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Adsorption of Citalopram on C60 Nano-cage as Anti-depression Drug Carriers

Saied Jamaladdin Emamjome Koohbanani, Sayed Ali Ahmadi*, Dadkhoda Ghazanfari, Enayatollah Sheikhhosseini

Department of Chemistry, Kerman Branch, Islamic Azad University, Kerman, Iran

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Abstract

In this study, we used the computational process by DFT with the B3LYP/6-311+G (d, p) quantum method to discover the reactivity properties and dope, and to determine the adsorption behavior of Citalopram on C60 (ih) as anti-depression drug carriers in the gas phase. We calculated chemical structural parameters such as dipole momentum (3.7193D) and electronic parameters (σ (6.45), μ (-2.70), ω (16.5), χ(2.70) and η(1.53)) which can determine the chemical reactivity of Citalopram. According to the calculated HOMO (-4.25eV) and LUMO (-1.15eV) energy value, Citalopram is a stable and chemical active compound and has chemical reactivity. It has six active sides, which lead to adsorb on C60 nano-cage as a drug carrier. This surface adsorption helps Citalopram transfer to biological systems much better.

Keywords: DFT, Bucky ball, Reactivity, Stability.

*__Corresponding author__: *Sayed Ali Ahmadi, Department of Chemistry, Kerman Branch, Islamic Azad University, Kerman, Iran. E-mail: ahmadi.iauk58@gmail.com, Tel.: +98 34 33201337, Fax: +98 34 33211405.*

Introduction

The availability of eight first-choice antidepressant agents for the treatment of major depression in Canada is prevalent. According to reports from epidemiological studies, in Ontario and five European countries, only 20% to 25% of the identified individuals experiencing a depressive episode which has received antidepressant therapy. In addition, more than 50% of patients with depression, who were followed up after 12 weeks of antidepressant treatment in family practice settings, discontinued the treatment. The availability of citalopram in Canada as an alternative antidepressant agent within the selective serotonin reuptake inhibitor (SSRI) class provides the clinicians with an additional choice in the pharmacological management of depression. The purpose of this review is to provide clinicians with the information to compare citalopram with existing antidepressant agents [1,2].

Nano-materials have been considered for application in optical devices, superconductors, fuel cells, catalysts, biosensors, drug, and gene delivery and so on. [3-6] Nano-materials as novel drug delivery systems have also been applied to improve the physicochemical and therapeutic effectiveness of the drugs [7-9]. Likewise, nanotechnology in pharmaceuticals and microbiology have showed promising applications to overcome the problem of antibiotic resistance [3, 10-12]. Over the past few years, researchers have evaluated various nano-sized antibacterial agents such as metal and metal oxide nanoparticles. Several types of metal and metal oxide nanoparticles such as silver (Ag), silver oxide (Ag_2O), titanium dioxide (TiO_2), zinc oxide (ZnO), gold (Au), calcium oxide (CaO), silica (Si), copper oxide (CuO), and magnesium oxide (MgO) have been known to show antimicrobial activity [13-19].

It has also been revealed that the size and surface area of carbon nano-materials are important parameters affecting their antibacterial activity; that is, increasing the nanoparticles' surface area by decreasing their size leads to improving their activity for interaction with bacteria [20, 21]. Bucky ball (C60) was applied as an absorbent [22] for some toxic and nontoxic chemical ingredients [23] in dies [24] and wastewater [25-28]. Density functional theory [29-33] and molecular dynamic calculation [34-36] were used for theoretical analysis in all fields of study [37], such as nano-cage [22]. In this study, the bucky ball (C60) was used as an absorbent of Citalopram in the gas phase by density functional theory with 6-311+G (d, p) basis set.

Experimental

The chemical quantum calculations were applied due to the Gaussian 03 [38] package that runs on the supercomputer. The full geometry optimization, electric field gradient, thermodynamic properties, electrical parameters were carried out by the density functional theory (DFT) with three-

parameter hybrid functional of B3LYP and the 6-311+g (d, p) basis set. Bucky ball C-C (C60 ih) was applied as an absorbent, and adsorption energy was calculated by the below formula:

$E_{ads}=E_{(B\text{-}Cit)}-(E_{\ Citalopram}+E_{buckyball})$

Result and discussion

In the previous studies, the results of calculations showed that the adoption of nano-cages with metallic atoms could modify their electrical properties, chemical activity, and reaction potential efficiently [39]. Therefore, B3LYP/6-311 + G (d, p) optimized all structures such as Citalopram, the bucky ball (C60, fullerene), and adopted Citalopram on the bucky ball. Figure 1 shows the optimized structure of Citalopram. There are six active sides in Citalopram: Two Ns, one O, one F, and two phenyl rings. These six places have different chemical and electrochemical positions in Citalopram. Figure 2 illustrates all the active positions in Citalopram. Density electron in each position has various effects of reacting on a chemical reaction. Two phenyl rings could improve the chemical behavior in the gas phase.

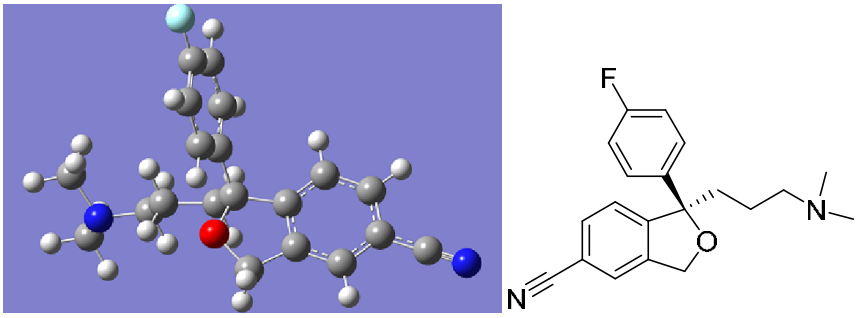

Figure 1. Optimized structure of Citalopram by B3LYP/6-311+G (d, p).

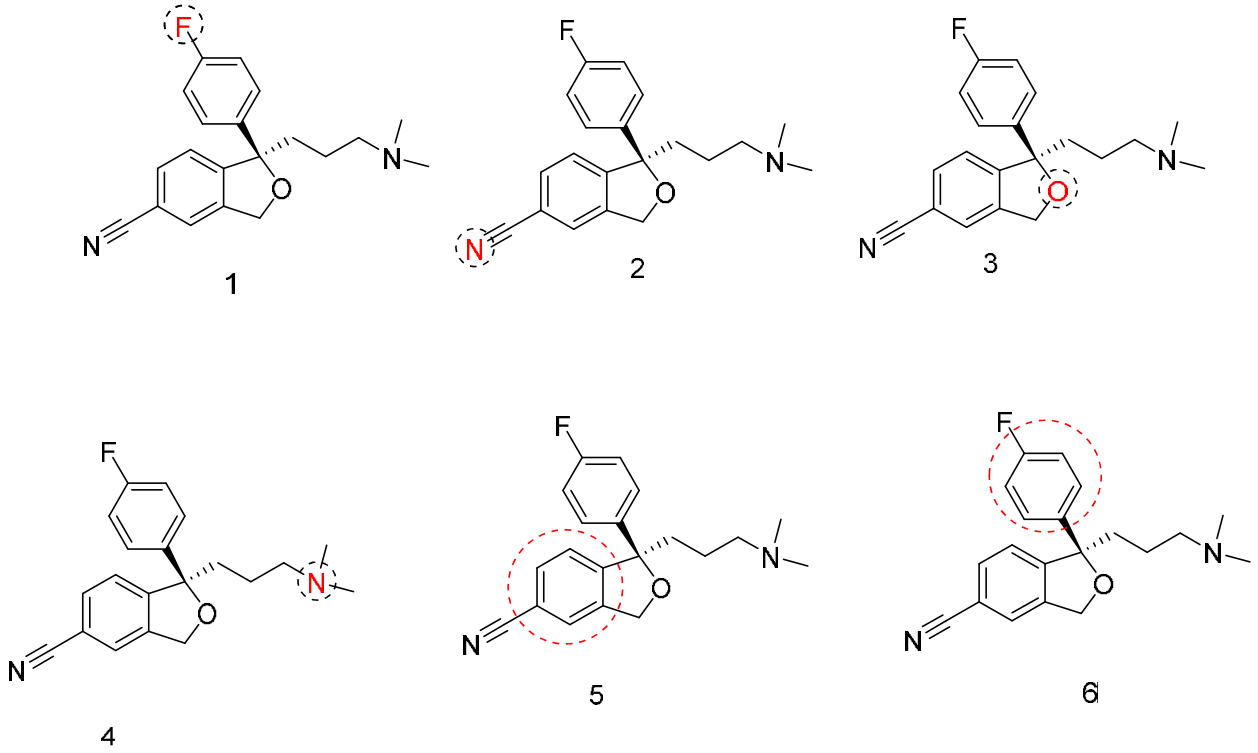

Figure 2. Different active places in Citalopram.

HOMO and LUMO energy are significant characters in chemical reactivity. The large amount of LUMO shows more electrons in the molecules. HOMO and LUMO energy can recognize and predict the strength and stability of chemical compounds. Based on the energies of these frontier orbitals, which are the nearby orbitals with various energy levels, the HOMO-LUMO band gap energy is where the most electron excitations can occur. When there is an extensive chemical aromatic system, in particular, small HOMO-LUMO band gaps cause π mobile electrons. Therefore, it is easy for the electron to jump to a higher level of energy that is close in energy. The higher mobility of π electrons in large conjugated π orbital systems resulted in the excellent distribution of the energy throughout the molecule, which makes stability. Hence, smaller HOMO-LUMO gaps correspond to better stability. This mobility of the π electrons further means that large aromatic systems (like graphene nanoribbons) have outstanding conductivity and make excellent semiconductors since their conduction band gap is small.

The movement of electrons is an electrical current. HOMO and LUMO are fascinating aspects of chemistry, which can provide a remarkable insight into the workings of reactions based on how orbitals interact to control the outcome of reactions. HOMO energy provides weak electrons to react in chemical reactions. According to the resulted amount of HOMO energy of Citalopram, it stated to participate in chemical reactions vigorously. It had electron-donating role in all chemical

reactions because of electronegative atoms (N, O, F), which are in the chemical structure of Citalopram. Table 1 shows data of Citalopram frontier (HOMO and LUMO) orbitals.

Table 1. Energy data and dipole momentum of Citalopram by B3LYP/6-311+G (d, p).

Citalopram	gas
Energy	-2782.35kJ
Dipole moment (Debye)	3.7193
HOMO	-4.25eV
LUMO	-1.15eV

The dipole momentum of chemical compound introduces polarity of compounds in reaction media. According to Table 1, the gas dipole momentum of Citalopram is 3.7193. It shows the polarity of Citalopram due to the electronegative atoms in the chemical structure of Citalopram (N atom).Citalopram has six active positions to adopt to C60 (Figure 3).

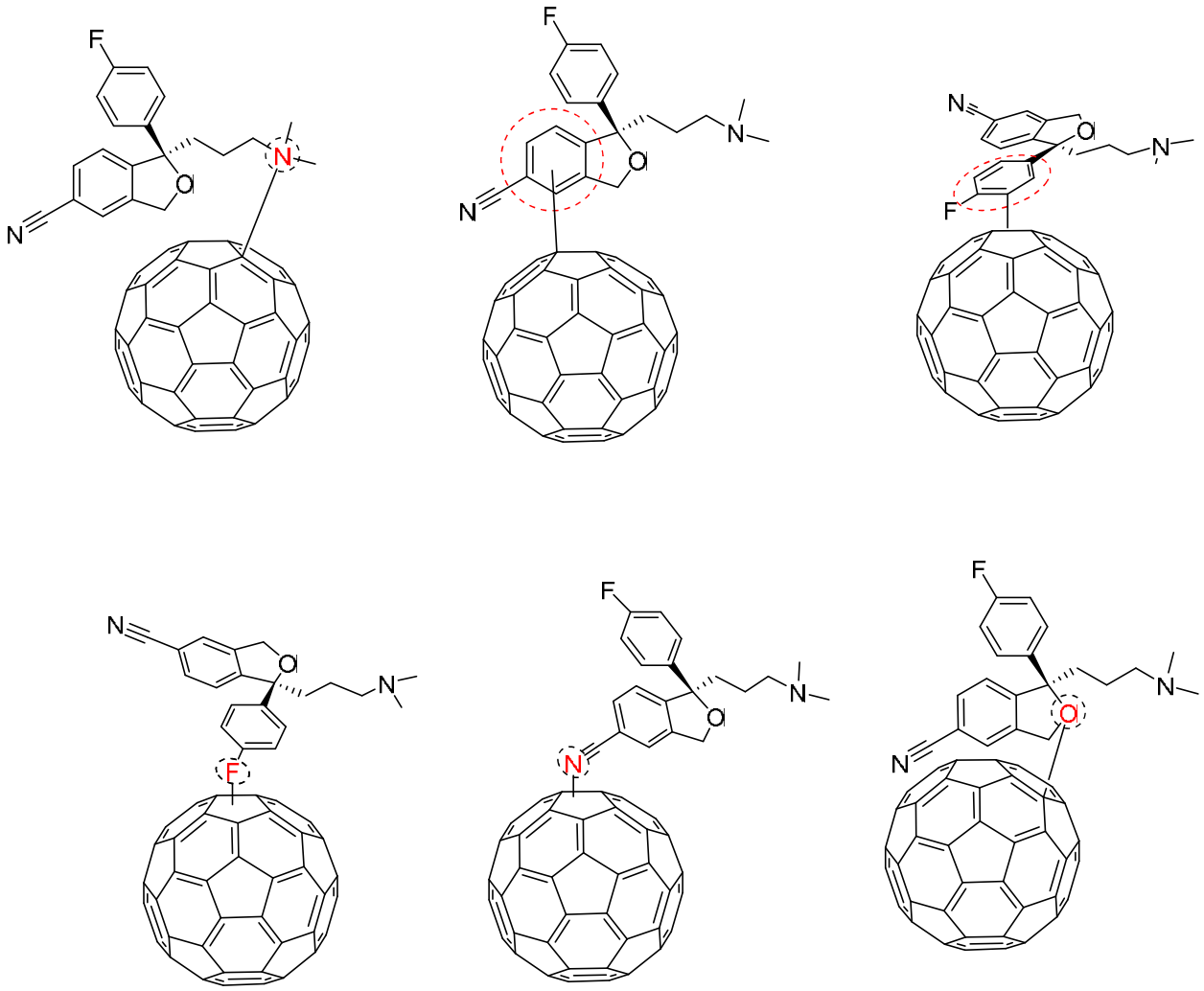

Figure 3. Citalopram -C60 complexes in different active sides (six different positions).

Citalopram has six active positions to adopt with C60 illustrated in Figure 3. C60 is (ih) symmetric system, which has the same situation to participate in chemical reactions. Each considered position makes no difference in reaction. Figure 4 shows the main and optimized structure of the bucky ball. Fullerene is a closed-cage nanoparticle, where the conjugation is extended through π-electrons. This structure is perhaps the main reason that fullerenes can absorb light and subsequently generate reactive oxygen species [40]. As soon as fullerene (C_{60}) is illuminated by photons, C_{60} will excite from the ground state to a highly short-lived (~1.3 ns) excited state. The excited state quickly decays to a lower triplet state with a longer lifetime (50–100 μs) [41].

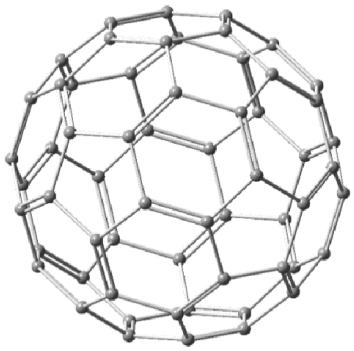

Figure 4. Optimized structure of C60(ih) by B3LYP/6-311+G(d, p) E(-738.33kJ).

Table 2. Electronic parameters of Citalopram in gas and water phase by B3LYP/6-311+G (d, p).

citalopram	IP (eV)	EA (eV)	μ (eV)	η (eV)	χ (eV)	σ (eV)	ω (eV)
gas	4.25	1.15	-2.70	1.55	2.70	6.45	16.5

Energy can be the capacity of doing work and heat supplement. Chemical potential energy is the saved energy in the chemical bonds. It is thermodynamically important and an applicable concept to many material sciences, such as chemistry, physics, biology, and chemical engineering. The thermodynamic parameters of a chemical material at a spatial pressure and temperature could be computed from the chemical potential. Under constant pressure, chemical and potential temperature can determine the stability of substances, chemical compounds, and solutions. Amount of chemical potential μ for Citalopram -2.70 in gas phase decided Citalopram is a stable chemical compound in gas phases. Negative energy shows hidden energy in the chemical bonds of Citalopram. The energy of an atom is defined as when the atom loses or gains energy through chemical reactions that cause the loss or gain of electrons.

A chemical reaction that releases energy is called an exothermic reaction, and a chemical reaction that absorbs energy is called an endothermic reaction. Since energy from an exothermic reaction is negative, it is given a negative sign; whereas, energy from an endothermic reaction is positive, so it has a positive sign. When an electron is added to a neutral atom (i.e., first electron affinity), energy is released; thus the first electron affinities are negative. However, more energy is required to add an electron to a negative ion (i.e., second electron affinity), which overwhelms any energy released from the electron attachment process; thereby second electron affinities are positive.

Citalopram has positive electron affinity energy (EA), which means it does not want to give electrons and wants to donate an electron. Reactivity parameters of a molecule, for example, electronegativity (χ), softness (σ), hardness (η), and electrophilicity index (ω), have been extracted from the theory of Koopman by DFT popular method. Electronegativity (χ) is a value of attracting the power of an atom or molecule achieved from HOMO and LUMO. η causes the stability and reactivity of a chemical molecule. σ illustrates the capacity acceptance electrons of chemical molecules.

Table 2 shows the reactivity parameters of Citalopram in the gas and water phase. Accordingly, it is recognized that Citalopram has high stability and reactivity in the chemical reactions. Adopting Citalopram occurred on C60. Table 3 demonstrates the energy of each complex in Figure 3. The energy of an electron in a single atom can be determines solely by the principal quantum number. However, the energy of an electron in multi-electron atoms depends on both on its principal quantum number (n) and its azimuthal quantum number. This difference in energy of various subshells residing in the same shell is mainly attributed to the mutual repulsion among the electrons in a multi-electron atom. In multi-electron atoms, there is repulsive force acting between various electrons apart from the attractive force between the nucleus and the electrons. Thus, the stability of an electron in a multi-electron atom is dependent on the total attractive interactions and the repulsive interactions.

The electron in an atom is only stable if the total attractive interaction is more than the total repulsive interaction. For bigger atoms, due to the presence of electrons in the inner shells, the electrons in the outer shell are deprived to experience the full positive charge of the nucleus. This effect is known as the shielding of the outer shell electrons from the nucleus by the inner shell electrons. The net positive charge experienced by the outer shell electrons is termed as the effective nuclear charge. The dipole momentum of each complex showed that all active sides could act in polar media as well. Relative adopting energy (Figure 5.) shows all active sides made stable structure in chemical media, and structure 5 is the most stable amount of all. Table 4 is comparative work of relative energy.

Table 3. Energy and dipole momentum in Citalopram-C60 complexes.

	1	2	3	4	5	6
E(kcal/mol)	-2154.214	-2851.206	-2504.380	-1706.693	-2265.033	-2035.439
μ(D)	1.8517	1.80	1.650	1.9874	1.2587	1.8154
ΔE(ads/kJ)	5527.019	8454.385	6997.716	3647.431	5992.4586	5028.164

Table 4. Comparative of other work on relative energy [42]

C60@Metronidazole	ΔE(ads/kcal/mol)
C60-N- Metronidazole	9.18
C60-O- Metronidazole	-0.25

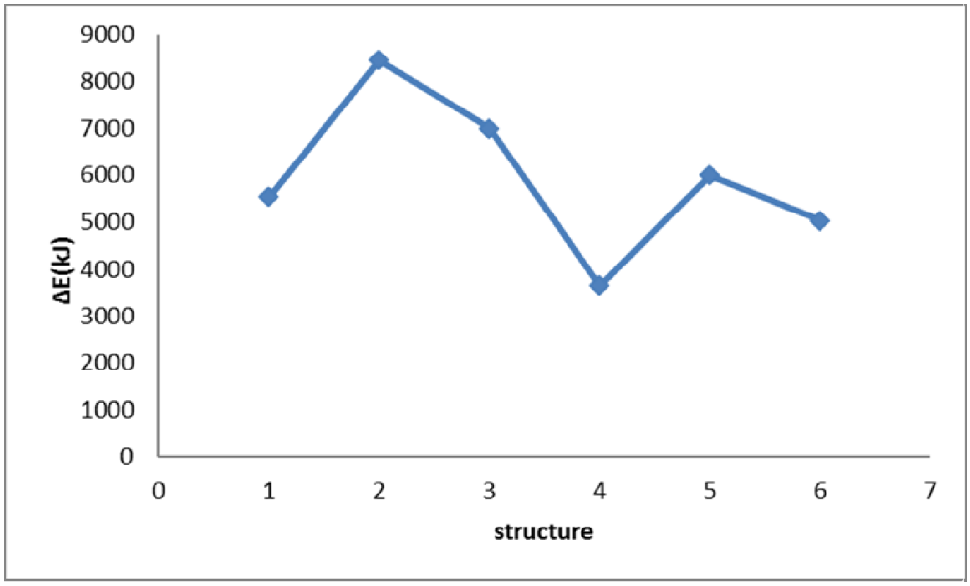

Figure 5. Diagram of relative energy

Conclusions

The present study considered the chemical reactivity of Citalopram and adopted it on the bucky ball (C60) applied by DFT B3LYP/6-311+G (d, p) in the gas phase. To have biological and medicinal applications, carbon nanostructures should be purified and functionalized. Their solubility should also be enhanced in physiological media. Finally, the application of carbon nano-composites composed of carbon nanostructures and metal nanoparticles could be considered a promising approach for disinfection purposes. However, further studies are necessary to understand the exact mechanisms of the antimicrobial activity of carbon nanostructures. The results of chemical structure, electronic parameters demonstrated that Citalopram was an active molecule, which could

adopt on C60 as a stable compound. Citalopram has six active sides, which are thermodynamically stable, and structure 2 is the most stable amount of all.

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