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Adsorption of Melphalan on the Surface of Single-Walled Carbon Nanotube: A DFT Study

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ABSTRACT: In this study, adsorption of melphalan on the surface of single walled carbon nanotube was studied computationally. For this purpose, the structures of carbon nanotube, melphalan and the derived products from the interaction of melphalan with carbon nanotube at two different configurations were optimized geometrically. Then, IR and frontier molecular orbital calculations were implemented on them in the temperature range of 298-398 K at 10˚ intervals. The obtained thermodynamic parameters including Gibbs free energy changes (ΔG_f) and formation enthalpy alterations (ΔH_f) have revealed that the adsorption of melphalan is exothermic, spontaneous, one-sided and experimentally feasible at the both evaluated configurations. The influence of temperature on the thermodynamic factors of the desired process was also inspected and the results indicate that 298.15 K is the best temperature for the carbon nanotube substitution on melphalan. The calculated specific heat capacity values have shown that the sensitivity of the produced carbon nanotube- melphalan derivatives to the heat and shock have declined significantly. Some HOMO-LUMO related parameters such as energy gap, electrophilicity, chemical hardness, maximum transferred charge index (ΔN_{max}) and chemical potential were also calculated and discussed in details.

Keywords: *Adsorption, Carbon nanotube, Density functional theory, Drug delivery, Fronier molecular orbitals, Melphalan, Thermochemistry*

INTRODUCTION

Melphalan is a chemotherapy medication that is used for the treatment of multiple myeloma, ovarian cancer, AL amyloidosis, and occasionally malignant melanoma. However, it is associated with many different adverse effects like nausea, hair loss, bone marrow suppression; sever rash, itching and allergic reactions. Therefore, finding a nanocarrier for this medicine for its delivery to the target tumour tissue is very important in order to decreasing the drug side effects and increasing its efficiency [1-4]. Moreover, single-walled carbon nanotube (SWCNT) is one of the allotropes of carbon. Indeed, it is a like graphene nanosheet that became cylindrical. SWCNT has several special properties that make it an ideal nanocarrier in the field of drug delivery such as high specific surface area, low density, high electrical and thermal conductivity, and excellent robustness. Owing to the aforementioned special traits

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SWCNTs have been applied in different traits including supercapacitors, electrochemical sensors, nanofiltration, adsorption, microextraction and drug delivery. In this respect, the performance of SWCNT as a nanocarrier for the delivery of melphalan was investigated by DFT computations for the first time in this research [5].

COMPUTATIONAL DETAILS

At the outset, the structures of melphalan, SWCNT and their derived products at two various configurations were designed by nanotube modeler 1.3.0.3 and Gauss View Softwares. Afterward, the designed structures were optimized geometrically. In the next step, IR and frontier molecular orbital calculations were implemented on them in the temperature range of 298-398 K at 10˚ intervals by spartan software. The computations were done in the atmospheric pressure and gaseous phase [6-8]. Density functional theory method and B3LYP/631G(d) basis set were chosen for the calculations because, in our former studies, this method and basis set had produced results that were in an admissible accordance with the experimental findings [9-13]. The evaluated reaction is as follows:

$$\text{Melphalan} + \text{SWCNT} \rightarrow \text{Melphalan} - \text{SWCNT} \qquad (1)$$

RESULTS AND DISCUSSION

In order to find the most stable configuration, melphalan interaction with SWCNT was scrutinized at 2 dif-

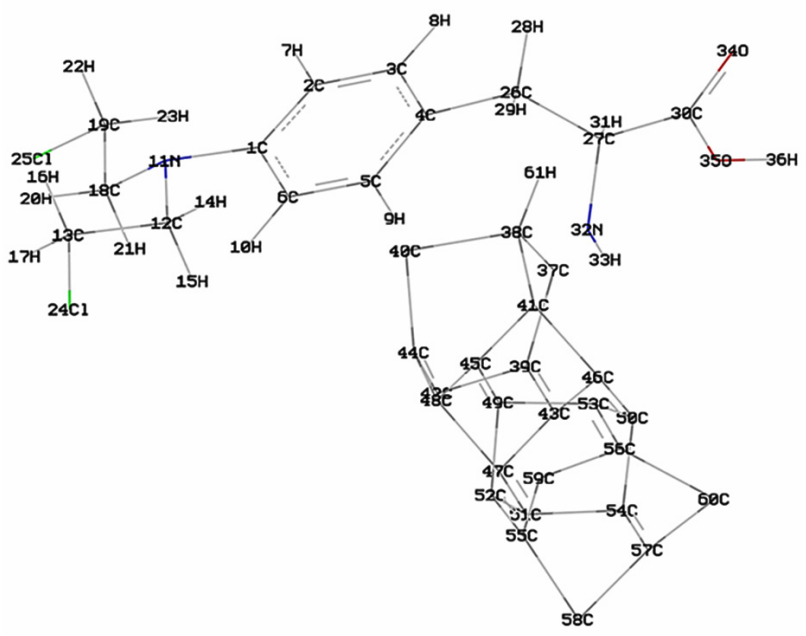

Fig. 1. Optimized Structure of I-Isomer.

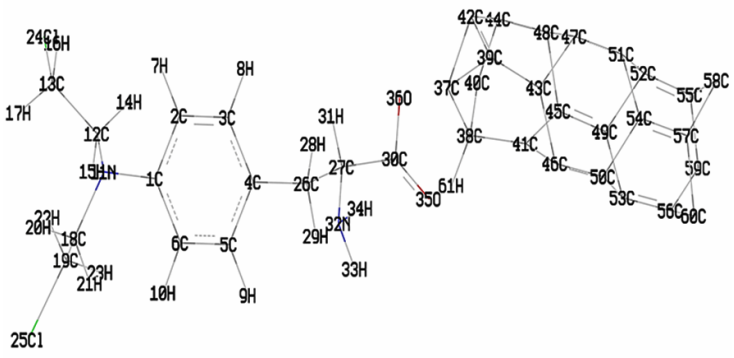

Fig. 2. Optimized Structure of II-Isomer.

ferent conformers. As the provided data at Figs 1 and 2 show clearly, in I-Isomer the drug is inserted near the nanostructure towards its amine functional group but in II-Isomer melphalan is located near SWCNT towards its OH functional group. It should be noted that on the basis of the carried out IR computations, it was not seen any negative frequency at all of the studied structures [7, 14].

Calculation and verifying the values of adsorption enthalpy changes (ΔH_{ad})

For acquiring enthalpy variations for the adsorption process of melphalan, the succeeding equation was utilized. In this formula, H_{th} represents the obtained thermal enthalpy for the reactants and products of the evaluated process and ΔE^{o} is the symbol of total energy changes of the system which can be calculated by subtracting the total energy of the products from the sum of the total energy of reactants [15, 16].

$$\Delta H_{ad} = \Delta E^{\circ} + (H_{th\ (Melphalan-SWCNT)} - (T_{th\ (Melphalan)} + H_{th\ (SWCNT)})) \quad (2)$$

The provided data in Table 1 clearly indicates that the reaction of melphalan and SWCNT is exothermic at both configurations because the achieved ΔH_{ad} values are negative for both isomers. The influence of temperature on this variable was also checked out. As it can be seen from the Table, temperature does not have an obvious effect on enthalpy changes. Because there is not a remarkable difference between the obtained ΔH_{ad} values at different temperatures. Hence, 298 K can be selected as the best temperature for the adsorption procedure of melphalan. The next hidden point in the Table is that II-Isomer has lower enthalpy changes in comparison to I-Isomer at all temperatures. Thus, it can be deduced that the formation of II-Isomer is more exothermic and experimentally possible than the formation process of I-Isomer [10, 12].

Calculation and inquiring the values of Gibbs free energy alterations (ΔG_f)

In order to calculate the Gibbs free energy changes, equation 3 was applied. In this equation, G_{th} stands for the thermal Gibbs free energy that was computed by the software for the reactants and products of the desired procedure. And ΔE^{o} is heeded as a symbol for the total energy changes of the system [9, 17].

$$\Delta G_{ad} = \Delta E^{\circ} + (G_{th\ (Melphalan-SWCNT)} - (G_{th\ (Melphalan)} + G_{th\ (SWCNT)})) \quad (3)$$

The obtained ΔG_f values are reported in Table 2. As it is obvious from the Table the adsorption of melphalan at both configurations are spontaneous due to the remarkable negative calculated Gibbs free energy changes. Moreover, the values of Gibbs free energy changes for II-Isomer are more negatives than I-Isomer. So, the synthesis process of II-Isomer is more spontaneous and experimentally feasible than the other product [18].

Table 1. The values of enthalpy changes for the adsorption of melphalan on the surface of SWCNT in the temperature range of 278.15-305.15 K.

ΔH (kJ/mol)		
Temperature (K)	I-Isomer	II-Isomer
278.15	-2437.7186	-2603.6216
281.15	-2437.7473	-2603.6543
284.15	-2437.7771	-2603.6881
287.15	-2437.8048	-2603.7218
290.15	-2437.8325	-2603.7565
293.15	-2437.8612	-2603.7922
296.15	-2437.8910	-2603.8280
299.15	-2437.9197	-2603.8637
302.15	-2437.9514	-2603.8984
305.15	-2437.9831	-2603.9331

Table 2. The values of Gibbs free energy changes for the adsorption of melphalan on the surface of SWCNT in the temperature range of 278.15-395.15 K.

ΔG (kJ/mol)		
Temperature (K)	I-Isomer	II-Isomer
278.15	-3091.9094	-3256.6494
281.15	-3084.4452	-3249.1182
284.15	-3084.2140	-3248.8930
287.15	-3083.9819	-3248.6689
290.15	-3083.7529	-3248.4469
293.15	-3083.5219	-3248.2229
296.15	-3083.2909	-3247.9989
299.15	-3083.0600	-3247.7760
302.15	-3082.8321	-3247.5531
305.15	-3082.6053	-3247.3303

Frontier molecular orbital and Structural analysis

Some of the chemical and structural traits of tetryl and its derivatives with graphene including the energy of HOMO and LUMO orbitals (E_H and E_L), the energy discrepancy between HOMO and LUMO molecular orbitals (HLG) [15, 19, 20], the electrophilicity index (ω), maximum transferred charge index (ΔN_{max}), chemical potential (μ), zero-point energy, density, chemical hardness (η), dipole moment, volume and weight were calculated and reported in Table 3. In chemistry, HOMO is the highest occupied molecular orbital and LUMO is the lowest unoccupied molecular orbital and the energy difference between them is described as energy gap which is usually represented by HLG symbol. It should be mentioned that this variable was calculated by using equation 4. The provided data in Table 3 demonstrate that the energy gap has decreased after the adsorption of melphalan on the SWCNT. And this decreasing is more sharply in the case of I-Isomer. Energy gap has a direct relationship with conductivity so that the compounds with low HLG are more conductive than compounds with high HLG values because a high amount of HLG implies that the substance needs more energy for transferring the electron to the excited state. Hence, it can be deduced that the conductivity of pure melphalan is lower than its derivatives with SWCNT owing to the decrementing trend of HLG [14, 21]. Chemical hardness was the next inspected parameter which was calculated by equation 5. Chemical hardness shows the softness of a compound. In fact, the materials which have a low amount of chemical hardness will be more chemically smoother and vice versa. In addition, this parameter is related to the reactivity of the structure. Due to the fact that soft compounds can alter their electron density more conveniently in comparison to hard substances, Therefore, soft molecules can participate in chemical reactions more easily because the electron transmission which is necessary for the implementation of reactions can be done better in this type of compounds. As it can be seen, chemical hardness has decremented after the adsorption of melphalan on the surface of SWCNT. So, melphalan-SWCNT derivatives are more chemically softer and more reactive than pure melphalan. The amount of chemical potential which is essential for obtaining electrophilicity and maximum transferred charge capacity was also calculated by equation 6. Chemical potential experienced a tangible decline by binding of melphalan to the surface of SWCNT [22].

$$HLG = E_{LUMO} - E_{HOMO} \quad (4)$$

Table 3. The values of Calculated E_H and E_L, HLG, chemical hardness (η), electrophilicity index (ω), the chemical potential (μ), the maximum amount of electronic charge index (ΔN_{max}), volume, weight, density, zero point energy and dipole moment

Chemical properties	Melphalan	I-Isomer	II-Isomer
Energy (au)	-1160.6635	-2557.3182	-2557.3872
E HOMO (eV)	-6.47	-4.4	-6.67
E LUMO (eV)	7	2.97	1.72
Dipole Moment (Debye)	5.97	14.93	13.25
Weight (amu)	307.221	559.024	593.469
Volume ($Å^3$)	281.61	542.51	558.17
Area ($Å^2$)	305.99	513.92	538.31
H° (kJ/ mol)	-1660.3	-2102.8	-2556.86
G° (kJ/ mol)	-1660.3	-2102.8	-2556.93
Gap Energy (eV)	13.47	7.37	8.39
Hardness (a.u.)	6.735	3.685	4.195
Chemical Potential (a.u.)	-0.265	-1.73	-2.475
Electrophilicity (a.u.)	0.0052	0.3464	0.7301
ΔN_{max} (a.u.)	-0.0393	0.4004	0.5899
ZPE (kj.mol)	1028.98	1338.6	1323.48

$$\eta = (E_{LUMO} - E_{HOMO}) / 2 \quad (5)$$

$$\mu = (E_{LUMO} + E_{HOMO}) / 2 \quad (6)$$

$$\omega = \mu^2 / 2\eta \quad (7)$$

$$\Delta N_{max} = -\mu / \eta \quad (8)$$

The electrophilicity index is an admissible criterion for checking out the tendency of a compound for absorbing the electron. This parameter was calculated by equation 7. When two molecules react with each other, one of them plays the role of a nucleophile whilst the other one acts as an electrophile. A material with high electrophilicity value will be more eager to absorb electron to it. The maximum transmitted charge capacity (ΔN_{max}) can be calculated by equation 8. A compound with a positive amount of ΔN_{max} will act as an electron acceptor and a material with a negative amount of ΔN_{max} will behave as an electron donor. As it can be witnessed, the amount of the both mentioned parameters have increased in melphalan-SWCNT derived products which substantiates that pure melphalan has a lower propensity towards electron in comparison to its derivatives with SWCNT.

The next evaluated parameter is dipole moment which has an obvious relationship with the solubility of the studied compound in polar solvents like water. At it can be seen, the dipole moment of I-Isomer is higher than the dipole moment of pure melphalan and II-Isomer. Therefore, I-Isomer has better solubility in polar solvents whereas the solubility of pure melphalan is relatively poor in comparison to I-Isomer [23].

CONCLUSION

In this research, melphalan interaction with SWCNT was investigated by DFT studies. The calculated Gibbs free energy changes and adsorption enthalpy variations confirmed the nanostructure has an exothermic and spontaneous interaction with melphalan. The values of bandgap, chemical potential, chemical hardness and dipole moments showed melphalan-SWCNT derivatives are more reactive and biocompatible in comparison to the pure drug molecule without nanostructure. The theoretical results showed SWCNT can be a potential nanocarrier for the delivery of melphalan.

REFERENCES

[1] Abolhasani Zadeh, F., Abdalkareem Jasim, S., Javed Ansari, M., Olegovich Bokov, D., Yasin, G., Thangavelu, L., Derakhshandeh, M. (2022). Boron carbide nanotube as targeted drug delivery system for melphalan anticancer drug. J Mol Liq., 354(2), 118796.

[2] Badawi, H.M., Khan, I. (2016). A comparative study of the vibrational spectra of the anticancer drug melphalan and its fundamental molecules 3-phenylpropionic acid and l-phenylalanine. J Mol Struct., 1109(2), 171–178.

[3] Celaya, C.A., Hernández-Ayala, L.F., Buendía Zamudio, F., Vargas, J.A., Reina, M. (2021). Adsorption of melphalan anticancer drug on C24, B12N12, B12C6N6, B6C12N12 and B6C6N12 nanocages: A comparative DFT study. J Mol Liq., 329 (2), 115528.

[4] Ehsani, E., Shojaie, F. (2021). DFT computational investigation of the reaction behavior of polyamidoamine dendrimer as nanocarrier for delivery of melphalan anticancer drug. J Mol Liq., 323(2), 114625.

[5] Y. Aboul-Enein, H., Berczynski, P., Kruk, I. (2013). Phenolic Compounds: the Role of Redox Regulation in Neurodegenerative Disease and Cancer. Mini Rev Med Chem., 13(2), 385–398.

[6] Mirzaei, M., Nouri, A. (2010). Journal of Molecular Structure: THEOCHEM The Al-doped BN nanotubes: A DFT study. J Mol Struct. (THEOCHEM), 942(2), 83–87.

[7] Mirzaei, M., Youse, M., Meskinfam, M. (2012). Density functional studies of oxygen-terminations versus hydrogen-terminations in carbon and silicon nanotubes. Solid State Sci., 14(7), 874–879.

[8] Mirzaei, M., Mirzaei, M. (2010). Electronic structure of sulfur terminated zigzag boron nitride nanotube: A computational study. Solid State Sci., 12(2), 1337–1340.

[9] Ahmadi, R., Jalali Sarvestani, M.R. (2018). Investigating the Effect of Doping Graphene with Silicon in the Adsorption of Alanine by Density Functional Theory. Phys Chem Res., 6(2), 639–655.

[10] Ahmadi, R., Jalali Sarvestani, M.R. (2020). Adsorption of Tetranitrocarbazole on the Surface of Six Carbon-Based Nanostructures: A Density Functional Theory Investigation. Russ J Phys Chem B, 14(2), 198–208.

[11] Ahmadi, R. (2020). Evaluating Adsorption of Proline Amino Acid on the Surface of Fullerene (C60) and Carbon Nanocone by Density Functional Theory. Chem Methodol., 4(2), 68–79.

[12] Ahmadi, R. (2019). Effect of B12N12 junction on the energetic and chemical features of PATO: A density functional theory investigation. Int J Nano Dimens., 10(2), 62–68.

[13] Jalali Sarvestani, M.R., Ahmadi, R. (2020). Trinitroanisole adsorption on the surface of boron nitride nanocluster (B12N12): A computational study. J Water Environ Nanotechnol., 5(2), 34–44.

[14] Mirzaei, M., Meskinfam, M. (2011). Computational studies of effects of tubular lengths on the NMR properties of pristine and carbon decorated boron phosphide nanotubes. Solid State Sci., 13(2), 1926–1930.

[15] Ahmadi, R., Ebrahimikia, M. (2017). Calculation of thermodynamic parameters of [2.4.6] three nitro toluene (TNT) with nanostructures of fullerene and boron nitride nano-cages over different temperatures, using density functional theory. Phys. Chem. Res., 5(2), 617–627.

[16] Beheshtian, J., Peyghan, A.A., Bagheri, Z. (2012). Quantum chemical study of fluorinated AlN nano-cage. Appl Surf Sci., 259(2), 631–636.

[17] Jalali Sarvestani, M.R., Ahmadi, R. (2019). Investigating the influence of doping graphene with silicon and germanium on the adsorption of silver (I). J Water Environ Nanotechnol., 4(2), 48–59.

[18] Mazurek, A.H., Szeleszczuk, Ł., Pisklak, D.M. (2020). Periodic DFT calculations- Review of applications in the pharmaceutical sciences. Pharmaceutics, 12.

[19] Methodologies, C. (2020). Adsorption of Tetryl on the Surface of B12N12: A omprehensive DFT Study. Chem Methodol., 4(2), 40–54.

[20] Mirkamali, E.S., Ahmadi, R. (2020). Adsorption of melphalan anticancer drug on the surface of boron nitride cage (B12N12): A comprehensive DFT study. J Med Chem Sci., 3(2), 199–207.

[21] Shahzad, H., Ahmadi, R., Adhami, F., Najafpour, J. (2020). Adsorption of Cytarabine on the Surface of Fullerene C20: A Comprehensive DFT Study. Eurasian Chem Commun., 2(2), 162–169.

[22] Afshar, M., Ranjineh Khojasteh, R., Ahmadi, R. (2020). Adsorption of lomustin anticancer drug on the surface of carbon nanotube: A theoretical study. Eurasian Chem Commun., 2(2), 595–603.

[23] Nasiri Moghaddam, T.S., Nikmaram, F.R., Ahmadi, R. (2017). Density Functional Theory Study of the Behavior of Carbon Nano cone, BP Nano cone and CSi Nano cone as Nano Carriers for 5-Fluorouracil Anticancer Drug in Water. Int J New Chem., 4(2), 72–77.

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