Journal of Physical and Theoretical Chemistry
of Islamic Azad University of Iran, 11 (1) 21-27: Spring 2014
(J. Phys. Theor. Chem. IAU Iran)
ISSN 1735-2126

A DFT study of interaction of folic acid drug on functionalized single-walled Carbon Nanotubes

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Received May 2014; Accepted June 2014

ABSTRACT

In this work, the structural and electronic properties of folic acid molecule on functionalized (7,0) zigzag single-walled carbon nanotube was studied in gas phase on the basis of density functional theory (DFT). Furthermore, covalent interaction of folic acid with single-walled carbon nanotube was investigated and its quantum molecular descriptors and binding energies were calculated. The DFT-B3LYP/6-311G(d) calculations revealed that the binding energies of single walled carbon nanotube with folic acid have negative values and decrease with increasing in the number of functionalization.

Keywords: Carbon nanotube; Folic acid; Density functional theory; Reactivity descriptors

INTRODUCTION

Folic acid, FA, is a water soluble compound and it is related to the B complex family of vitamins [1-2]. According to the research that has done in 1945, this drug is an effective material in the treatment of Gilbert's syndrome that is common hereditary disorder which causes of high concentration bilirubin. Also, folic acid deficiency is one of the causes certain type of anemia which is macrocytic anemia [3].Carbon nanotubes belong to the family of fullerenes, the third allotropic of carbon after graphite and diamond [4-5]. They are very stable molecules and this stability has caused some drawbacks in integrating the nanotubes with the current technology. The functionalization process is the most promising strategy for overcoming these difficulties. CNTs because of their extraordinary structural, mechanical, chemical, physical, electronic properties are important for basic science studies and practical applications and their important application is in the field of biomedical, biomaterials and biosensors technology for drug delivery systems [6-7]. However, theoretical studies have shown that an understanding on the mechanism of drug uptake by carbon nanotubes and its release at target cells without inflicting damage to normal cells is essential to justify successful application of CNTs as carrier

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vehicles [8]. Recently the interaction of functionalization SWCNTs with folic acid has been investigated because of the importance of such compounds as carriers in drug delivery systems [9-10] and since folic acid is an attractive ligand, it is useful for targeting cell membranes and enhancing CNTs endocytosis by the folate receptor [11-12]. Theoretical studies by Lu et al. demonstrated that SWCNTs are the most reactive due to their small diameter which is a determining parameter in nanotubes reactivity [13,14]. Computational studies on structural properties of drug interaction with carbon nanotube, for example interaction of carbon nanotubes with carboplatin [15], glycine [16], nimesulide [17], nifedipine [18] and different amino acids [19] have also been investigated theoretically using different computational methods. The present work indicates the results of quantum chemical calculations [20] on the electronic and structural properties interaction folic acid with covalent functionalization single-walled carbon nanotube. We calculated the dipole moments, molecular orbital energy analysis, and quantum molecular descriptors including electronic chemical potential (μ), global hardness (□), energy gap, and electronegativity (χ) of the complexes using Koopmans' theorem [21].

COMPUTATIONAL METHODS

In this work we studied, the interaction of folic acid drug molecules with covalently functionalized (7,0) zigzag SWCNT of finite length by simulation methods. We considered a (7,0) zigzag SWCNT consisting of 56 carbon atom that terminated with 14 hydrogen atom forming eight layer of carbon atoms along the tube axis. The C–C bond length in SWCNT is 1.42 A, which corresponds to C=C bond with sp^2 hybridization. The geometries of folic acid and f-SWCNT were individually optimized in gas phase. Also, folic acid molecule loaded with f-SWCNT was geometrically optimized (Fig. 1). The electronic and structural properties of the (7,0) zigzag single-walled carbon nanotube (SWCNT) and folic acid adsorbed on SWCNT were derived by means of density functional theory (DFT) method (Hohenberg and Kohn, 1964; Parr and Yang, 1989) with the B3LYP functional (Becke's three-parameter hybrid exchange functions using the Lee–Yang–Parr gradient-corrected correlation) (Becke, 1993; Lee Met al., 1988). For all systems, a geometry optimization calculation was performed using 6-311G(d) basis set. All calculations were carried out using the Gaussian 09 program [22].

The binding energy was calculated using the following equation [23]:

E_b=E(FA/SWCNT)-E(SWCNT)-E(FA) (1)

where E(FA/SWCNT) is the total electronic energy of the adsorbed folic acid molecule on the f-SWCNT after full geometry optimization. E(SWCNT) and E(FA) are the electronic energies of the SWCNT with functionalized group, and the folic acid molecule respectively. The energy corresponding to HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) respectively indicate the ionization potential of the molecule and electron affinity value. It is known that DFT methods give lower LUMO–HOMO gaps than HF methods, and that is why we use a hybrid method B3LYP for the calculation of the LUMO–HOMO gaps [24]. A high LUMO–HOMO energy gap represents greater stability and low reactivity of the chemical species. Also using the Koopmans' theory I= $-E_{HOMO}$ is the first vertical ionization energy and A= $-E_{LUMO}$ is the electron affinity of the molecule [25].

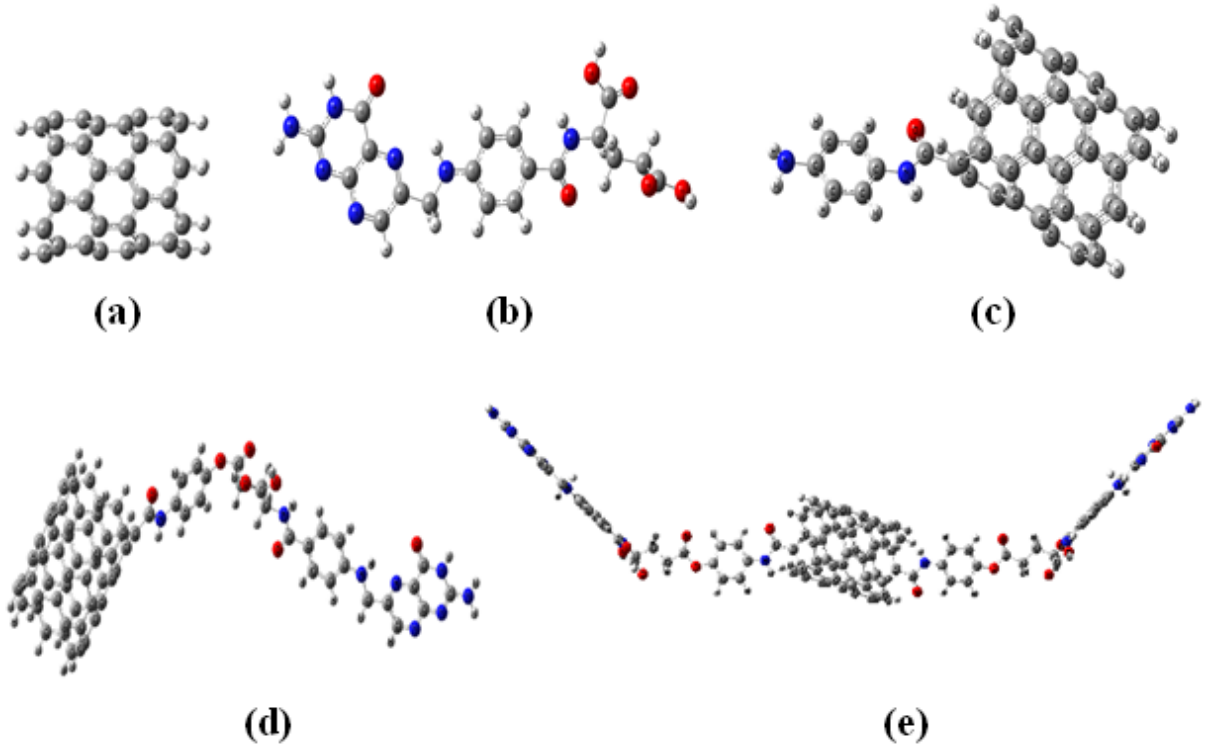

Fig.1. Optimized geometries of (a) (7,0) zigzag SWCNT, (b) Folic acid drug molecules, (c) (7,0)-SWCNT functionalized (d) and (e) functionalized (7,0)-SWCNT with one and two FA drug molecules.

RESULTS AND DISCUSSION

Fig. 1 shows the optimized structures of (7,0) zigzag carbon nanotube, folic acid molecule, and folic acid loaded onto (7,0)-SWCNT functionalized. For better understanding the nature of the interaction of (7,0)-SWCNT and FA, we examined the electronic structures of the functionalized (7,0) zigzag single-walled carbon nanotube with folic acid. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) in FA, and (7,0)-SWCNT are shown in Fig. 2 and FA loaded on (7,0)-SWCNT functionalized in Fig. 3. In (7,0) zigzag SWCNT the HOMO and LUMO orbitals integrated distributed throughout nanotube axis, which shows that covalent functionalization is preference throughout the nanotube (Fig. 2). For mono functionalized SWCNT–FA (Fig. 3), HOMO and LUMO are delocalized along C-C bonds parallel to nanotube axis. From the optimized geometries the stability and reactivity of system were determined by their global hardness (□) value, global softness (S), ionization potential, and energy gap. An increase in hardness leads to increase in stability and decrease in reactivity of the system. We observed the increase in functionalization leads to the decrease the energy gap in compare with SWCNT and FA drug. The energy gap characterizes the molecular chemical

stability and it is important parameter in determining molecular electrical properties. It is well known that molecules with high energy gap are kinetically stable. The calculation results of quantum molecular descriptors for functionalized single-walled carbon nanotube, folic acid drug molecules and f-SWCNT loaded with one and two folic acid drug are shown in Table 1. In order to investigate the interaction of FA drug with f-SWCNT the resulting binding energies given by Eq. (1) are studied.

Table 1. Quantum molecular descriptors for functionalized (7.0) zigzag SWCNT, FA, and functionalized SWCNT with FA drug molecules in gas phase (eV)

Descriptors	**Folic acid**	**f-SWCNT**	**f-SWCNT–1FA**	**f-SWCNT–2FA**
HOMO energy	-5.513	-4.150	-4.204	-3.988
LUMO energy	-2.378	-3.627	-3.683	-3.461
LUMO - HOMO gap	3.135	0.523	0.521	0.520
Electron affinity (A)	2.378	3.627	3.683	3.461
Ionization potential (I)	5.513	4.150	4.204	3.988
Global hardness (□)	1.567	0.261	0.260	0.263
Chem. Potential (μ)	3.945	3.888	3.943	3.724
Electronegativity (χ)	-3.945	-3.888	-3.943	-3.724

Table 2. Binding energies of FA, functionalized (7,0) zigzag SWCNT with one and two FA drug molecules, respectively

Parameter	FA	f-SWCNT–1FA	f-SWCNT–2FA
Binding energy (kcal/mol)	-	-13.612	-29.402

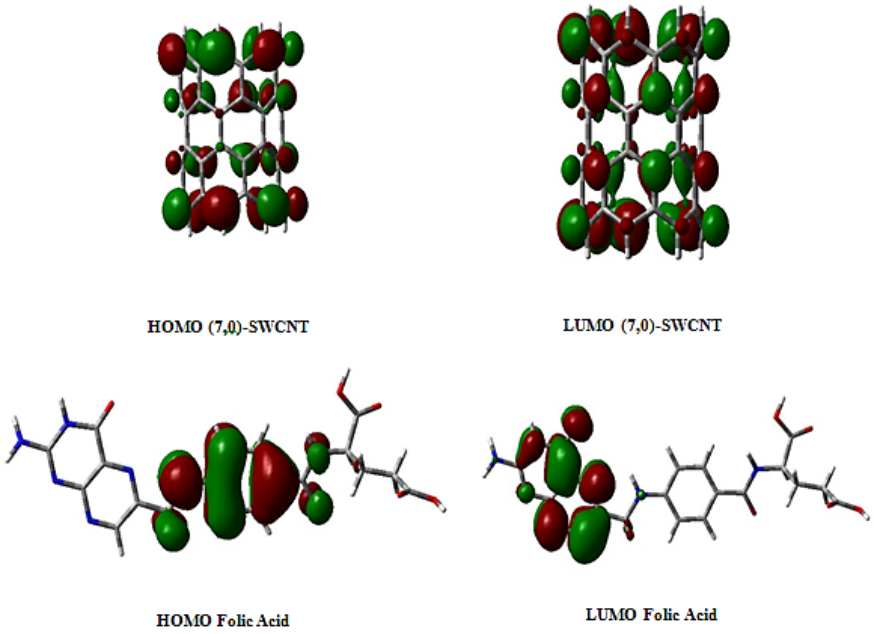

Fig. 2. DFT calculated HOMO and LUMO orbitals for (7,0)-SWCNT and FA drug molecules.

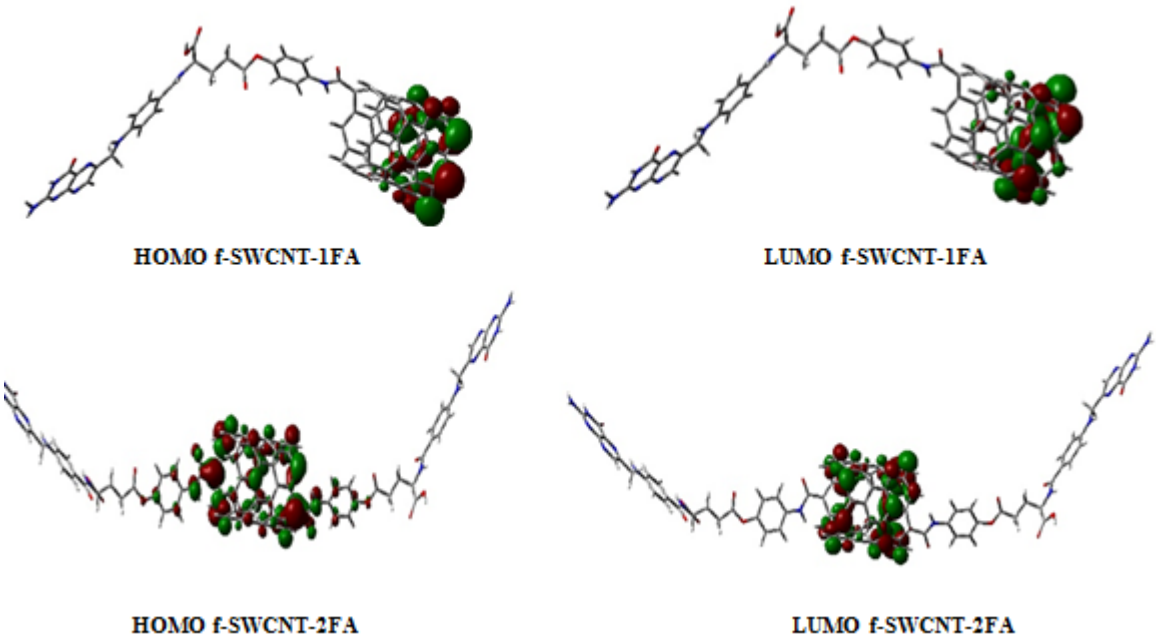

Fig. 3. DFT calculated HOMO and LUMO orbitals for functionalized (7,0)-SWCNT with one FA and two FA drug molecules.

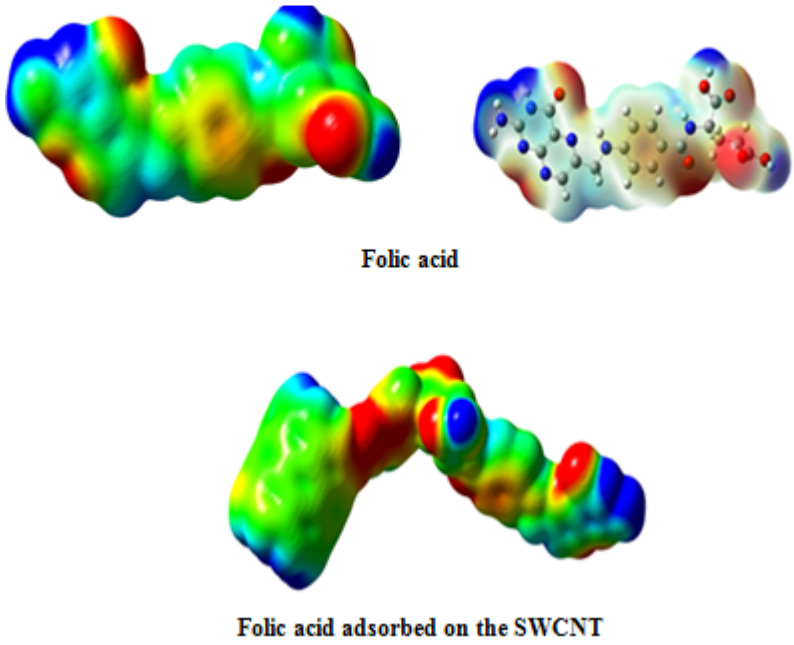

Fig. 4. The molecular electrostatic potential surface of folic acid and folic acid adsorbed on the SWCNT.

Tables 2 indicates that the binding energy values for mono functionalized and bi functionalized SWCNT are negative, this means that with increase in functionalization, the binding energy decreases indicating increase in thermodynamic stability of the system.

The MEP is a useful and important property to study of reactivity that an electrophile will be attracted to regions where the electron distribution effect is dominant (negative regions). The MEP means that the maximum of the negative region which is red and is suitable for the electrophilic attack and the maximum of the positive region which is blue and is preferred site for nucleophilic attack. The importance of MEP is that it can be simultaneously used to display molecular size, shape as well as positive, negative and neutral electrostatic potential regions in terms of color grading. For folic acid adsorption on (7,0) zigzag SWCNT, the MEP plot shows a strong positive electrostatic potential (blue color) and weak negative electrostatic potential (red color) occur at the end and opposite end regions of nanotubes, respectively, where the hydrogens are located (Fig. 4).

CONCLUSION

In this work we showed, a theoretical study on adsorption of FA drug on sidewall of functionalized (7.0)-SWCNT. Our results showed that thermodynamically covalent functionalization of SWCNT is favorable and energetically the SWCNT-FA system is stable. Also B3LYP calculation with 6-311G(d) basis set performed to obtained binding energies, dipole moment, molecular electrostatic potential, HOMO and LUMO energies. The results clearly indicated that electronic properties can be used for prediction of strength interaction between drug molecules and single-walled carbon nanotube. Table 1 shows that increasing the number of folic acid drug molecules loaded on(7,0)-SWCNT leads to

decrease in global hardness and energy gap, signifying that stability of the system decreases with functionalization. Finally, chemical shift of carbon nanotube sidewalls using covalently functionalized is effective method by which delivery of drug molecules, loading and treatment can be investigate.

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