Study of DFT calculations on the interaction and molecular properties of the drug molecule carmustine with the surface of a carbon nanotube (8,0) from different directions

Majid Kia[1,*]- Narges Bakhshi[2]
[1] Department of Chemistry, Rasht Branch, Islamic Azad University, Rasht, Iran
[2] Department of Microbiology, Rasht Branch, Islamic Azad University, Rasht, Iran

ABSTRACT

This research involved drawing the structures and optimizing the drug molecule carmustine and a single-walled carbon nanotube (8,0) using Gaussian09, GaussView, and Nanotube Modeler software. By employing Density Functional Theory (DFT) and the 6-31G basis set, we examined the interaction of the drug molecule carmustine with the surface of the carbon nanotube from various angles.
Additionally, we calculated physical properties such as ionization potential, chemical potential, electron affinity, hardness, softness, and the gap between the Highest Occupied Molecular Orbital (HOMO) and Lowest Unoccupied Molecular Orbital (LUMO) of the drug molecule both before and after placement on the nanotubes. The results indicate that the drug molecule shows the highest absorption and interaction with the carbon nanotube surface when approached from the oxygen side.

Keywords: Gaussian, DFT, Carbon Nanotube, Carmustine, molecular properties

1. *INTRODUCTION*

Carmustine is used as an alkylating agent to treat various types of brain cancer, including glioma, glioblastoma multiforme, medulloblastoma, astrocytoma, multiple myeloma, and lymphoma (both Hodgkin's and non-Hodgkin's). It is also used as part of a chemotherapeutic protocol in preparation for hematological stem cell transplantation, a type of bone marrow transplant, in order to reduce the white blood cell count in the recipient.Carbon nanotubes (CNTs) have exceptional electrical conductivity, heat conductivity, and mechanical properties. They are considered the best electron field emitters available. CNTs are polymers of pure carbon that can be reacted and manipulated using the well-known and rich chemistry of carbon.
There has been significant practical interest in the conductivity of CNTs. CNTs with specific combinations of structural parameters (N and M) indicating the amount of twist in the nanotube can be highly conducting, making them metallic. Their conductivity is influenced by their chirality (degree of twist) and diameter. CNTs can exhibit either metallic or semi-conducting behavior electrically.
Carbon nanotubes are remarkable objects with the potential to revolutionize the technology world. Their fascinating physical, optical, and electrical properties make them a promising material for future research. This research primarily focuses on the physical properties of CNTs and provides an overview of factors that affect these properties, such as structural differences, purity, tube diameter, and density.
In the current research, our main goal is to theoretically study the absorption of drug molecules on the surface of carbon nanotubes. Therefore, theoretical calculations were performed using the DFT method and 6-31g basis set. We hope that the results presented could provide improved conditions for the use of nanostructures, particularly carbon nanotubes, as drug carriers.[1] to [3]

2. *Methodology*

In this research, the carmustine drug molecule and carbon nanotube were drawn using GaussView and Nanotube Modeler software, respectively. They were then optimized using the Density Functional Theory (DFT) method and 6-31g basis set in the Gaussian09 program. Next, the optimized drug molecule was positioned near the surface of the carbon nanotube from various directions, and the binding energies (BE) were calculated using the following equation:

$BE=E_{CNT\text{-}DRUG} - (E_{CNT} + E_{DRUG})$ (1)

E_{CNT} and E_{DRUG} represent the electronic energies of a carbon nanotube (8,8) and the drug molecule carmustine, respectively. Additionally, $E_{CNT\text{-}DRUG}$ is associated with the total electronic energy of nanotubes loaded with the drug molecule carmustine after full geometric optimization. The quantum molecular descriptors for the nanotubes were determined as follows:

$\mu = -(I + A)/2$ (2)
$\chi = -\mu$ (3)
$\eta = (I - A)/2$ (4)
$S = 1/2\eta$ (5)
$\omega = (\mu^2/2\eta)$ (6)
$\Delta N_{max} = -\mu/\eta$ (7)

Where I ($-E_{HOMO}$) represents the energy of the Fermi level and A ($-E_{LUMO}$) is the initial value of the conduction band. The electronegativity (χ) is calculated as the negative of the chemical potential (μ), expressed as: $\chi=-\mu$. Furthermore, hardness (η) can be estimated using Koopmans' theorem. I ($-E_{HOMO}$) stands for the ionization potential, and A ($-E_{LUMO}$) represents the electron affinity of the molecule. The maximum amount of electronic charge, ΔN_{max}, that the electronic system can accept is determined by Eq. (7) [4]and [7] to [11].

3. *Results and discussion*

The optimized structures of the anticancer drug molecule, zigzag carbon nanotube (8,0), and the structures in which the carmustine drug molecule approaches the surface of the nanotube through oxygen and chlorine are presented in Figures 1 and 2.

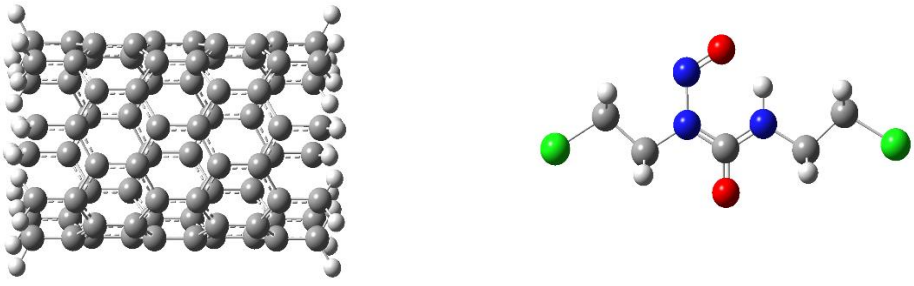


Fig. 1. *Optimized geometrical parameters of CNT(8,0) and Carmustine*

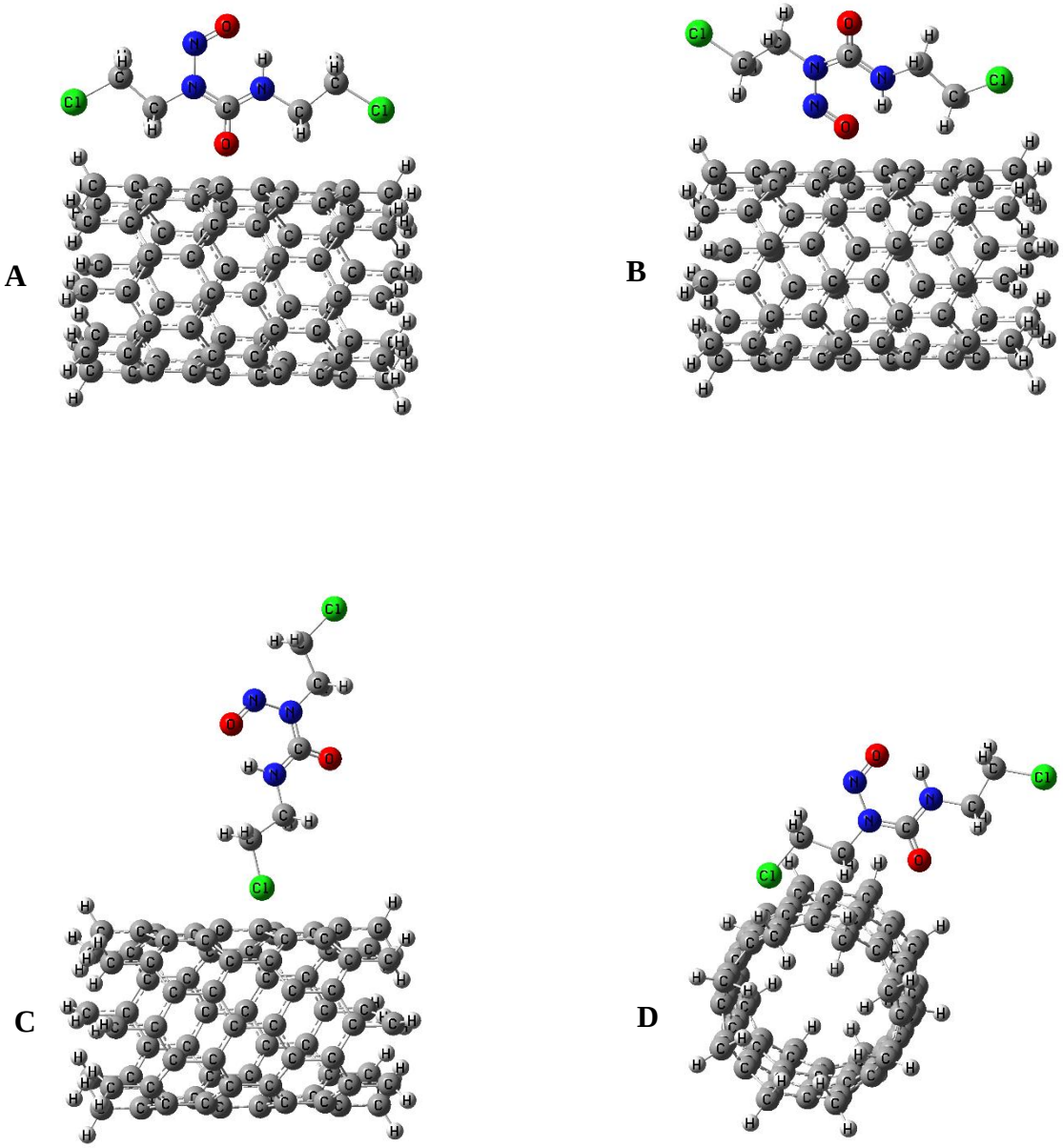


Fig. 2. *Optimized geometrical parameters of Carmustine on the surfaces of CNT(8,0) from the side of chlorine and oxygen atoms*

Table 1. *E_{HOMO} and E_{LUMO}, bond gap (Eg), adsorption energy (E_{ad}), energy of Fermi level (E_F), chemical potential (μ),* electron affinity (A), *hardness (η), softness (S), ΔN_{max}, and electrophilicity (χ) of carmustin adsorbed on the CNT(8,0). The parameters are in units of eV.*

property	carmustine	CNT(8,0)	CNT-DRUGO1(A)	CNT-DRUGO2(B)	CNT-DRUGCl1(C)	CNT-DRUGCl2(D)
E_{HOMO}	-6.98	-3.30	-3.22	-3.57	-3.28	-3.18
E_{LUMO}	-2.82	-2.90	-2.86	-3.16	-3.02	-2.84
E_{gap}	4.16	040	0.36	0.41	0.26	0.34
E_{ad}	-	-	-183.73	-184.53	-179.33	-175.53
E_F	-4.90	-3.10	-3.04	-3.36	-3.15	-3.01
$I=-E_{HOMO}$	6.98	3.30	3.22	3.57	3.28	3.18
$A=-E_{LUMO}$	2.82	2.90	2.86	3.16	3.02	2.84
$\eta = (I - A)/2$	2.08	0.20	0.18	0.20	0.13	0.17
$\mu = -(I + A)/2$	-4.90	-3.10	-3.04	-3.36	-3.15	-3.01
$S = 1/2\eta$	1.04	0.10	0.09	0.10	0.06	0.08
$\omega = (\mu^2/2\eta)$	5.77	24.02	25.67	27.62	38.16	26.65
$\Delta N_{max} = -\mu/\eta$	2.35	15.50	16.89	16.41	24.23	17.70

The amount of absorption depends on the chemical potential. The more negative the numerical value of the chemical potential, the greater the absorption. Therefore, based on the values obtained for the chemical potential, it can be concluded that the absorption rate of the carmustine drug molecule on the carbon nanotube surface is higher in structure B (-3.36 eV).

Additionally, the interaction energies of branches A, B, C, and D are equal to -183.73, -184.53, -179.33, and -175.53 electron volts, respectively. Therefore, the amount of interaction of the carmustine drug molecule is higher due to the more negative interaction energy in structure B. This result is in perfect agreement with the absorption of structure B. It can be said that the most interaction and absorption of the drug molecule occur in structure B and from the side of oxygen.

HOMO (Highest Occupied Molecular Orbital) and LUMO (Lowest Unoccupied Molecular Orbital) are molecular orbitals. They are very important electronic parameters for chemists and physicists. The LUMO is referred to as the innermost orbital containing available locations to accept electrons [5].

The eigenvalues of the LUMO-HOMO energy gap reflect the chemical activity of the molecule [6].The difference between the HOMO and LUMO molecular orbitals indicates the energy gap (E_{gap}). The higher the gap energy, the less energy the electron transfer from HOMO to LUMO requires, making electron transfer easier and increasing electrical conductivity.

The results obtained show that when the carmustine drug molecule approaches the surface of the carbon nanotube, the gap energy of the drug molecule decreases significantly. In structures a, b, and c, there is a decrease in gap energy, while in structure d, the gap energy remains almost constant.

According to the results, structure C has the lowest gap energy (0.26 eV) and the highest electrical conductivity, while structure B has the highest gap energy (0.41 eV) and the lowest electrical conductivity.

The density of states (DOS) of a material gives a measure of the number of energy states available in the system that electrons are allowed to occupy. DOS is an essential quantity to predict a material's conductivity. Calculating the density of states for small structures shows that the distribution of electrons changes as dimensionality is reduced.

The density diagram shows the interaction mode of the carmustine drug molecule with CNT(8,0) in structures A, B, C, and D in Figure 3. In the graph of the state density function, the boundary distance between virtual orbitals (red line) and occupied orbitals (green line) indicates the energy gap. This reveals that the lowest bandgap is associated with structure C, while the highest energy gap is linked to structure B.

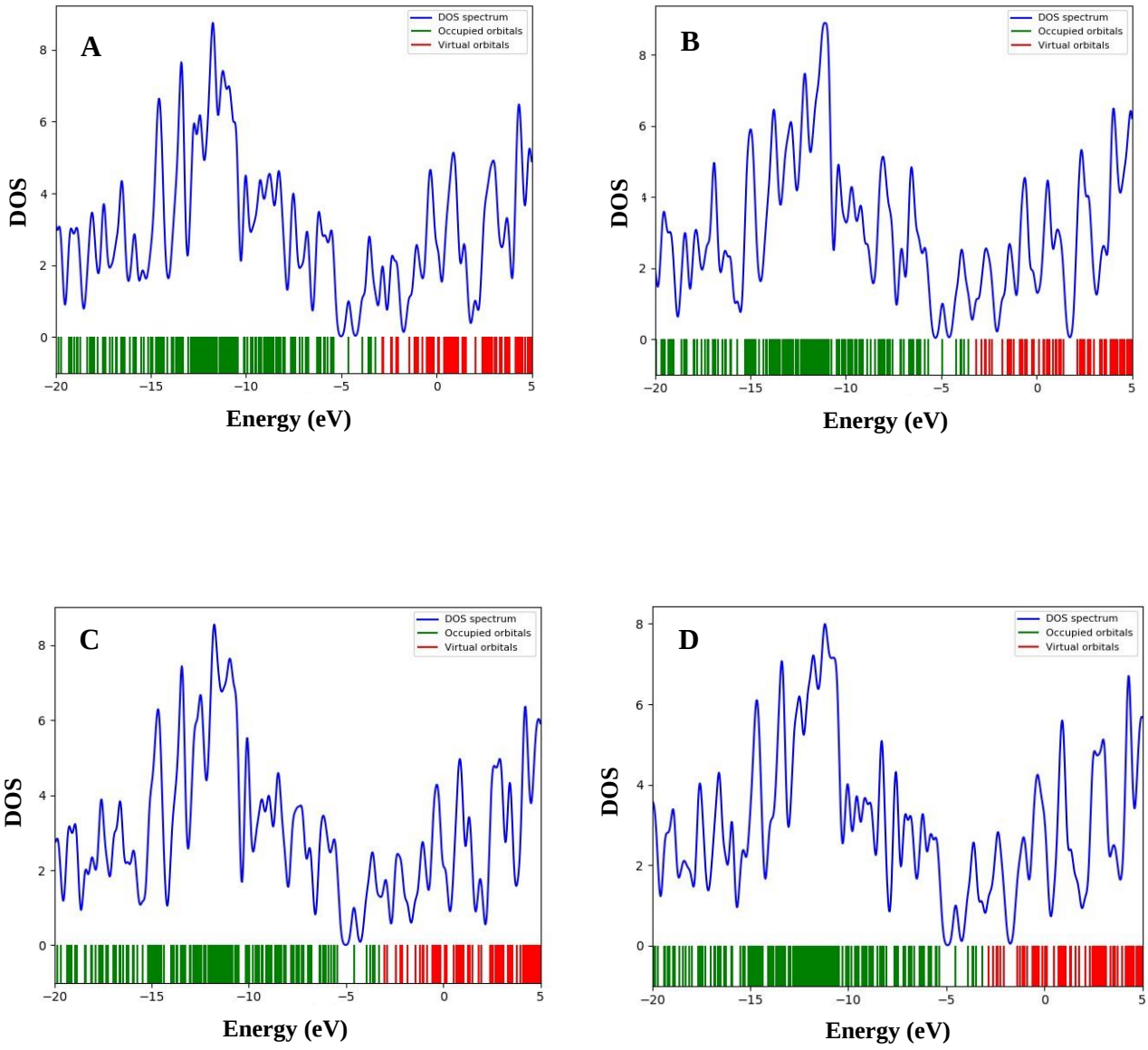
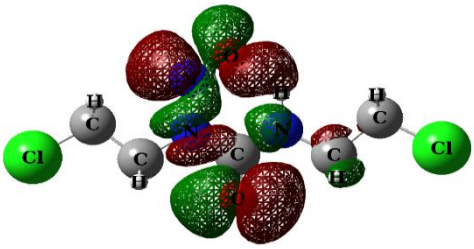
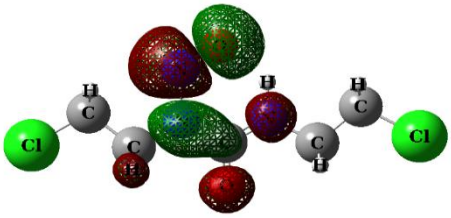


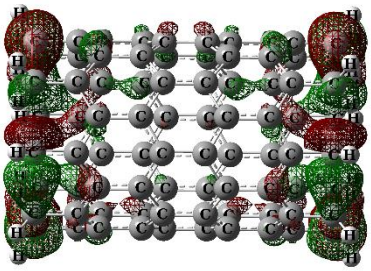
Fig. 3. *Calculated density of state (DOS) plots for carmustine adsorbed on the CNT(8,0)*



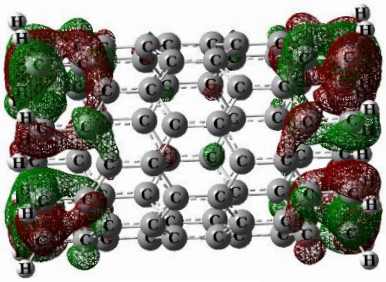
HOMO



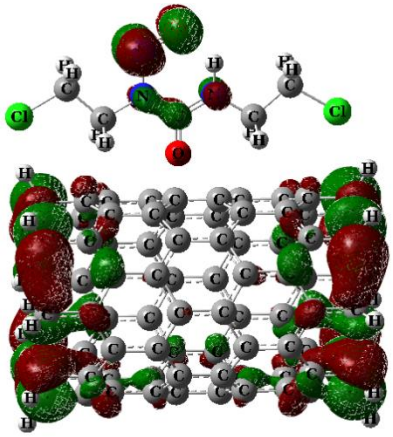
LUMO



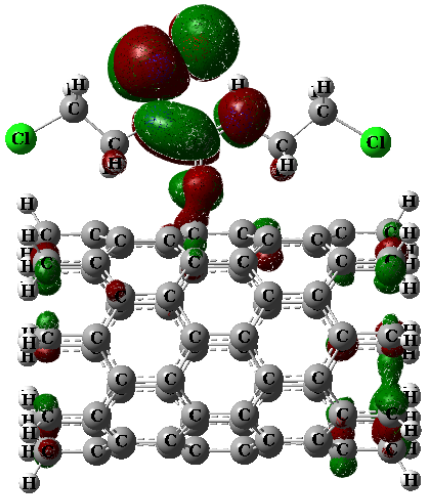
HOMO



LUMO



HOMO A



LUMO A

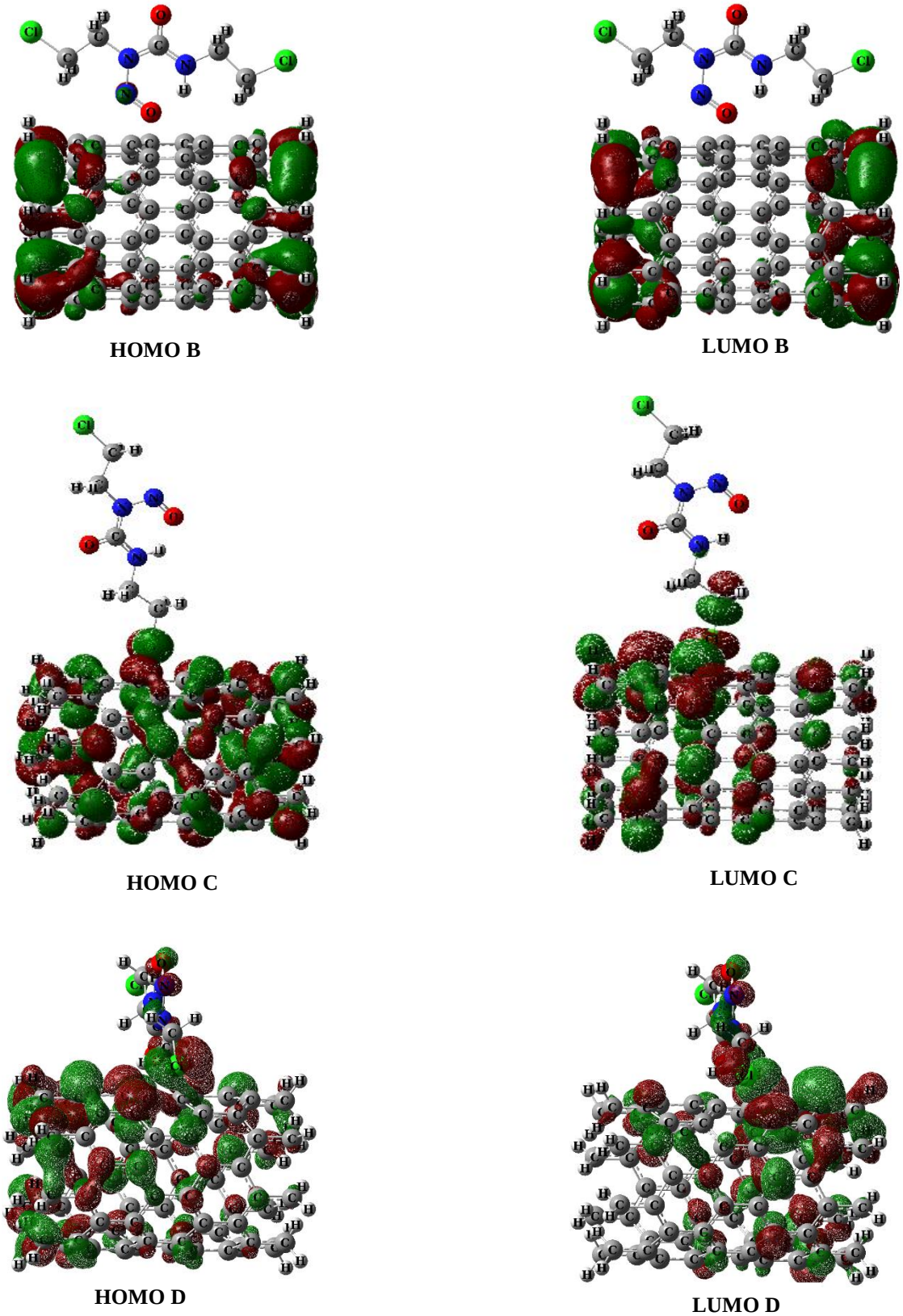


Fig. 4. *The surfaces of HOMO and LUMO of carmustine,CNT(8,0) and carmustine-adsorbed (8,0) SWCNTs.*

In the drug molecule carmustine, the concentration of the HOMO and LUMO molecular orbitals is located in the center of the molecule and on the oxygen and nitrogen atoms. In CNT(8,0), however, these orbitals are found at the ends of the nanotubes and on the terminal carbon atoms.
In structure A, mostly HOMO molecular orbitals are observed on oxygen and nitrogen atoms away from the nanotube, as well as at both ends of the nanotube. LUMO molecular orbitals are only present in the carmustine drug molecule and around oxygen and nitrogen atoms. Therefore, it can be concluded that in structure A, electron transfer occurs from the nanotube to the carmustine molecule.
In structure B, the concentration of HOMO and LUMO molecular orbitals is on the carbon atoms at both ends of the nanotube. In structure C, the dispersion of HOMO molecular orbitals is mainly around the chlorine atom near the nanotube and throughout the nanotube. However, the density of LUMO molecular orbitals on the chlorine atom of the carmustine molecule is close to the nanotube and on the same side of the nanotube.
Additionally, in structure D, the HOMO molecular orbitals are located on the chlorine atom of the carmustine molecule, and in the nanotube, the HOMO and LUMO orbitals are mainly distributed on the carbon atoms close to the drug molecule but on the opposite side of the nanotube.
The hardness index for CNT(8,0) is 0.2 eV. After the carmustine molecule approaches its surface in nanostructures A, B, C, and D, the hardness index becomes 0.18, 0.20, 0.13, and 0.17, respectively. It is evident that the hardness index decreases in nanostructures A, C, and D, while remaining constant in B. A decrease in the hardness index signifies a decrease in stability and an increase in reactivity. Therefore, it can be inferred that nanostructure C is the least stable and most reactive among the nanostructures.
Furthermore, the ionization potential and electron affinity *of nanostructure B are 3.57 and 3.16 eV, respectively, which are the highest among the nanostructures. This indicates that nanostructure B has the highest resistance to electron loss and the greatest tendency to absorb electrons.*

REFERENCES

[1] *Y-H. Li, T-H. Hung, C-W. Chen, Carbon 47 (2009) 850.*
[2] *N. Saikia, R.C. Deka, Chem. Phys. Lett. 500 (2010) 65.*
[3] *M.K. Shukla, M. Dubey, E. Zakar, R. Namburu, J. Leszczynski, Chem. Phys. Lett. 496 (2010) 128.*
[4] *A. Soltani, M.R. Taghartapeh, H. Mighani, A.A. Pahlevani, R. Mashkoor, Appl. Surf. Sci. 259 (2012) 637.*
[5] *Sertbakan, T.R. (2017) Structure, Spectroscopic and Quantum Chemical Investigations of 4-Amino-2-Methyl-8-(Trifluoromethyl) Quinoline. Celal Bayar University Journal of Science, 13, 851-861.*
[6] *Suresh, D.M., Amalanathan, M., Sebastian, S., Sajan, D., Joe, I.H., Jothy, V.B. and Nemec, I. (2013) Vibrational Spectral Investigation and Natural Bond Orbital Analysis of Pharmaceutical Compound 7-Amino-2,4-Dimethylquinolinium formate—DFT Approach. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 115, 595-602.*
[7] *R. G. Parr, L. V. Szentpaly, S. Liu. J. Am. Chem. Soc. 121(1999) 1922-1924.*
[8] *J. C. Phillips, Phys. Rev. 123 (1961) 420.*
[9] *T. Koopmans, Physica1 (2006) 104.*
[10] *K. K. Hazarika, N.C. Baruah, R. C. Deka. Struct. Chem. 20 (2009) 1079-1085.*
[11] *X. M. Li, W. Q. Tian, X. R. Huang, C. C. Sun, L. Jiang, J. Mol. Stru. (THEOCHEM) 901 (2009) 103- 109.*