Comparison of the Electron Donor-Acceptor and Sensing Capacity of The Selected CNTs in Drug Delivery Applications

Serap Senturk Dalgic, Fatma Kandemirli

Abstract **— Carbon nanotubes (CNT) have remarkable properties in drug delivery applications. Here, the size, shape, and functionalization effect on the electron-donor acceptor and sensing capability of the selected CNTs for drug delivery applications have been investigated using density functional theory (DFT). The anti-oxidative activity and toxicity have been calculated using quantum molecular / Frontier Molecular Orbital (FMO) parameters. The electrophile (w) values vary according to CNTs and the groups of drugs interacting with CNT. The electro-donating and electro-accepting powers have been computed based on the electron affinity and the ionization potential parameters. Therefore, the size, doping effect and electron-donor-acceptor MAP (DAM) of the studied CNTs have been thoroughly discussed. These findings define the system, paving the way for promising sensors in practical applications. These CNT sensors can be used to detect, recognize, and carry drugs for their medicinal applications, underscoring the relevance and importance of our research.**

Keywords**— Carbon nanotubes, Computational materials science, Materials science and technology, Nanotechnology, Nano sensors.**

I. INTRODUCTION

Carbon nanotubes (CNTs) have outstanding physicochemical properties [1]. Despite their toxic properties, CNTs are of great interest as biosensors or drug delivery systems in biomedical and tissue engineering [2]-[11]. Studies have shown that the toxicities of CNTs can be reduced by chemical functionalization, depending on the type of CNT [4],[5]. Many factors have been shown to mediate CNT toxicity, including shape, size, length, and diameter [6}. However, there is no consensus on the exact effect of all these factors on the CNT's toxicity, so building a picture of such factors will help in the future design of safer CNTs. On this line, we have focused on investigating the toxicity of CNTs that can be used in drug delivery applications.

Concerning the interaction of drugs with CNTs, perspectives of the Density Functional Theory (DFT) of chemical reactivity, electrophilicity(ω), and chemical hardness (η) investigations exist to define the electron donor-acceptor capability of drugs [12]- [14]. Parr et al. denoted electrophilicity as an "electrophilic" power [15]. Gazquez et al. [16] define the other response functions, such as the electro-donating (w^-) and electro-accepting (w+) powers, in terms of vertical IP and vertical EA values. Those response functions have been used to create the systems' donor-acceptor maps (DAMs) [17],[13],[14].

To understand the antioxidant or toxicity capacity of the drug on the pristine and Si-doped SWCNTs, we have selected Ribavarin(RBV) drug and single wall carbon nanotubes (SWCNTs). In our previous study [11], the adsorption and sensing properties of RBV on pristine and Si-doped CNTs have been investigated. Here, toxicity properties related to the electron donor-acceptor capacity of the drug-SWCNTs complexes have been considered. We have used chemical quantum calculations based on the Density Functional Theory (DFT) method to compare their electron donor-accepting capacities. We proposed a computational model to classify SİZE DEPENDENCY of electron donating and electron accepting properties of the molecules. It provides a new perspective on the antioxidative and toxic properties of drugs, depending on their size.

II. MATERIALS AND METHOD

The Ribavarin (RBV) drug molecule adsorption on two different (4,0) and (6,0) pristine and Si-doped SWCNTs (Si-SWCNTs) has been investigated by the DFT implemented in the Gaussian 09W [18]. The two samples of SWCNTs with different lengths are selected. The Si-doped CNTs with 31C and 8H atoms (Si-C31H8) as CNT1 with 9.206Å length and (4,0) diameter; another one, with 35 C and 12 H atoms (Si-C37H12) as CNT2 with 7.223Å and (6,0) diameter (in Fig. 1) were chosen for the comparison. The optimizations of all geometric structures were performed using M062X functional in conjunction with the 6-31G(d) level of theory by Gaussian 09W. In our previous study [11], we have a comparative investigation of the change in different sensing, electronic and structural properties before and after adsorption of RBV drug onto the nanotubes with different diameters and lengths. The effect of metal doping of small sized (4,0) and (6,0) CNTs on sensing properties and nano-carriers of RBV in drug delivery studies have been presented in Ref. [11].

Here, to give further insights into the geometric stability, sensitivity and reactivity of the studied systems, the electronic properties taken into account, such as chemical quantum descriptors and Frontier molecular orbital (FMO) analysis, were carried out. Fig.1 shows the optimized molecular structure of the selected pristine CNTs.

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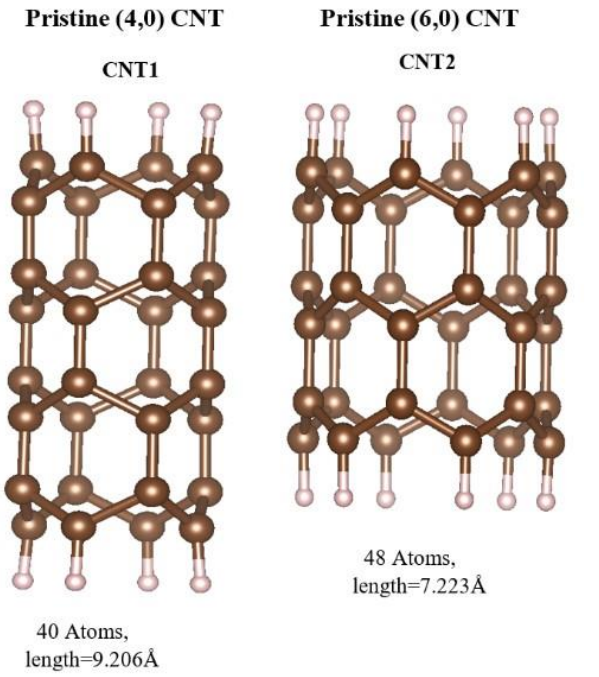


Fig. 1 (Color online) Side views of optimized pristine CNTs in different diameters and lengths (C brown, H pink)

Global quantum descriptors used in computational chemistry are a form of mathematical function that helps understand the molecules predicted in terms of quantum mechanical properties. Parameters such as electronic chemical potential (μ) (negative of electronegativity (-χ)) defined by $(\frac{\partial E}{\partial N})_V$, chemical hardness (η*) due to $\eta * = (\partial^2 E/\partial^2 N)_V$, and electrophilicity (ω) were computed by the following equations proposed by Parr and co-workers [15],

$$\mu = -\chi = -\frac{IP+EA}{2}, \qquad \eta * = IP - EA \tag{1}$$

$$\omega = \frac{\mu^2}{2\eta} \tag{2}$$

where IP and EA denote the ionization potential and electron affinity, respectively. The global hardness (η) indicates the system's resistance to charge transfer; that is, the higher the hardness value, the higher the electronic stability of the molecule.

The electrophilicity index (ω) proposed by Parr and co-workers [15] is the capacity of the molecule to accept an arbitrary number of electrons. To obtain some approximate expressions for the electrophilicity index (ω), we consider the ground state and valance state parabola models studied by Parr and co-workers [15] where the total energy of system taking into account with the electron number. They pointed that the energy of system at the ground state could produce using the Equations (1-2) from the maximal flow of electrons between the donor and acceptor by

$$\omega^* * \approx \frac{(IP+EA)^2}{8(IP-EA)} \tag{3}$$

It has been found a correlation between electrophilicity index (ω*) and electron affinity of some number of natural atoms/molecules in the ground state parabola model [ ].The second model of Parr and co-workers is the valance state parabola model. Within this model, chemical hardness (η) and electrophilicity (ω) are given by

$$\eta = (IP - EA)/2 \tag{4}$$

$$\omega \approx \frac{(IP+EA)^2}{4(IP-EA)} = 2\omega^* \tag{5}$$

Other parameters that correlate with the antioxidative activity of the studied complex structures are HOMO and LUMO energies, E_{HOMO} and E_{LUMO}, respectively. HOMO is always the highest occupied molecular orbital and LUMO is the lowest occupied molecular orbital. The energy of E_{LUMO} is related to the EA, while E_{HOMO} is due to the IP as IP=-E_{HOMO}, EA=-E_{LUMO} using the Koopmans relations.

Gazquez and co-workers [16] have taken into account the hardness definition given in Eq. (4) in terms of E_{HOMO} and E_{LUMO} energies by (η=(E_{LUMO}-E_{HOMO})/2 .

Gazquez and co-workers have also proposed the electron donating (w-) and electron accepting(w+) powers in terms of vertical IP and vertical EA values by the following equations,

$$\omega^+ = \frac{(IP+3\,EA)^2}{16(IP-EA)} \tag{6}$$

$$\omega^- = \frac{(3IP+\,EA)^2}{16(IP-EA)} \quad . \tag{7}$$

On this line, global response functions are defined so that chemical reactivity can be understood easily. Using the above equations, the computed DAM of neutral, cationic, and anionic systems is most beneficial for classifying any substance regarding its electron-donating-accepting capability. Thus, the DAM of the studied compounds presents a qualitative comparison among them.

III. RESULTS AND DISCUSSION

As mentioned above, two samples of pristine and Si-SWCNTs were optimized separately before creating the drug/CNTs (here after SWCNTs called as CNTs) complex structures. All the single point calculations, we have minimized the all structures and their positive frequencies. We have examined the interactions between RBV and CNTs with different diameters and length in our previous study [11]. We referee it for the details of DFT calculations. Here, we are focusing on the correlation of the electron accepting/ electron donating power for netural systems which is proportional with the electrophilicity of w*, between electron affinity of the studied RBV/CNTs or RBV/Si-CNTs complexes composed with RBV drug and CNTs/Si-CNTs.

Electronic properties of RBV drug, CNTs, Si-CNTs and their complexes formed with the interaction of drug and surfaces, EA, IP, η, ω, ω* are summarized in Table 1.

The lowest IP values among the complex structures given in Table 1 are the RBVdrug/Si-CNT2(6,0) complexes.

Since IP, which is the first antioxidant mechanism, indicates the ease of donating electrons to the studied complexes due to electron abstraction, structures with lower IP values can be oxidized more easily. However, molecule presenting a low electrophilicity power may be considered as a nucleophile.

TABLE I Electron affinity (EA), Ionization potential (IP),

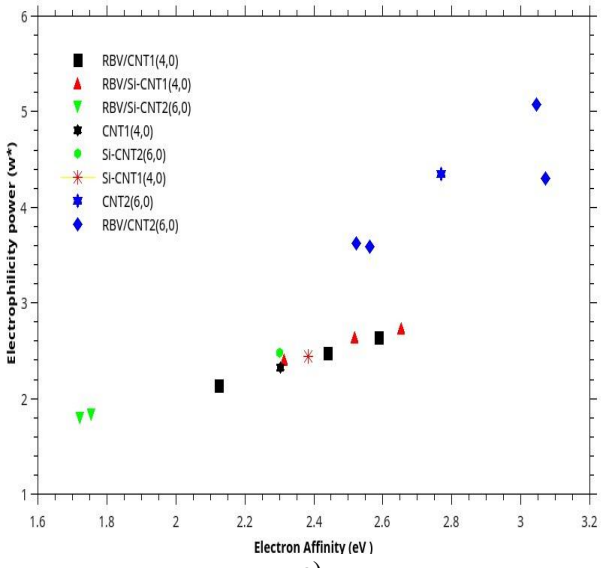
chemical hardness (η), electrophilicity (ω) and electrophilicity (ω*) of ground state model (All energies are in e V).

Structure		EA	IP	η	ω	ω*
	RBV	0.330	8.638	4.153	2.420	1.210
CNT (4,0) CNT1		2.304	6.219	1.958	4.638	2.319
	H_{27}	2.125	6.014	1.944	4.259	2.130
	H_{18}	2.441	6.352	1.955	4.942	2.471
	H_{25}	2.589	6.502	1.956	5.282	2.641
(4,0)Si -CNT1		2.383	5.874	1.745	4.882	2.441
	O_1	2.519	5.814	1.647	5.271	2.635
	O_3	2.654	6.395	1.870	5.471	2.735
	N_8	2.315	5.433	1.559	4.814	2.407
(6,0) CNT2		2.769	4.139	0.685	8.704	4.352
	O_1	2.522	3.984	0.730	7.243	3.621
	O_3	3.045	4.418	0.686	10.15	5.075
	H_{25}	3.071	4.931	0.930	8.605	4.302
	O_5	2.562	4.109	0.774	7.187	3.593
(6,0)Si -CNT2		2.301	4.947	1.323	4.962	2.481
	O_4	1.722	4.008	1.143	3.590	1.795
	O_5	1.755	4.063	1.154	3.667	1.833

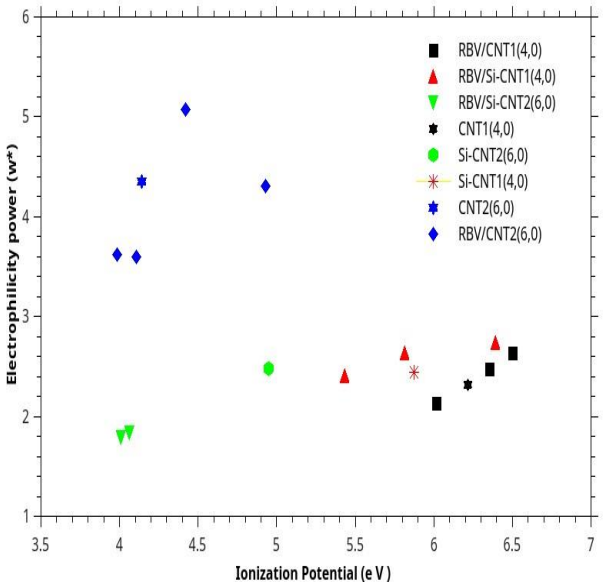
The electrophilicity of (6,0) CNT2 is greater than (4,0) CNT2. So, (6,0) CNT2 is more easily oxidized than (4,0) CNT2. Similarly, Si doped (6,0) CNT2 is oxidized more easily than (4,0) CNT1. When RBV is bonded to (6,0) CNT2 and (4,0) CNT1 with the O3 atom, the oxidation ability of the complex decreases. EA refers to the energy change resulting from the addition of a single electron, whereas the energy decrease associated with maximum electron flux is characterized by ω.

Although the relationship between electron affinity and electrophilicity power w* is similar in the complexes obtained with (4,0) CNT1, (6,0) CNT2 and Si doped (4,0) CNT1, the electrophilic power in (6,0) CNT is higher than the electron affinity.

We are focusing on the correlation of the electron accepting/ electron donating power of the electrophilicity of w*, between electron affinity/ionization potential of the studied systems. We proposed that correlation can be deduced from Eq. 3 and IP / EA values of the systems and shown in Figs 2, respectively. Figs 2. have shown the size dependency of electrophilicity w*.



a)



b)

Fig. 2. Correlation between the electrophilicity power (w*) and (a) Electron Affinity (EA) , (b) Ionization Potential (IP), (All energies are in e V)

In Fig. 2a, it is clear that there are a linear relation between EA and w* for the complex structures of RBV/CNTs except RBV/CNT2(6,0). In Fig. 2b, the size effect is clearly shown as the linearity between the IP and w* was occurred for each CNTs with different diameters.

We have calculated the electron powers for donating (w-) and accepting(w+) using the IP and EA values for neutral systems given in Table 1 using the equations (6) and (7). With the parameters of w+ and w-, it is possible to determine the Electron Donor-Acceptor Map (DAM) of studied complexes. The computed DAM graph for neutral RBV, CNTs, Si-CNTs, RBV/CNTs and RBV/Si-CNTs is illustrated in Fig. 3.

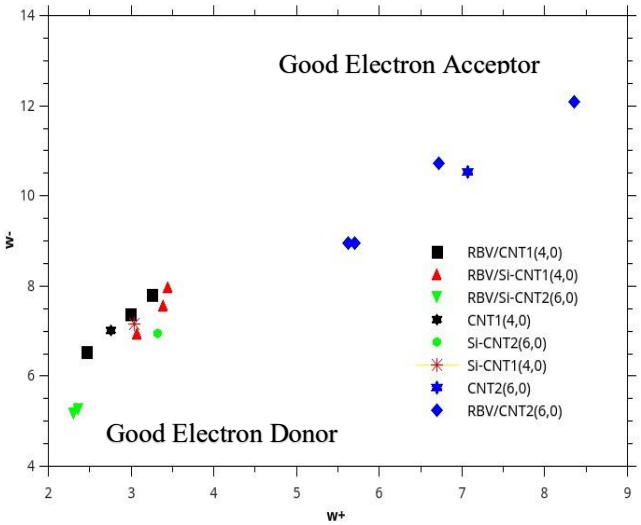


Fig. 3. Electron Donor-Acceptor Map (DAM) of RBV drug on pristine and Si-CNTs with different diameters. (values are in e V)

To investigate the oxidant capacity of CNTs for RBV drug, the analysis of the electron donor-acceptor properties was obtained using the DAM for each studied systems. It was noted in Fig. 3, that the electron acceptor capacity increases with the diameter increases of CNTs from (4,0) to

(6,0) zigzag CNTs.

Results of Fig. 3 indicate that the complex structures of RBV drug with Si-CNT2(6,0) are the best electron donors. The best electron acceptor complex structures are composed of RBV drug with prıstine (6,0) CNTs.

Molecules having low ω^- values are good electron donor while, molecules having high ω^+ values are good electron acceptor molecules.

These results for RBV drug are important to show the reactivity of these complexes helps to explain the toxicity. The RBV/CNT2(6,0) complexes are good oxidant complexes since they are the good electron acceptor. Thus pristine (6,0) CNT2 is more oxidant than others such as the smaller diameter one and Si doped CNT2 with their complexes. It is agreeing with literature. Thus the long size CNTs may be more toxic then smaller ones. [5], [6],[13].

Fig. 3 shows RBV/Si-CNT2(6,0) complexes are good electron donor, thus RBV molecule is a good antioxidant molecule on Si-CNT2(6,0).

IV. Conclusions

The relationship between the electron accepting/electron donating power and w* electrophilicity of the RBV drug and CNTs was studied. w* values were obtained from equation 3.

We have found that the electron acceptor capacity increases with the diameter increases of CNTs from (4,0) to (6,0) zigzag CNTs. Prıstine (6,0) CNT2s are better oxidant than others since they are good electron acceptors. Thus, Prıstine (6,0) CNT2s may be the most toxic in the studied systems. However, Si-CNT2(6,0) complexes can be the less toxic because it is worse electron acceptor.

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