Structural, energetic and electrical properties of encapsulation of penicillamine drug into the CNTs based on vdW-DF perspective

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HIGHLIGHTS

• We have studied the various diameters and kinds of SWCNTs.
• Detailed information of structure, electronic properties, stability and reactivity descriptor data provided.
• Introducing suitable SWCNTs as an efficient carrier for penicillamine drug.
• The vdW forces can be effects on the binding properties.

GRAPHICAL ABSTRACT

The binding energies of the complex of penicillamine with (14,0) CNT is about 15 kcal/mol which is in the range of physisorption and suitable for drug delivery.

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ABSTRACT

First-principles van der Waals density functional (vdW-DF) calculation using GGA/PBE functional and DZP basis set implemented in the SIESTA package was carried out to investigation the encapsulation of penicillamine drug into the both armchair and zigzag single wall carbon nanotubes (SWCNTs). The results reveal that the drug encapsulated inside the CNT cavity is weakly bounded. The obtained results of binding energies indicated that incorporation of drug is favored inside the zigzag SWCNTs compared with armchair counterparts. We address here the role of vdW interaction for penicillamine drug when inclusion in the CNTs. It worth mentioning that encapsulation of vdW forces can be effects on the binding properties. The electronic structures and Mulliken charge population are analysed for the energetically most favorable complexes which shows that encapsulated penicillamine changes slightly the electronic properties of SWCNTs and trivial charges are transferred from drug to CNTs during encapsulation process.

Global reactivity descriptor values such as electronegativity (χ), global hardness (η), global softness (S), electronic chemical potential (μ), and electrophilicity index (ω) were calculated. We anticipated that these findings supply the new way and value information for help in the experimental study and future applications.

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1. Introduction

The discovery of carbon nanotubes (CNTs) in 1991 by Iijima [1] have attracted deal of attention because, structural, unique properties and special geometry is used in biological application [2–4], pharmaceutical drug delivery system [5–7], electronic devices and transistor [8, 9] and other applications. CNTs exhibit enormous benefits to be applied as drug delivery vehicles. For instance, CNTs have large hollow space for encapsulation of drug molecule. Furthermore, SWCNTs may have metallic or semi-conducting nature depending on size and chirality and provide ideal surroundings to shield encapsulated drug from degradation.
Drug delivery by CNTs, recommend several biochemical problems about the interaction between drugs and carbon nanotube when drug encapsulated inside the nanotube. There are several experimental \cite{10,11} and theoretical \cite{12} studies concerning this matter. The main challenge in biomedical application of carbon nanotubes is low solubility in organic media, that for solves this problem we modification by functionalization for example by 1,3-dipolar cycloaddition \cite{13} Diels–Alder \cite{14} surfactant molecules \cite{15}. Also this compound used delivery of drug with low toxicity \cite{16}. They play an important role in biomolecule delivery for instance nucleic acids \cite{17,18} proteins \cite{19,20} vitamin A \cite{21}, carriers of drugs \cite{22,23}. We can use carbon nanotubes for treatment of diseases for instance tuberculosis \cite{24} and cancer \cite{24}. Farm-ancedeh and Ghazanfary considered the interaction between zig-zag and armchair BNNT nanotubes and collagen amino acid for drug delivery based on DFT method \cite{25}. C.Deca et.al investigated adsorption of isoniazid drug on the pristine and B-doped nanotubes based on theoretical study \cite{26}. Darvish Ganji and Sabet carried out theoretical study on the complex formation of fluorouracil drug and cucurbit[n]urils \cite{27}. In previous study we illustrate the interaction on lamivudine drug with CNTs \cite{28} and oxazepam drug with CNT \cite{29} based on vdW-DF treatment.

In present study, we elucidated the interaction between penicillamine drug and series of metallic and semiconducting nanotubes and then considered orientation and electronic structures based on vdW-DF calculations.

2. Computational details

The ab initio calculations of the CNTs and penicillamine drug are studied based on the density functional theory (DFT) \cite{30,31}, using the SIESTA code \cite{32–34} which solves the standard Kohn–Sham equations and has been demonstrated to be very efficient for large atomic systems. In order to avoid interaction between two layers, the vacuum space is applied 30 Å. In addition, it is important to investigate nonlocal corrections pertaining to dispersion interactions. Because conventional DFT methods do not describe van der Waals interactions, we implement the fully self-consistent vdW-DF at the theoretical GGA level, with the PBE exchange functional being favorable for calculating vdW interactions \cite{28,29,35} in DFT and the standard norm-conserving Troullier–Martins pseudo-potentials \cite{36}. For a better description of physical quantities, a high dense Brillouin zone sampling is necessary and the Monkhorst-Pack block was set to $1 \times 1 \times 5$ denser for geometry optimization. It was increased to $1 \times 1 \times 15$ for the determination charge transfer and density of states (DOS). A cut-off energy of 150 Ry was set for grid integration which presents a good accuracy. The relaxed atomic structures of the tubes were obtained by minimization of the total energy using Hellmann–Feynman forces, including Pullay-like corrections. Structural optimizations were performed using the conjugate gradient algorithm until the residual forces were smaller than 0.02 eV Å$^{-1}$. The valence electrons of all systems were explained by means of a double-$ζ$-pseudoatomic basis set consisting of polarization functions (DZP). The range of those basis functions was controlled by the energy shift parameter, which was set to 0.05 eV.

3. Results and discussion

To evaluate the interaction between a penicillamine drug and CNTs, we first calculated the binding energy ($E_b$) of penicillamine-CNT complexes. The binding energy calculations in the systems under consideration were obtained according to the following equation:

$$E_b = E_{CNT-Penicillamine} - (E_{CNT} + E_{Penicillamine})$$

where $E_{CNT-Penicillamine}$, $E_{CNT}$, $E_{Penicillamine}$ are the total energies of the relaxed Penicillamine-CNTs complex, isolated CNTs and isolated penicillamine respectively. According to this definition, a negative $E_b$ values indicates that the inclusion of penicillamine drug in to the CNTs is energetically favorable.

Pristine drug molecule and Drug@SWNTs complexes (Figs. 1, and 2) when penicillamine drug is encapsulated in the SWNTs were separately geometry optimized.

The binding energy values of single penicillamine molecule included in to the various types of SWCNTs with different diameters, such as armchair (6,6)(7,7)(8,8)(9,9) and zigzag (10,0), (11,0)(12,0)(13,0)(14,0)(15,0) nanotubes were computed as shown in Table 1 density functional theory (DFT) results demonstrated that among all selected armchair and zigzag nanotubes, CNT (8, 8) and CNT (14, 0) can form the most binding strengths complex.

The binding energies and equilibrium distances between the closest atom of the Penicillamine drug (H atom) and CNT8,8 are around $–0.245$ eV (–5.647 kcal/mol), 3.51 Å respectively. The same calculations are carried out for penicillamine@CNT14,0 complex. The binding energy and equilibrium distances between the closest atom of the Penicillamine drug (H atom) and CNT14,0 are around $–0.643$ eV (–14.821 kcal/mol), 2.98 Å respectively. (see Fig. 2(a) and (b)).

The calculated binding energies all the considered Drug@CNTs complexes are summarized in Table 1. Here it is useful to compare the binding energies of these complexes with van der waals(vdW) forces as shown is Table 1. All these binding energy are increased when the vdW interactions are included. As a result the binding energies for the Drug@CNT8,8 and Drug@CNT14,0 complexes are changed from $–0.245$ eV (–5.647 kcal/mol) and $–0.643$ eV (–14.821 kcal/mol) to $–0.265$ eV (–6.108 kcal/mol) and $–0.646$ eV (–14.89 kcal/mol) respectively which indicates dominant role of vdW interaction in this process. Furthermore, we compare the pristine CNTs diameters before and after the encapsulation of drug molecule in to the aforementioned CNTs from 10.81 Å, 10.96 Å to 11.10 Å.
Table 1
The calculated binding energies of Drug@CNTs in presence vdW and non-vdW interactions.

<table>
<thead>
<tr>
<th>Drug@CNTs</th>
<th>6,6</th>
<th>7,7</th>
<th>8,8</th>
<th>9,9</th>
<th>10,0</th>
<th>11,0</th>
<th>12,0</th>
<th>13,0</th>
<th>14,0</th>
<th>15,0</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_b$ (eV)-NonVdw</td>
<td>3.57</td>
<td>0.347</td>
<td>-0.245</td>
<td>0.083</td>
<td>5.249</td>
<td>1.803</td>
<td>-0.171</td>
<td>-0.336</td>
<td>-0.643</td>
<td>-0.470</td>
</tr>
<tr>
<td>$E_b$ (eV)-Vdw</td>
<td>3.55</td>
<td>0.324</td>
<td>-0.265</td>
<td>0.0714</td>
<td>5.246</td>
<td>1.804</td>
<td>-0.177</td>
<td>-0.339</td>
<td>-0.646</td>
<td>-0.466</td>
</tr>
</tbody>
</table>

Fig. 2. Geometric parameters of the optimized structure of (a) Drug@CNT8,8 (b) Drug@CNT14,0 complexes (c) binding distance between closest atom of Drug@CNT8,8 (d) Drug@CNT14,0.
respectively as shown in Fig. 3. With increase in CNTs diameter for armchair nanotubes the binding energies will be increased but for Drug@CNT9,9 is decreased. The same findings are achieved for zigzag counterparts as increase in CNTs diameter for zigzag nanotubes the binding energies will be increased but for Drug@CNT15,0 is decreased which illustrate that diameter of CNTs play a key role in determining the reactivity CNTs. Based on the change in the electronic structure of these systems, a negligible value of electrons is transferred in the encapsulation process between CNTs and drug molecule. Upon the Mulliken population analyses (MPA) [37] exhibit that about (0.053 e) and (0.055 e) charge transferred from the penicillamine drug molecule to the CNT(8,8) and (14,0) complexes respectively. The molecular orbital contribution plays a vital role in determining the charge transfer phenomenon. It can be seen that the electron density of HOMO are localized on the penicillamine drug while LUMO are contributed on the CNTs for both of the stable complexes which is consistent with obtained results of charge transfer (see Fig. 4(a) (b) (d) (e)).

The isosurface plots of total electron density are shown in Fig. 4 (c and f). As results a weak overlapping of electron clouds between CNTs and drug molecule was observed. To deeper understand of nature of bonds between drug molecule and selected CNTs we illustrated analysis of electron structure based upon the density of states (DOSs). As shown in Fig. 5(a and b) a negligible change in the DOS spectra for both energetically favorable complexes before and after encapsulation process can be found. In other words, there is no distinct difference between pristine CNTs and Drug@CNTs complexes and there is not the new peak near of the fermi level.

The low difference the Fermi level of CNT8,8 (\(E_f = -4.585 \text{ eV}\)) and Drug@CNT8,8 (\(E_f = -4.573 \text{ eV}\)) and also CNT14,0 (\(E_f = -4.574 \text{ eV}\)) and Drug@CNT14,0 (\(E_f = -4.555 \text{ eV}\)) noticeably indicates a weak charge transfer between them in the encapsulation phenomenon (see Table 2). This finding shows the presence of physical interaction between them.

To have better understand of these interactions, the partial density of states (PDOSs) of the H atom of drug molecule and C atom of CNT8,8 and CNT14,0 were considered (see Fig. 6(a and b)). The obtained results show that the S orbital of H atom of drug molecule and Py orbital of C atoms of both selected CNTs overlapped in the range of \(-5 \text{ eV}\) to \(5 \text{ eV}\).
Fig. 4. The calculated orbital localized (a) HOMO (b) LUMO (c) Total density of Drug@CNTR8,8 complex and (d) HOMO (e) LUMO and (f) Total density of Drug@CNTR14,0 complex.
The above results shows that the penicillamine drug encapsulated inside the CNTs cavity is weakly bounded. The study of electronic structure, binding energy and Mulliken analysis indicated that there presences weak interaction between penicillamine drug and armchair and zigzag nanotubes. It can be found that CNTs can not to be ideal material for drug delivery.

Furthermore, we used the quantitative chemical concepts in density functional theory (DFT) [38] such as chemical potential ($\mu$) [39], global hardness ($\eta$) [40], global softness ($S$), electrophilicity index ($\omega$) [41], electronegativity ($\chi$) for realize of molecular reactivity.

The stability of molecule is related to hardness which is tool to understand chemical reactivity.

$$\eta = \frac{1}{2} (I - A)$$  \hspace{1cm} (1)

$$S = \frac{1}{2\eta}$$  \hspace{1cm} (2)

$$\mu = -\chi = -\frac{1}{2} (I + A)$$  \hspace{1cm} (3)

where $I = -E_{\text{HOMO}}$, highest occupied molecular orbital energy) is the ionization potential and $A = -E_{\text{LUMO}}$, lowest unoccupied molecular orbital energy) is the electron affinity. From the Koopmans’ [42] theorem for closed shell molecules, we can say that, $I$ and $A$ values can be replaced by the Frontier orbital energies given by HOMO and LUMO:

$$I = -E_{\text{HOMO}} \text{ and } A = -E_{\text{LUMO}}$$  \hspace{1cm} (4)

The electrophilicity index defined by Parr [43] and provides information about the activity and toxicity of molecules is given as below equation

$$\omega = \frac{\mu^2}{2S}$$  \hspace{1cm} (5)

The quantum molecular descriptors for the Drug@CNTs, pristine Drug and pristine CNTs are depicted in Table 3.

When penicillamine drug encapsulated in to the armchair and zigzag SWCNTs the quantum molecular descriptors are changed. In metallic complexes the hardness, electrophilicity and electronic chemical potential of complex will be decreased which means that stability of the complexes are lower than pristine CNTs, as well softness will be reduced as shown in Table 3 while for energetically favorable zigzag complex the hardness before and after encapsulation around remained unchanged and electrophilicity is decreased. In other words, encapsulation process inside the zigzag nanotubes does not affect on the hardness index. The hardness of Drug@CNT8,8 complex is smaller compared with Drug@CNT14,0 complex which indicates reactivity of Drug@CNT8,8 system is higher compared with Drug@CNT14,0 system (see Table 3). On the other hand, the small harness value means the chemical activity and as a result low chemical stability. In addition, between complex aforementioned, Drug@CNT14,0 has higher value of electron affinity compared with armchair complex counterparts which indicate that it can easily accept the electrons. As shown in Table 2 we found that with increase in nanotubes diameter the gap energies are increased while for zigzag complexes at first increased form (10,0) to (11,0) and decreased for (12,0) and then increased form (13,0) to (15,0) which indicated that chirality plays a vital role in nanotubes reactivity.

The gap energies difference of CNTs in Drug@CNT8,8 and Drug@CNT14,0 complexes before and after encapsulation process are investigated. The obtained results shows that these changes are negligible a round 0.013 eV and 0.010 eV respectively that indicates high reactivity and conductivity of these complexes as shown in Table 3. It can be seen that the chemical potential ($\mu$) values for armchair complexes are increased which means that reactivity are improved. We also compared the chemical potential for energetically preferable complexes of both armchair and zigzag
and after inclusion process of zigzag SWCNTs is lower than Drug@CNT8,8 and also the gap energy difference of CNTs before is good agreement with obtained results of hardness value. As a chemical potential Isolated Drug and pristine CNTs.

### Table 3

<table>
<thead>
<tr>
<th>Species</th>
<th>$\mu$ (eV)</th>
<th>$\chi$ (eV)</th>
<th>$\eta$ (eV)</th>
<th>$S$ (eV)</th>
<th>$\omega$ (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNT6.0@Drug</td>
<td>-4.47</td>
<td>4.47</td>
<td>0.5385</td>
<td>0.929</td>
<td>18.55237</td>
</tr>
<tr>
<td>CNT7.2@Drug</td>
<td>-4.484</td>
<td>4.484</td>
<td>0.5235</td>
<td>0.956</td>
<td>19.20368</td>
</tr>
<tr>
<td>CNT8.8@Drug</td>
<td>-4.581</td>
<td>4.581</td>
<td>0.61</td>
<td>0.819</td>
<td>17.20128</td>
</tr>
<tr>
<td>CNT9.9@Drug</td>
<td>-4.563</td>
<td>4.563</td>
<td>0.566</td>
<td>0.883</td>
<td>18.39308</td>
</tr>
<tr>
<td>CNT10.0@Drug</td>
<td>-4.504</td>
<td>4.504</td>
<td>0.346</td>
<td>1.44</td>
<td>29.31505</td>
</tr>
<tr>
<td>CNT11.0@Drug</td>
<td>-4.427</td>
<td>4.427</td>
<td>0.4555</td>
<td>1.097</td>
<td>21.51298</td>
</tr>
<tr>
<td>CNT12.0@Drug</td>
<td>-4.546</td>
<td>4.546</td>
<td>0.106</td>
<td>4.716</td>
<td>97.48168</td>
</tr>
<tr>
<td>CNT13.0@Drug</td>
<td>-4.578</td>
<td>4.578</td>
<td>0.269</td>
<td>1.858</td>
<td>38.95555</td>
</tr>
<tr>
<td>CNT14.0@Drug</td>
<td>-4.572</td>
<td>4.572</td>
<td>0.409</td>
<td>2.222</td>
<td>25.55401</td>
</tr>
<tr>
<td>CNT15.0@Drug</td>
<td>-4.606</td>
<td>4.606</td>
<td>0.089</td>
<td>5.617</td>
<td>119.1867</td>
</tr>
<tr>
<td>Pristine CNT6.6</td>
<td>-4.522</td>
<td>4.522</td>
<td>0.357</td>
<td>0.897</td>
<td>18.43718</td>
</tr>
<tr>
<td>Pristine CNT7.7</td>
<td>-4.511</td>
<td>4.511</td>
<td>0.579</td>
<td>0.863</td>
<td>17.88567</td>
</tr>
<tr>
<td>Pristine CNT8.8</td>
<td>-4.591</td>
<td>4.591</td>
<td>0.0635</td>
<td>0.828</td>
<td>17.46254</td>
</tr>
<tr>
<td>Pristine CNT9.9</td>
<td>-4.627</td>
<td>4.627</td>
<td>0.622</td>
<td>0.804</td>
<td>17.20991</td>
</tr>
<tr>
<td>Pristine CNT10.0</td>
<td>-4.563</td>
<td>4.563</td>
<td>0.309</td>
<td>1.62</td>
<td>33.69089</td>
</tr>
<tr>
<td>Pristine CNT11.0</td>
<td>-4.525</td>
<td>4.525</td>
<td>0.5045</td>
<td>0.992</td>
<td>20.29299</td>
</tr>
<tr>
<td>Pristine CNT12.0</td>
<td>-4.468</td>
<td>4.468</td>
<td>0.0145</td>
<td>34.48</td>
<td>688.3801</td>
</tr>
<tr>
<td>Pristine CNT13.0</td>
<td>-4.528</td>
<td>4.528</td>
<td>0.3335</td>
<td>1.499</td>
<td>30.73881</td>
</tr>
<tr>
<td>Pristine CNT14.0</td>
<td>-4.553</td>
<td>4.553</td>
<td>0.404</td>
<td>2.475</td>
<td>25.6557</td>
</tr>
<tr>
<td>Pristine CNT15.0</td>
<td>-4.455</td>
<td>4.455</td>
<td>0.018</td>
<td>27.77</td>
<td>575.0694</td>
</tr>
<tr>
<td>Drug</td>
<td>-3.467</td>
<td>3.467</td>
<td>2.0255</td>
<td>0.243</td>
<td>2.928158</td>
</tr>
</tbody>
</table>

CNTs. It was found that the CNT8,8@Drug complex has a higher chemical potential ($\mu$) compared with zigzag counterparts which is good agreement with obtained results of hardness value. As a result, due to the harness of Drug@CNT14,0 is lower than Drug@CNT8,8 and also the gap energy difference of CNTs before and after inclusion process of zigzag SWCNTs is lower than armchair counterparts, we can concluded that Drug@CNT14,0 is better than Drug@CNT8,8 but is not suitable vehicle for drug delivery.

### 4. Conclusion

In the present study, we report a theoretical study of encapsulation of penicillamine drug molecule into the both armchair and zigzag CNTs. Our obtained results indicated that zigzag nanotubes was energetically favorable than armchair counterparts. In addition, the vdW forces play a vital role in the structural stability. Based on molecular orbital, for both energetically favorable complexes the HOMOS orbital are localized on the penecillamine drug whereas LUMO are contributed on the CNTs which confirmed with a help mullicken charge population analysis. Analysis of electronic structure and mullicken population indicates that both of armchair and zigzag nanotubes with penicillamine drug molecule are interact weakly. Some theoretical findings such as binding energies, charge transfer, density of states plots and total density introduce the CNTas an efficient carrier for delivery of penicillamine drug in nanomedicine domain.

### References