Int. J. Nano Dimens., 11 (4): 346-354, Autumn 2020

ORIGINAL ARTICLE

Adsorption of Metronidazole drug on the surface of nano fullerene C_{60} doped with Si, B and Al: A DFT study

Mohammad Hossein Fekri, Rahim Bazvand, Mousa Soleymani, Maryam Razavi Mehr*

Department of Chemistry, Ayatollah Borujerdi University, Borujerd, Iran.

Received 04 June 2020; revised 16 August 2020; accepted 28 August 2020; available online 05 September 2020

Abstract

In this research, the quantum mechanics calculations were carried out to elucidate the adsorption behavior of metronidazole drug on the surface of pristine as well as doped C60 fullerene with Si, B and Al using density functional theory (DFT) at B3LYP/6-31G (d,p) level. After optimization of the structures, various parameters such as HOMO and LUMO energies, gap energy, adsorption energy, chemical hardness, chemical potential, dipole moment, electrophilicity index and thermodynamics data were calculated. The results showed that by substitution of the carbon atom in the C60 fullerene with Si, B and Al, the amounts of gap energy and chemical hardness are decreased, while those of chemical potential and electrophilicity index are increased. It means that the doping of C60 by Si, B and Al leads to an increase in drug reactivity. Also, the binding and stabilization energies are increased by doping of C60. The thermodynamic results suggested that substitution on the pristine C60 leads to a more negative in the value of the Gibbs energy and subsequent spontaneous process.

Keywords: *Chemical Potential; C60 Fullerene; Density Functional Theory (DFT); Doping; Metronidazole.*

How to cite this article

Fekri MH., Rahim Bazvand, Soleymani M., Razavi Mehr M. Adsorption of Metronidazole drug on the surface of nano fullerene C_{60} doped with Si, B and Al: A DFT study. Int. J. Nano Dimens., 2020; 11 (4): 346-354.

INTRODUCTION

Metronidazole (**Met.**) is an anti-protozoan and positive/negative gram anti-bacterial drug. That is used against the bacterial diseases such as liver, stomach and skin infections, joints, brain, and breathing organ. In addition, it is delivered for various types of stomach ulcers. It is applied for the outside intestine amoebiasis treatment. It has not shown a significant effect on intestinal parasites, so it must be applied along with an intestinal amoebae for inhibition of the infection. Metronidazole effectively eradicates infections in intestinal and extra hepatic tissues [1].

Molecular interactions of the drugs are of importance in various processes of pharmacology, drug design, imaging, *etc*. Therefore, the interactions of drugs with the nanomaterials have been extensively studied [2-6]. Employing of the nanostructures as drug delivery carriers is one of the most mentioned items in this area. Nanostructures can be considered as a very effective drug delivery system which can increase the drug efficiency due the following reasons: biocompatibility; ability to slowly release the drug in a controlled manner; protection of the drug's molecular structure; being smaller than the cell; increasing the drug's shelf life; reducing the dose required for the patient. Carbon nanostructures such as nanotubes, graphene, and fullerenes have received an extensive attention in pharmaceuticals science. Due to the small size of these nanostructures, they can pass from the membranes easily and insert to the cell [7-9]. In recent years, attention to the computational chemistry has been increased in order to study the drug delivery systems. In fact, the development of drug delivery systems requires deeper studies containing more details [10-15]. In the recent years, fullerenes are one of the nanostructures

* Corresponding Author Email: *m.h.fekri@abru.ac.ir*

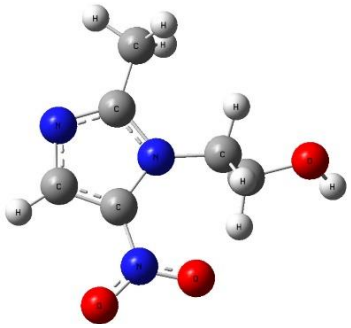

Fig. 1. Optimuzed structure of Metronidazole (Met) drug.

employed as a drug carrier. However, they have been less investigated by computational methods compared to the other nanomaterials. $C_{30}B_{15}N_{15}$ Hetero fullerene as a carrier of isoniazid drug and interaction of fullerene doped with 5-fluorouracil drug are some of the studies which have been reported by employing density functional theory (DFT) [16]. The drug must be protected from any chemical and enzymatic degradations before arriving to the target. Doping of the nanostrucures with different functional groups is one of the common methods to increase its specific surface area. Therefore, some researchers have attempted to increase the charge capacity of drugs by doping of the nano materials. For example, Khodadadi *et al*. utilized nitrogen-doped graphene quantum dots to deliver methotroxate anticancer drug. Their results showed that the quantum dots of graphene doped with nitrogen improve the drug performance [17, 18].

In this research, Gauss View software was used to design **Met.**, pristine C_{60}, and doped with Si-, B-, and Al-doped C_{60} and their complexes. The energies of the highest occupied and the lowest unoccupied molecular orbitals (HOMO & LUMO), gap energy (E_g) and general characteristics such as chemical potential (μ), chemical hardness (η), maximum charge transfer (ΔN_{max}), electrophilicity index (ω), *etc*. were calculated. [19-25].

MATERIALS AND METHODS

The configuration optimizing of all structures were performed with Gaussian 09 [26] in theoretical level of B3LYP/6-31G (d,p). For this purpose, **Met.** (Fig. 1) was attached to prior C_{60} and Si-, B-, and Al-doped C_{60} in different sites with the C, N, and O atoms which are abbreviated as C-Met, N-Met, and O-Met, respectively. All of these three ways have been evaluated in this work. For the recognition of the best interaction sites, molecular electrostatic potential (MEP) calculations were carried out on all of the structures. The HOMO-LUMO values were also extracted from the Gaussian 09 output.

Adsorption energy ($E_{ads.}$) of Met-Nanocarriers was calculated using the following equation:

$$E_{ads.} = [E_{complex}] - [E_{cage} + E_{Met.}] \quad (1)$$

Where E_{Met}, $E_{complex}$, and E_{cage} are the energies of **Met.**, fullerene- drug complexes, and pristine fullerene, doped fullerene with silicone, boron, and aluminum, respectively.

In order to evaluate the nanocarrier, drug and complex reactivity, quantum descriptors such as global hardness (η), chemical potential (μ), electrophilicity index (ω), maximum charge transfer (ΔN_{max}), electronegativity (χ) and Fermi level (E_{FL}) were calculated. These indexes were estimated through the following equations:

$$E_g = E_{LUMO} - E_{HOMO} \quad (2)$$

$$\mu = -\frac{IP + EA}{2} \quad (3)$$

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

$$\omega = \frac{\mu^2}{2\eta} \quad (5)$$

$$\Delta N_{max} = -\frac{\mu}{\eta} \quad (6)$$

$$\chi = -\mu \quad (7)$$

$$E_{FL} = \frac{E_{LUMO} + E_{HOMO}}{2} \quad (8)$$

In these equations, E_{HOMO} and E_{LUMO} refer to

the energies of HOMO and LUMO, respectively. IP and EA show the ionization and electron affinity energies. In addition, the thermodynamic parameters ($\Delta H_{ads.}$, $\Delta S_{ads.}$, $\Delta G_{ads.}$) were calculated to evaluate the drug adsorption possibility by the carriers [27, 28].

RESULTS AND DISCUSSIONS

Several feasible configurations were chosen for approaching of **Met.** to the fullerene cage. For this purpose, MEP calculations were carried out on drug, nanocages, and their complexes, in which red and blue colors present the regions with high (more nucleophilic) and low (more electrophilic) density electron, respectively. MEP calculations on the molecular surfaces of an individual **Met.** molecule are shown that O and N atoms may be considered as feasible active sites potentially (Fig.2). On the other hand, the CH_3 group in drug is indicated with the blue color presenting a high electron affinity. In the doped fullerene, the blue regions observed for Al-doped C_{60} is more intensive than those for Si- and B-doped C_{60}. This despite the fact that distribution of MEP is also changed to interaction cage-C_{60} with **Met.**

The dipole moment plays a key role in the solubility. In fact, the overall polarity and solubility in water is increased for these nanocages-drug complexes when the dipole moment is increased (Table 1). Since water is the main part of the body, these conclusions suggest that the doping may modify fullerenes drug delivery. As presented in Table 1, C_{60} has a zero value of dipole moment suggesting it is a non-polar molecule. Doping of the fullerene with the Si, B and Al atoms leads to a significant change in the dipole moment. The metronidazole drug presents a dipole moment value of 4.34 Debye, while the C_{59}Al-C-Met nanocage shows the highest one.

In the next step, the bond lengths between drug and nanocarriers were calculated from optimized structures. The results suggested that the bond length for Met-C_{60} is lower than that for Met-cages (Table 1). C_{59}Al-C-Met shows the greatest amounts for bond length. In all cases, the bond length for O-cage is lower than that for C- and N-cages. Because the oxygen atom is the more electronegative than, the carbon and nitrogen atoms.

The stability of the drug-nanocarrieres were evaluated by calculation of the adsorption energy (Table 2). The results showed that when **Met.** with the nanocages, adsorption energies will be become negative. While, these values for undoped-C_{60} are very low. Thus, adsorption of the drug is almost unstable on the undoped fullerene from the C-, N-, and O- sites. Finally, negative adsorption energies of drug-doped nanocages leads to an increase in the stability. The highest adoption energy was observed in the C_{59}Si-O-Met system (-61.73 kcal mol^{-1}). Then, the thermodynamic parameters were calculated to investigate the drug adsorption possibility from energetic point of view (Table 2). It is clear that, all of Gibbs free energies values are negative in value except for the C_{60}-C-Met and C_{60}-N-Met systems. This suggests that adsorption of **Met.** on the Si-, B-, and Al-nanocarriers is spontaneous. The C_{59}Si-O-Met system showed the highest Gibbs free energy. Therefore, it can be concluded that doping leads to enhancement of adsorption performance. Adsorption enthalpy values are negative in value for all complexes except for the C_{60}-C-Met and C_{60}-N-Met systems. This illustrates that the drug adsorption process is exothermic. The C_{59}Si-O-Met system presented the highest enthalpy (-59.60 kcal mol^{-1}). In all systems, the adsorption entropy is negative in value, which shows that the drug adsorption process takes place with decreasing of disorder in agreement with the adsorption mechanism.

Calculation of the HOMO and LUMO orbital images of the drug, pure and doped C_{60} and drug–doped complexes showed that these orbitals are located on the ring and the NO_2 groups (S-1). In addition, the frontier molecular orbitals of the C_{60} fullerene are almost symmetric. In the doped fullerenes, density of orbitals on the doped atom is higher than the other ones (specially for the Al-nanocages). HOMO orbitals in C_{59}Si-N-Met and C_{60}-N-Met and LUMO orbitals in C_{59}Al-N-Met, C_{59}B-N-Met, C_{59}Si-N-**Met.** systems are and located on the drug and the fullerene cages does not have a share in them. E_g is a quantity that determines the reactivity of a molecule. According to Table 3, E_g of C_{60} is higher (2.87 eV) than doped-C_{60}: C_{59}Si, C_{59}B, and C_{59}Al with values of 2.24, 2.54, and 2.22 eV, respectively, and thus the doped molecules show higher tendency to chemical interaction with **Met.**. On the other hands, E_g of **Met.** equals to 4.35 eV. The value of E_g for drug-nanocages is lower than pure C_{60} and **Met.**. Also, the Table presents the values of E_g for N-nanocages: C_{59}-N-Met, C_{59}Si-N-Met, C_{59}B-N-Met, and C_{59}Al-N-Met (0.51, 0.35, 1.46, and 1.04 eV) which are very low compared

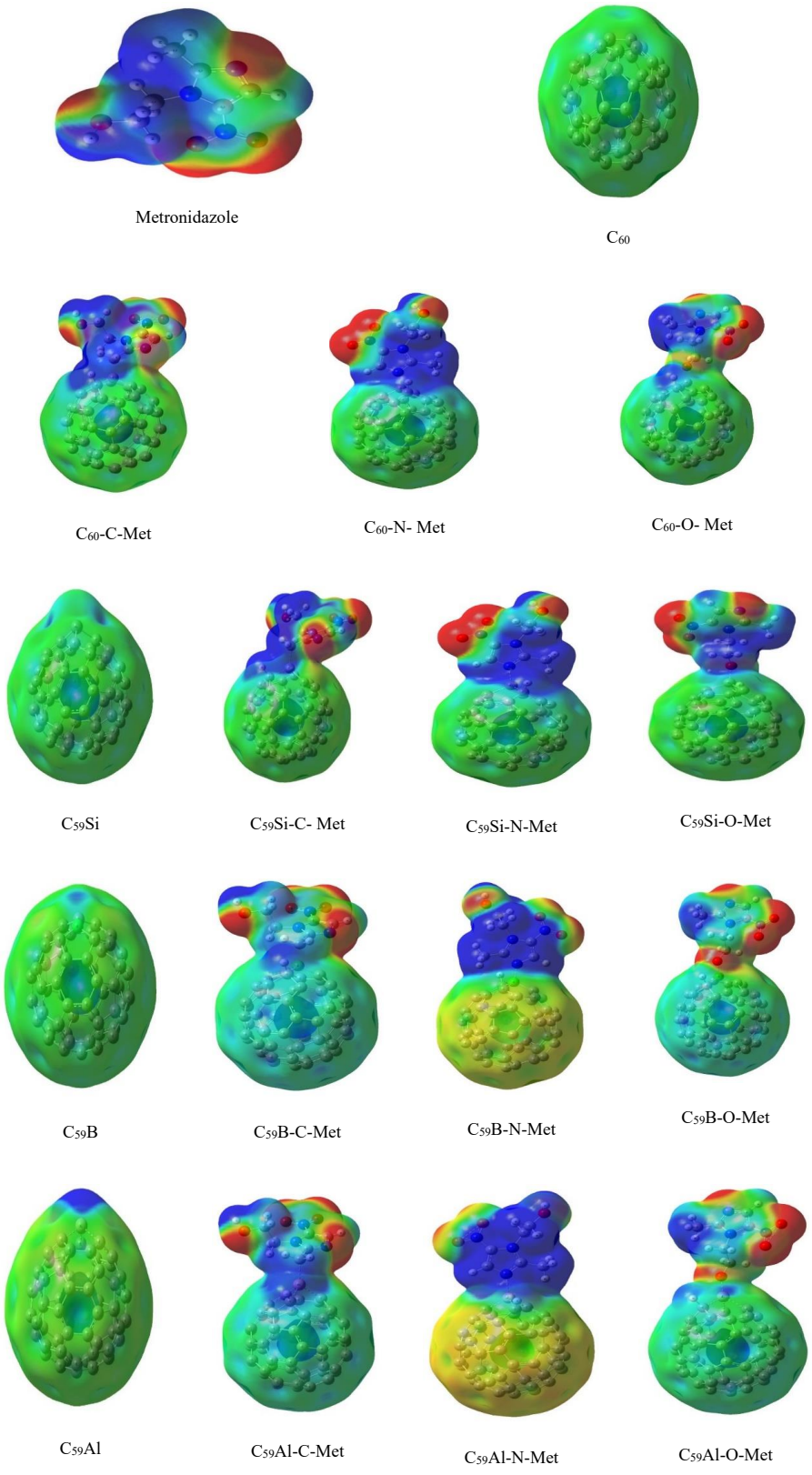

Fig. 2. The MEP images of drugs and drug-nanocarriers.

Table 1. Interatomic distance of drug-complex (in A°) and dipole moment (in D).

	R	μ
Metronidazole	-	4.34
C_{60}	-	0.00
C_{60}-C-Met	1.580	4.52
C_{60}-N-Met	1.519	5.74
C_{60}-O- Met	1.476	4.46
$C_{59}Si$	–	0.28
$C_{59}Si$-C- Met	1.934	5.13
$C_{59}Si$-N- Met	1.850	6.53
$C_{59}Si$- O- Met	1.723	4.45
$C_{59}B$	-	0.48
$C_{59}B$-C-Met	1.680	6.68
$C_{59}B$-N-Met	1.627	11.20
$C_{59}B$- O-Met	1.490	7.12
$C_{59}Al$	-	2.88
$C_{59}Al$-C-Met	2.018	6.37
$C_{59}Al$-N-Met	1.997	14.68
$C_{59}Al$- O-Met	1.747	5.96

Table 2. Absorption energies and thermochemical parameters for drug-nanocages (kcal. mol^{-1}).

	E_b	ΔH_{ad}	ΔG_{ad}	ΔS_{ad}
C_{60}-C-Met	1.26	3.32	16.95	-0.046
C_{60}-N- Met	7.74	9.18	23.02	-0.046
C_{60}-O- Met	-1.97	-0.25	-0.08	-0.001
$C_{59}Si$-C- Met	-38.07	-36.32	-24.37	-0.040
$C_{59}Si$-N- Met	-20.77	-20.28	-8.30	-0.040
$C_{59}Si$-O- Met	-61.73	-59.60	-47.54	-0.040
$C_{59}B$-C- Met	-0.99	-0.43	12.69	-0.044
$C_{59}B$-N- Met	-29.65	-27.53	-14.59	-0.043
$C_{59}B$-O- Met	-23.12	-23.18	-8.74	-0.048
$C_{59}Al$-C- Met	-23.65	-23.23	-11.97	-0.038
$C_{59}Al$-N- Met	-44.79	-43.65	-30.25	-0.045
$C_{59}Al$-O- Met	-57.20	-56.11	-45.15	-0.037

to the other systems (≈ 2.2-2.7 eV). Fermi level is the highest energy state occupied by electrons in a material at absolute zero temperature. The Fermi levels (E_{FL}) for **Met.**, fullerene, and nanocages are in agreement with the E_g values. In order to better understand the electronic changes in the evaluated systems after drug absorption, density of states (DOS) curves were calculated (Fig. 3).

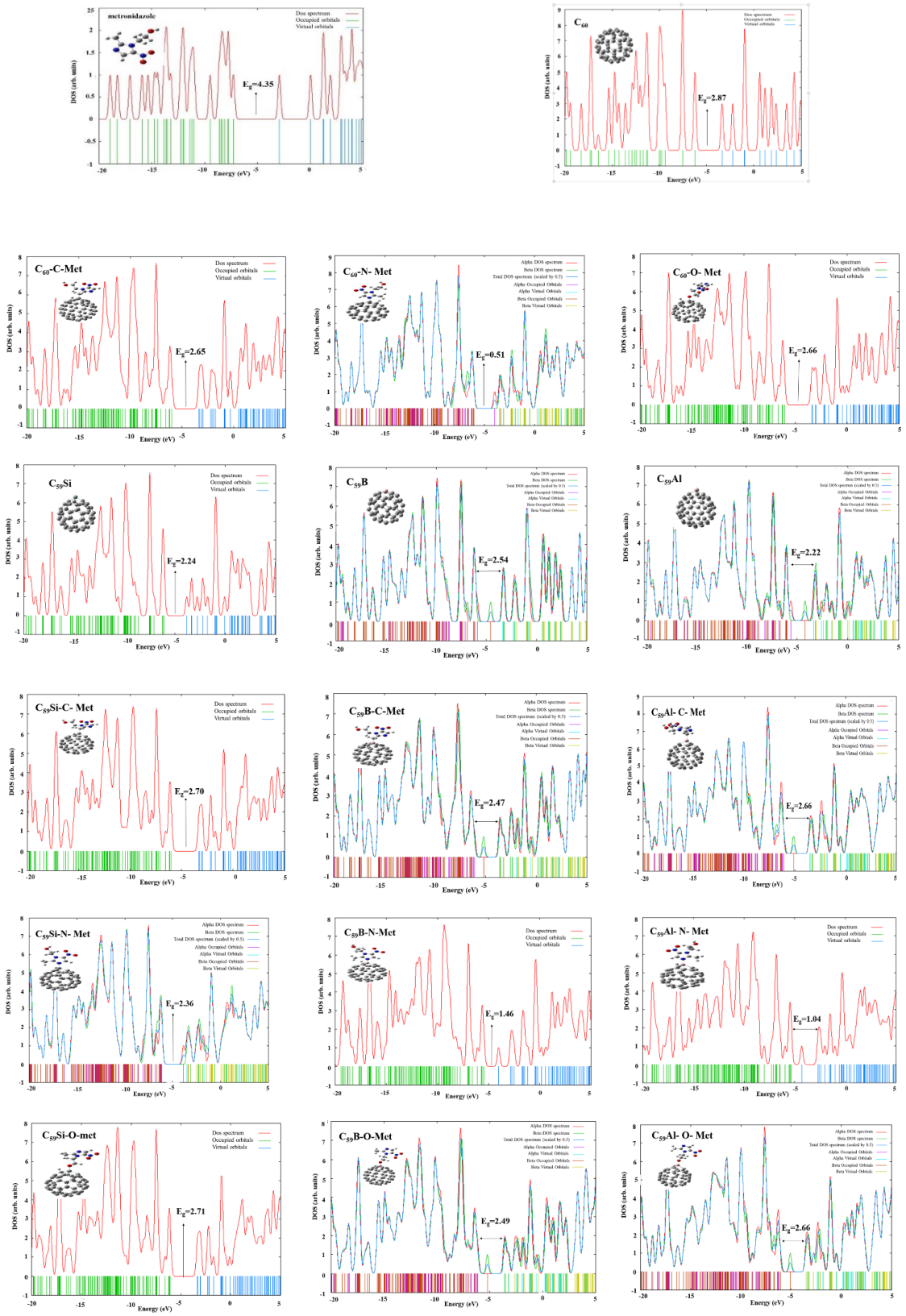

Fig. 3. Schematic of optimized structures and DOS plots for drugs and drug-nanocarriers.

Table 3. Molecular orbitals energies and quantum descriptors (eV).

	E_{HOMO}	E_{LUMO}	E_g	μ	η	ω	ΔN_{max}	χ	E_{FL}
Metronidazole	-7.29	-2.94	4.35	-5.11	2.17	6.00	2.35	5.11	-5.11
C_{60}	-6.25	-3.38	2.87	-4.81	1.43	8.06	3.36	4.81	-4.81
C_{60}-C-Met	-6.01	-3.36	2.65	-4.68	1.32	8.30	3.55	4.68	-4.68
C_{60}-N-Met	-3.99	-3.48	0.51	-3.73	0.25	27.57	14.92	3.73	-3.73
C_{60}-O-Met	-6.09	-3.43	2.66	-4.76	1.33	8.50	3.58	4.76	-4.76
C_{59}Si	-6.07	-3.83	2.24	-4.95	1.12	10.91	4.42	4.95	-4.95
C_{59}Si- C- Met	-6.03	-3.33	2.70	-4.68	1.35	8.11	3.47	4.68	-4.68
C_{59}Si- N- Met	-3.89	-3.53	0.36	-3.71	0.18	38.49	20.61	3.71	-3.71
C_{59}Si- O- Met	-6.08	-3.37	2.71	-4.72	1.35	8.24	3.50	4.72	-4.72
C_{59}B	-5.91	-3.37	2.54	-4.64	1.27	8.47	3.65	4.64	-4.64
C_{59}B- C- Met	-6.10	-3.63	2.47	-4.86	1.23	9.58	3.95	4.86	-4.86
C_{59}B- N- Met	-5.49	-4.03	1.46	-4.76	0.73	15.56	6.52	4.76	-4.76
C_{59}B- O- Met	-6.13	-3.64	2.49	-4.89	1.25	9.56	3.91	4.89	-4.89
C_{59}Al	-5.60	-3.38	2.22	-4.49	1.11	9.05	4.05	4.49	-4.49
C_{59}Al- C- Met	-6.22	-3.56	2.66	-4.89	1.33	8.98	3.68	4.89	-4.89
C_{59}Al- N- Met	-5.35	-4.31	1.04	-4.83	0.52	22.35	9.29	4.83	-4.83
C_{59}Al- O- Met	-6.18	-3.52	2.66	-4.85	1.33	8.83	3.65	4.85	-4.85

Chemical potential (μ) values shows the affinity to the electron attraction. The negative values of chemical potential show that the charges transfer between two particles are spontaneously. The electron transfer occurs from a molecule with a higher chemical potential to a molecule with a lower one. In this work, the electronic chemical potentials (μ) for all drug-cage complexes are negative and in the range of -3.7 to -4.95 eV. According to Table 3, the chemical potential of the drug is higher than other compounds, indicating that the electron transfer in the corresponding complexes takes place from the drug to the fullerenes. Hence, increment of the reactivity in the doped fullerene can be concluded with the drug adsorption.

Chemical hardness indicates resistance to change in the electron density of a chemical system, and can explain the system stability. The chemical hardness of fullerene is reduced after doping and also absorption of drug. According to results, chemical hardness has reduced after drug adsorption by doped-C_{60} from toward the N-site of drug. Table 3 presents that chemical hardness for N- nanocages including C_{60}-N-Met, C_{59}Si-N-Met, C_{59}B-N-Met, and C_{59}Al-N-Met have the lowest values (0.25, 0.18, 0.73, and 0.52 eV, respectively).

In organic chemistry, an electrophile is an electron absorbent, which are in positive or neutral modes. They have certain empty orbitals for electron absorption. When two molecules react each other, one molecule acts as a nucleophile, while the other plays the role of an electrophilic. Electrophilicity power (ω) is a parameter related to HOMO and LUMO that indicates the reactivity of the structure. In fact, the electrophilicity index is the energy stability when the system accepts electrons. In this work, the ω values are high (≈8-38.5 eV) for all of molecules. Also, this parameter is higher for nanocages-N-Met than the other ones (≈15.5-38.5 eV).

The most electrical charge that an electrophilic system can accept is called ΔN_{max} [21]. In other words, ΔN_{max} indicates the charge capacity of a molecule. According to the ΔN_{max} equation (eq. 6), by increasing the chemical potential, the chemical hardness is decreased and the electrophilicity power is increased. When the system possesses more electron deficiencies, it becomes more positive, and thus, it is expected that the possibility of electron transfer to the system is increased. The results related to ΔN_{max} (Table 3) show that the level of this parameter in N-nanocages-Met is higher than the other molecules (≈6.5-20.6 eV). The results suggest that by attachment of **Met.** to the nanocages from toward nitrogen site has higher values of electrophilicity and electrical charge compared to the two other alternative ways (carbon and oxygen sites).

CONCLUSION

We performed DFT calculations to study interactions of the C_{60} fullerene with Metronidazole Drug. Furthermore, Si-, B-, and Al-doped C_{60} fullerenes were also studied. All of possible interactions drug to nanocages from different towards (C-, N, and O-) are carried out and finally, following results were extracted:

The MEP images displayed that the reigns containing O and N in the metronidazole drug have the affinity to the nucleophile role in the reaction. While, the CH_3 group has the affinity to play the electrophile role in the reaction. Doping of the fullerene with the Si, B and Al atoms leads to perceptible changes in the dipole moment. The C_{59}Al-C-Met nanocage has the highest value of dipole moment. In all nanocages-Met, bond length of O-cage is lower than that of C- and N-cages due to the more electronegativity of oxygen compared to the carbon and nitrogen atoms. The negative adsorption energies of drug-doped nanocages leads to increasing their stability. The highest adsorption energy was shown in the C_{59}Si-O-Met system (-61.73 kcal mol^{-1}). These results confirm that the adsorption of **Met.** on the Si-, B-, and Al-nanocarriers are spontaneous. The C_{59}Si-O-Met system showed the highest Gibbs free energy. The value of E_g for drug-nanocages is lower than that for pure C_{60} and **Met.**. Also, the values of E_g for N- nanocages C_{59}-N-Met, C_{59}Si-N-Met, C_{59}B-N-Met, and C_{59}Al-N-Met were found to be 0.51, 0.35, 1.46, and 1.04 eV, respectively, which are very low compared to the other systems (≈2.2-2.7 eV). Chemical potential (μ) for all drug-cages are negative in range of -3.7 to -4.95 eV. Chemical hardness has reduced after drug adsorption by doped-C_{60} from toward the N-site of drug. The ω parameters for all of the molecules is high (≈8-38.5 eV). Also, this parameter for nanocages-N-Met is higher than other cages (≈15.5-38.5 eV).

It can be concluded as a general perspective that doping of C_{60} with Si, B, and Al atoms improves the C_{60} performance as a nanocarrier in drug delivery systems.

CONFLICTS OF INTEREST

The authors do not have any personal or financial conflicts of interest.

REFERENCES

[1] Freeman C. D., Klutman N. E., Lamp K. C., (1997), Metronidazole. *Drugs*. 54: 679-708.

[2] Mirzaei M., (2013), Effects of carbon nanotubes on properties of the fluorouracil anticancer drug: DFT studies of a CNT-fluorouracil compound. *Int. J. Nano Dimens*. 1: 175-179.

[3] Faramarzi R., Falahati M., Mirzaei M., (2020), Interactions of fluorouracil by CNT and BNNT: DFT analyses. *Adv. J. Sci. Eng*. 30: 62-66.

[4] Mirzaei M., Gülseren O., Hadipour N., (2016), DFT explorations of quadrupole coupling constants for planar 5-fluorouracil pairs. *Comput. Theor. Chem*. 15: 67-73.

[5] Kouchaki A., Gülseren O., Hadipour N., Mirzaei M., (2016), Relaxations of fluorouracil tautomers by decorations of fullerene-like SiCs: DFT studies. *Phys. Lett. A*. 3: 2160-2166.

[6] Harismah K., Sadeghi M., Baniasadi R., Mirzaei M., (2017), Adsorption of vitamin C on a fullerene surface: DFT studies. *J. Nanoanalysis*. 4:1-7.

[7] Nikfar Z., Shariatinia Z., (2017), DFT computational study on the phosphate functionalized SWCNTs as efficient drug delivery systems for anti-osteoporosis zolendronate and risedronate drugs. *Phys. E*. 91: 41-59.

[8] Zhao L., Li H., Tan L., (2017), A Novel fullerene-based drug delivery system delivering Doxorubicin for potential lung cancer therapy. *J. Nanosci. Nanotechnol.* 17: 5147-5154.

[9] Zhang Q., Wu Z., Li N., Pu Y., Wang B., Zhang T., Tao J., (2017), Advanced review of graphene-based nanomaterials in drug delivery systems: Synthesis, modification, toxicity and application. *Mater. Sci. Eng: C*. 77: 1363-1375.

[10] Kamel M., Raissi H., Morsali A., Shahabi, M., (2018), Assessment of the adsorption mechanism of Flutamide anticancer drug on the functionalized single-walled carbon nanotube surface as a drug delivery vehicle: An alternative theoretical approach based on DFT and MD. *Appl. Surf. Sci.* 434: 492-503.

[11] Zhang L., Peng G., Li J., Liang L., Kong Z., Wang H., Jia L., Wang X., Zhang W., Shen J. W., (2018), Molecular dynamics study on the configuration and arrangement of doxorubicin in carbon nanotubes. *J. Mol. Liq.* 262: 295-301.

[12] Hasanzade Z., Raissi H., (2018), Density functional theory calculations and molecular dynamics simulations of the adsorption of ellipticine anticancer drug on graphene oxide surface in aqueous medium as well as under controlled pH conditions. *J. Mol. Liq.* 255: 269-278.

[13] Shafiei F., Hashemianzadeh S. M., Bagheri Y., (2019), Insight into the encapsulation of gemcitabine into boron-nitride nanotubes and gold cluster triggered release: A molecular dynamics simulation. *J. Mol. Liq.* 278: 201-212.

[14] Ahmadi R., Pourkarim S., (2015), Investigation of fullerene (C_{60}) effects on chemical properties of Metoprolol: A DFT study. *Int. J. Bio-Inorg Hybrid Nanomater*. 4: 249-254.

[15] Ahmadi R., Jalali Sarvestani M. R., Sadeghi B., (2018), Computational study of the fullerene effects on the properties of 16 different drugs: A review. *Int. J. Nano Dimens*. 9: 325-335.

[16] Hazrati M. K., Bagheri Z., Bodaghi A., (2017), Application of $C_{30}B_{15}N_{15}$ heterofullerene in the isoniazid drug delivery: DFT studies. *Phys. E*. 89: 72-76.

[17] Geng D., Yang S., Zhang Y., Yang J., Liu J., Li R., Sham T. K., Sun X., Ye S., Knights, S., (2011), Nitrogen doping effects on the structure of graphene. *Appl. Surf. Sci.* 257: 9193-9198.

[18] Khodadadei F., Safarian S., Ghanbari N., (2017), Methotrexate-loaded nitrogen-doped graphene quantum dots nanocarriers as an efficient anticancer drug delivery system. *Mater. Sci. Eng: C*. 79: 280-285.

[19] Fekri M. H., Omrani A., Jamehbozorgi S., Razavi Mehr M., (2019), Study of electrochemical and electronical properties on the some schiff base Ni complexes in DMSO solvent by computational methods. *Adv. J. Chem. A*. 2: 14-20.

[20] Naderi E., Mirzaei M., Saghaie L., Khodarahmi G. H., Gulseren O., (2017), Relaxations of methylpyridineone tautomers at the C_{60} surfaces: DFT studies. *Int. J. Nano Dimens*. 8: 124-131.

[21] Mebi C. A., (2011), DFT study on structure, electronic

properties and reactivity of cis-isomers of [$(NC_5H_4$-S)$_2$Fe(CO)$_2$]. *J. Chem. Sci.* 123: 727-731.

[22] Rezaei-Sameti M., Ataeifar F., (2018), The theoretical study of adsorption HCN gas on the surface of pristine, Ge, P and GeP-doped (4, 4) armchair BNNTs. *Iran. Chem. Commun.* 6: 280-292.

[23] Hasan M., Kumer A., Chakma U., (2020), Theoretical investigation of doping effect of Fe for $SnWO_4$ in electronic structure and optical properties: DFT based first principle study. *Adv. J. Chem. A*. 3: 639-644.

[24] Nabati M., Bodaghi-Namileh V., (2020), Evaluation of medicinal effects of Isoxazole ring isosteres on zonisamide for autism treatment by binding to Potassium voltage-gated channel subfamily D member 2 (Kv 4.2). *Adv. J. Chem. A*. 3: 462-472.

[25] Nabati M., Bodaghi-Namileh V., (2020), Molecular modeling of 3-(1, 3-Dioxoisoindolin-2-yl) benzyl Nitrate and its molecular docking study with phosphodiesterase-5 (PDE5). *Adv. J. Chem. A*. 3: 58-69.

[26] Frisch M. J., Trucks G. W., Schlegel H. B., Scuseria G. E., Robb M. A., Cheeseman J. R., Scalmani G., Barone V., Mennucci B., Petersson G. A., Nakatsuji H., Caricato M., Li X., Hratchian H. P., Izmaylov A. F., Bloino J., Zheng G., Sonnenberg J. L., Hada M., Ehara M., Toyota K., Fukuda R., Hasegawa J., Ishida M., Nakajima T., Honda Y., Kitao O., Nakai H., Vreven T., Montgomery Jr. JA., Peralta J. E., Ogliaro F., Bearpark M., Heyd J. J., Brothers E., Kudin K. N., Staroverov V. N., Kobayashi R., Normand J., Raghavachari K., Rendell A., Burant J. C., Iyengar S. S., Tomasi J., Cossi M., Rega N., Millam J. M., Klene M., Knox J. E., Cross J. B., Bakken V., Adamo C., Jaramillo J., Gomperts R., Stratmann R. E., Yazyev O., Austin A. J., Cammi R., Pomelli C., Ochterski J. W., Martin R. L., Morokuma K., Zakrzewski V. G., Voth G. A., Salvador P., Dannenberg J. J., Dapprich S., Daniels A. D., Farkas Ö., Foresman J. B., Ortiz J. V., Cioslowski J., Fox D. J., GAUSSIAN 09, Revision A.1, *GAUSSIAN Inc,. Wallingford, CT*., 2009.

[27] Ghasemi A. S., Ramezani Taghartapeh M., Soltani A., Peter J., (2019), Adsorption behavior of Metformin drug on boron nitride fullerenes: Thermodynamics and DFT studies. *J. Mol. Liq.* 275: 955–967.

[28] Ahmadi R., (2017), Study of thermodynamic parameters of (TATB) and its fullerene derivatives with different number of Carbon (C_{20}, C_{24}, C_{60}) in different conditions of temperature, using density functional theory. *Int. J. Nano Dimens*. 8: 250-256.

[29] Ahmadi R., Boroushaki T., Ezatti M., (2015), The usage comparison parameters, gap band energy, ΔN_{max} at Xylometazoline medicine ratio its medical conveyer nano. *Int. J. Nano Dimens*. 6: 19-22.