cylindrical. Kroto and Curl are known as discoverers of fullerene. In 1990, Wolfgang Kratschmer and Donald Huffman et al described the first practical method C_{60} [21]. This material was prepared for the first time with formula C_{60} in 1985 by Richard Smalley, Robert Curl, James Heath, Sean O'Brien, and Harold Kroto at Rice University of Texas State [22]. Low solubility of the fullerenes in fluids limits application of these materials as medicinal effective material. But hydrophobic size, three-dimensionality and electron properties cause its use as medicine. For example, their spherical form causes ability and position of fullerene molecules in enzymes or cells hydrophobic solutions. This action causes interesting medicinal properties which increases the rate of such characters by adding nano properties of these structures [23-25]. The electrophilicity concept was expressed for the first time in 1999 by Parr and *et all* [26]. The electrophilicity and the maximum amount of electronic charge indices are related to electronic charge, when the system acquires an additional or removal electronic charge. The maximum amount of electronic charge index, ΔN_{max}, describes the charge capacity of the molecule that the electrophone system may accept, it is given by (1) equation [26]. A positive value of ΔN_{max} index (a.u.) for a system indicates, that acts as an electron acceptor, whereas a negative value of ΔN_{max} index indicates that acts as an electron donor. The electrophilicity Index, ω, in atomic units is a measure of electrophilic power of a molecule it is given by (2) equation. When two molecules react with each other, one molecule behaves as a nucleophile, whereas the other one acts as an electrophone. A higher electrophilicity index shows higher electrophilic power of a molecule. So the quantity of ω describes the propensity of the system to acquire additional electronic charge from the environment, which is described by (1) equation [26]. In equations (3) and (4), μ and η are the chemical potential and the chemical hardness respectively. Both quantities may be approximated based on the energies of frontier molecular orbital's (E_{HOMO} and E_{LUMO}) as (equations 3 and 4). The low values of μ and η, characterize a good electrophone species [26].

$$\Delta N_{max}=\frac{-\mu}{\eta} \quad (1)$$

$$\omega=\frac{-\mu^2}{2\eta} \quad (2)$$

$$\mu=\frac{1}{2(E_{HOMO}+E_{LUMO})} \quad (3)$$

$$\eta=\frac{(E_{HOMO}+E_{LUMO})}{2} \quad (4)$$

COMPUTATIONAL METHODS

The structures of Captopril (CA) and nano fullerene Captopril (FCA) were designed primarily using of Gauss View 3.1 and nanotube modeler 1.3.0.3 soft wares (Fig.1). The optimization and natural bond orbital (NBO) calculation were done with water solvents with Polarized Continuum Model (PCM) and then in the gas phase. Finally obtained results were compared with each other. The optimization and NBO calculations of all systems are done by density functional theory (DFT) using B3LYP method and the standard 6-31G basis set, by Gaussian W98 suit of programs. Total computations were done under 1 atmosphere pressure and 298 Kelvin temperature [27-28].

RESULTS AND DISCUSSION

On the basis of these results, some separate issues such as energetic characters, electrophilicity, chemical potential, chemical hardness values were discussed of which results in this section.

Dipole moment

The results show that when structure of Captopril is linked to nano fullerene, the dipole moment in FCA increased. This parameter is an effective factor which has direct relationship with solubility and the more amount of this parameter, causes the more solubility inside the polar solvent (Table 1).

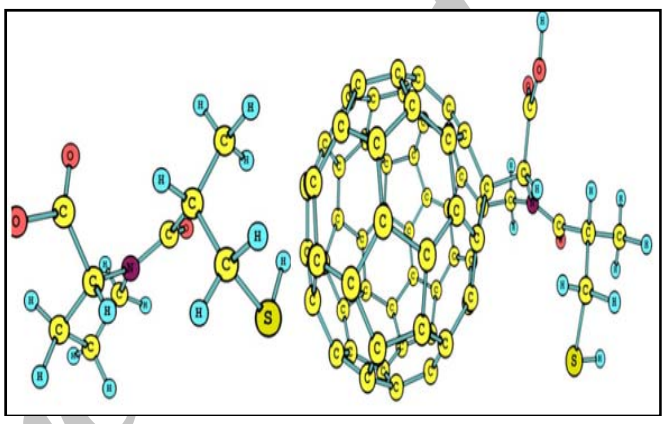

Fig. 1. Show of CA and FCA obtained by B3LYP/6-31G level of theory.

Table 1. Calculated E HOMO and E LUMO (a.u.), chemical hardness, η, chemical potential, μ, electrophilicity index, ω, and the maximum amount of electronic charge index, ΔN_{max}, in atomic units and dipole moment (Debye) for CA and FCA obtained by B3LYP/6-31G level of theory

	Gas Phase		Liquid Phase	
	CA	**FCA**	**CA**	**FCA**
HOMO (a.u.)	-0.23132	-0.2223	-0.24341	-0.2165
LUMO (a.u.)	-0.02942	-0.1244	-0.0249	-0.1187
HLG (a.u.)	0.2019	0.0979	0.2185	0.09778
Hardness (a.u.)	0.10095	0.04896	0.1093	0.04889
Chemical Potential (a.u.)	-0.13037	-0.17337	-0.1342	-0.1675
Electrophilicity (a.u.)	0.08418	0.3069	0.0824	0.2872
ΔNmax (a.u.)	1.2914	3.5406	1.2280	3.4277
Dipole moment (Debye)	4.1115	5.0674	6.0588	6.7763

HOMO and LUMO indices

The FCA has band gap less than CA. A small HOMO-LUMO Gap (HLG) in atomic units automatically means small excitation energies to the excited states. Therefore FCA is more conductive than CA (Table 1).

Chemical potential

In order to compare the obtained results, consider them. The results show that when structure of Captopril is linked to fullerene, the chemical potential (a.u.) of FCA decreased, in the gas and liquid phase (Table 1).

Chemical hardness

FCA has chemical hardness less than CA. A concise definition of chemical hardness (a.u.) offers that a hard molecule has a large HOMO-LUMO gap and a soft molecule has a small HOMO-LUMO gap, so FCA is softer than CA. Soft molecules with a small gap, will have their electron density changed more easily than a hard molecule. So FCA is more reactive than CA (Table 1).

Electrophilicity index

Electrophilicity value (a.u.) in FCA increased. The electrophilicity index is a measure of electrophilic power of a molecule. When two molecules react with each other, one molecule behaves as a nucleophile system, whereas the other one acts as an electrophone system. A higher electrophilicity index shows higher electrophilicity of a molecule. So FCA has higher electrophilicity than CA, therefore FCA is a more strong Lewis acid (Table 1).

Maximum amount of electronic charge index

As mentioned above, most electron charge which a system accepts can be calculated by ΔN_{max} parameter. The obtained results for this parameter were obtained like the previous parameters, For FCA it is increased. A positive value of ΔN_{max} indicates that charge flows to system, or our system acts as an electron acceptor, whereas a negative value of ΔN_{max} indicates that charge flows from system or our system acts as an electron donor. So FCA is an electron acceptor or a Lewis acid (Table 1).

Natural Charges and valence electrons

The result of valence electron population in atomic units, for carbons, nitrogen, oxygens and hydrogens atoms in similar position for FCA and CA show that generally in FCA valence electron population is lower than CA, so C_{60} has power of electron affinity (Table 2).

CONCLUSION

In this paper, the structural and electronic structures of CA and FCA have been investigated theoretically by performing DFT calculations at the B3LYP/6-31G level, in the gas phase and the liquid phase. The results show that FCA has band gap less than CA, also chemical hardness in FCA is lower than CA, so FCA with notice to electrophilicity and ΔN_{max} parameter, is more soft strong acid than CA. In terms of chemical reactivity we can conclude that soft molecules will be more reactive than hard molecules for unimolecular reaction such as isomerization and dissociation. This work can be useful for pharmaceutical researches because this action causes interesting medicinal properties.

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Table 2. Valance electron population in atomic units, for carbon, nitrogen, sulfur, oxygen and hydrogen atoms in similar position for FCA and CA obtained by B3LYP/6-31G level of theory in the gas phase.

	valance population (a.u.)	
Atoms	FCA	CA
C_{31}[a]=C_1[b]	4.03692	4.45532
C_{55}=C_2	4.06413	4.47863
C_{66}=C_8	3.18617	3.18955
C_{62}=C_4	4.12223	4.15626
C_{64}=C_6	4.23974	4.26219
C_{71}=C_{13}	3.28413	3.28588
C_{73}=C_{15}	4.34399	4.3386
C_{79}=C_{21}	4.55957	4.55488
C_{75}=C_{17}	4.69025	4.68886
S_{82}=S_{24}	6.07146	6.08576
N_{61}=N_3	5.45395	5.45605
H_{69}=H_{11}	0.48646	0.49051
H_{63}=H_5	0.70765	0.72467
H_{70}=H_{12}	0.70981	0.72317
H_{65}=H_7	0.72805	0.75603
H_{80}=H_{22}	0.73491	0.73728
H_{74}=H_{16}	0.73534	0.73491
H_{81}=H_{23}	0.73964	0.74415
H_{76}=H_{18}	0.74275	0.74614
H_{77}=H_{19}	0.74292	0.74033
H_{78}=H_{20}	0.76073	0.76388
H_{83}=H_{25}	0.84762	0.84865
O_{67}=O_9	6.55264	6.55276
O_{72}=O_{14}	6.58929	6.60562
O_{68}=O_{10}	6.7011	6.71086

[a]: left atom related to FCA [b]: right atom related to CA

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