Relaxations of fluorouracil tautomers by decorations of fullerene-like SiCs: DFT studies

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Decorations of silicon carbide (SiC) fullerene-like nanoparticles by fluorouracil (FU) and its tautomers are investigated through density functional theory (DFT) calculations. Two models of fullerene-like particles including Si12C8 and Si8C12 are constructed to be counterparts of decorated hybrid structures, FU@Si12C8 and FU@Si8C12, respectively. The initial models including original FU and tautomeric structures are hybridized and then combined for further optimizations in the hybrid forms. Covalent bonds are observed for FU@Si12C8 hybrids, whereas non-covalent interactions are seen for FU@Si8C12 ones. The obtained properties indicated that Si12C8 model could be considered as a better counterpart for interactions with FU structures than Si8C12 model. The results also showed significant effects of interactions on the properties of atoms close to the interacting regions in nanoparticles. Finally, the tautomeric structures show different behaviors in interactions with SiC nanoparticles, in which the SiC nanoparticles could be employed to detect the situations of tautomeric processes for FU structures.

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1. Introduction

Fluorouracil (or 5-fluorouracil, FU) has been used as an anticancer drug to treat various types of cancers for several years [1]. The advantages of this drug have still kept it useful for medical treatments of patients, but on the other hand, too many side effects are arisen for its users [2]. Therefore, considerable efforts have been dedicated to recognize various aspects of this drug and the method to increase its safety for patients for many years [3,4]. By the introduction of nanotechnologies, combinations of nanostructures with FU derivatives are proposed to be helpful for medical purposes [5–8]. Researchers of various fields have drastically explored other novel materials in addition to pioneering fullerenes and carbon nanotubes [9,10]. As a result, several types of nanostructures are now recognized including nanoparticles [11], nanocones [12], nanorods [13], nanorings [14], graphenes [15], and some other types. The results also indicated the possibilities of existence of non-carbon nanostructures, which could show polarities versus non-polar carbon nanostructures [16,17]. Stabilities and properties of silicon carbide (SiC) nanostructures have been investigated computationally and experimentally [18–20]. Earlier researches demonstrated that both carbon and non-carbon nanostructures could be physically or chemically decorated by other atoms and molecules to make new hybrid systems with new properties [21–23]. Among Those, biologically related decorations of nanostructures could be expected to make more useful compounds for applications in life sciences and technologies [24]. Within this research, we investigated decorations of two representative SiC fullerene-like nanoparticles by FU species to construct SiC–FU hybrids (Fig. 1) through quantum computations. In addition to the original di-keto form, we also considered other keto-enol and di-enol tautomeric structures of FU for decorations of SiC nanoparticles. The tautomeric structures could lead to mutations in biological systems; therefore, they are important to be carefully examined for organic and bioorganic compounds [25]. Our obtained results revealed that different situations of decorated systems depend on tautomeric structures and combined SiC nanoparticles.

2. Computational details

Density functional theory (DFT) calculations are performed to employ the B3LYP exchange-correlation functional and the 6-31G* standard basis set as implemented in the Gaussian 98 program [26]. The models include the original di-keto, tautomeric keto-enol, di-enol forms of FU and two models of SiC fullerene-like
nanoparticles (Fig. 1, panel A). The hydrogen atoms were moved to other proper atomic positions in the FU structure to make keto-enol and di-enol tautomers [27]. To construct the SiC fullerene-like nanoparticles, two systems with twenty atoms for each one, Si$_{12}$C$_8$ and Si$_8$C$_{12}$, were constructed based on the presence of Si–Si and C–C direct bonds. After constructing the initial models, all individual models were optimized to their minimum-energy levels. Subsequently, the original and tautomeric FU structures were allowed to relax on the surface of each pre-optimized SiC nanoparticles and construct the FU-decorated SiC hybrids (FU@SiC) (Fig. 1, panels B and C). The optimization processes yielded molecular properties (Table 1): dipole moments and various types of energies including total energies, binding energies, and energies for the highest occupied molecular orbitals (HOMO) and the lowest unoccupied ones (LUMO). To evaluate binding energies, differences of energies for hybrid structure and singular counterparts are employed: $E_B = E_{FU@SiC} - E_{FU} - E_{SiC}$. It is notes that the basis set superposition error (BSSE) [28] has been corrected for non-covalent interacting FU@SiC hybrids. To evaluate energy gaps, differences of HOMO and LUMO states are employed: $E_G = E_{LUMO} - E_{HOMO}$. Additionally, atomic scale properties were determined by evaluations of chemical shifts ($\delta$) for all atoms of the optimized structures. It is known that the chemical structures of materials could be efficiently detected by nuclear magnetic resonance (NMR) spectroscopy as a
versatile technique among the characterizing techniques \[29\]. To evaluate \( \delta \) values, chemical shielding tensors \( (\sigma_{ij}) \) were computed based on the gauge-included atomic orbital (GIAO) approach and then converted to isotropic chemical shielding \( (\sigma_{iso}) \) through the equation: \( \sigma_{iso} \text{(ppm)} = (\sigma_{11} + \sigma_{22} + \sigma_{33})/3 \) \[30\]. Subsequently, the obtained \( \sigma_{iso} \) values were converted to \( \delta \) values using the references of tetramethylsilan (TMS) for Si, C, and H atoms, water \((H_2O)\) for O atoms, and ammonia \((NH_3)\) for N atoms in the equation \( \delta \text{(ppm)} = \sigma_{iso,Reference} - \sigma_{iso,Sample} \) \[29\]. The chemical shieldings originated from the electronic sites of atoms, could reveal insightful information about the electronic properties of structures \[30,31\].

### 3. Results and discussion

#### 3.1. Optimized molecular properties

Optimized molecular properties including total energies \( (E_T) \), binding energies \( (E_B) \), energies of the highest occupied molecular orbitals and the lowest unoccupied molecular orbitals \( (E_{HOMO} \) and \( E_{LUMO} \)), and dipole moments \( (D_M) \) for the individual and hybrid models of this work \( (\text{Fig. 1}) \) are listed in Table 1. The individual models are the original and tautomeric forms of FU and two models of SiC fullerene-like nanoparticles include SiC\(_2\) and SiC\(_1\). The criterion of making two nanoparticles is to consider existence of Si-Si bond in the SiC\(_2\) model and C-C bond in the SiC\(_1\) one as well as Si-C bond in both models. The tautomer structures are constructed based on movement of H atoms among N\(_3\), O\(_2\), and O\(_4\) atomic positions. The hybrid structures are constructed through decorations of SiC\(_2\) and SiC\(_1\) nanoparticles by the available FU structures to make FU@SiC\(_2\) hybrids \( (\text{Fig. 1, panels B and C}) \). The results of optimized energies indicate that the most stable structure is the original di-keto form of FU and the most unstable structure is FU\(_3\), a keto-enol form with movement of H\(_1\) to O\(_4\) atomic position. Comparing the results of total energies indicates that the stabilities for other tautomers are ordered as FU\(_3\) > FU\(_2\) > FU\(_1\) > FU\(_4\). The results are in agreement with earlier results on uracil and FU tautomer structures \[27\]. The results for \( E_{HOMO} \) and \( E_{LUMO} \) also demonstrated that the orbital levels and the gaps between them are changed due to tautomerizations, in which the results reveal the changes of electronic properties for molecular systems of tautomers. Different magnitudes for \( E_{HOMO} \) and \( E_{LUMO} \) are seen for the SiC nanoparticles and different gaps are also seen for the two structures based on their atomic components. Different magnitudes for dipole moments are also obvious for the individual tautomers and also for two SiC nanoparticles, in which the value of \( D_M \) for SiC\(_2\) is larger than SiC\(_1\) structure.

There are two sets of FU@SiC\(_2\) hybrids based on the components of SiC nanoparticles; SiC\(_2\)\(_1\) and SiC\(_1\)\(_2\). A quick look at the B and C panels of \( \text{Fig. 1} \) indicates that the situations of interactions are different for the FU tautomers on the surface of two SiC nanoparticles. After optimizations, covalent attachments are seen for the SiC\(_2\)\(_1\) nanoparticles, whereas only non-covalent interactions are seen for the SiC\(_1\)\(_2\) nanoparticles. The trend shows the importance of atomic components in the structural behaviors of molecular interactions. Comparing the values of \( E_T \) for FU@SiC\(_2\)\(_1\) and FU@SiC\(_1\)\(_2\) hybrids indicates that the stabilities are different for the two hybrid systems, in which stronger interactions are seen for the FU@SiC\(_2\)\(_1\) hybrids in panel B of \( \text{Fig. 1} \) rather than the FU@SiC\(_1\)\(_2\) hybrids in panel C. The results for FU@SiC\(_1\)\(_2\) hybrids indicate that the obtained stabilities are different for the hybrid structures as could be seen by the magnitudes of \( E_T \), in which the most stable hybrid structure is FU@SiC\(_1\)\(_2\) among the investigated hybrids. Interestingly, the H atom of O\(_4\) is moved to Si\(_1\) atom of SiC nanoparticle and also the covalent attachment is seen for N\(_3\) and Si\(_2\) atom in the hybrid structure. With the exception of FU\(_2\)@SiC\(_1\)\(_2\), all other hybrids in this set include covalent bonds with almost similar strengths. However, physical interactions are only seen for FU\(_3\)@SiC\(_1\)\(_2\) and the results of \( E_T \) show the least stability for this structure among available hybrids. As it was shown earlier, the results of \( E_T \) for individual tautomers indicated FU\(_2\) is the least stable structure, in which the same result is also detected for FU\(_2\)@SiC\(_1\)\(_2\) hybrid. However, the stability for the original FU structure in the hybrid form is lowered in comparison with the original individual FU structure. Due to the special properties of SiC\(_1\)\(_2\) nanoparticle, the stability for FU\(_2\) is increased in the FU\(_2\)@SiC\(_1\)\(_2\) hybrid. Magnitudes of \( E_B \) also approve the values of stabilities, in which the most stable structure is FU\(_2\)@SiC\(_1\)\(_2\) and the least stable structure is FU\(_5\)@SiC\(_1\)\(_2\). The stabilities for other FU@SiC\(_1\)\(_2\) hybrids are almost similar. Different magnitudes for energies of HOMO and LUMO levels and also their gaps were observed for the hybrid structures, meaning changes of electronic properties of molecular orbitals of the investigated structures. The values of \( D_M \) indicate that the polarities are significantly changed during the hybridizations, in which remarkable magnitudes are seen for FU\(_1\)\(_2\), FU\(_0\), and FU\(_3\)@SiC\(_2\)\(_8\).
hybrids. As mentioned earlier, the interactions between FU tautomers and SiC\(_{12}\) nanoparticles are all non-covalent (Fig. 1, panel C), in which the stabilities of FU@Si\(_{12}\)C\(_8\) are lower than the stabilities of FU@Si\(_{12}\)C\(_8\) hybrids. Among the FU@Si\(_{12}\)C\(_8\) hybrids, the most stable structure is seen for the original FU on the Si\(_{12}\)C\(_8\) nanoparticle. The results of \(E_B\) also approve that the interaction between FU and Si\(_{12}\)C\(_8\) nanoparticle is stronger than other hybrid structures of FU−FU \@\@ SiC\(_{12}\). The stabilities and interaction strengths are almost similar for other hybrid structures. 

The levels for HOMO and LUMO still detect the effects of hybridizations in the FU@Si\(_{12}\)C\(_8\) hybrids but the magnitudes of gaps are larger in comparison with the FU@Si\(_{12}\)C\(_8\) hybrids. However, the magnitudes of \(D_M\) for FU@Si\(_{12}\)C\(_8\) hybrids are smaller than FU@Si\(_{12}\)C\(_8\) ones. Comparing the results for individual SiC nanoparticles and hybrids, reveals the influence of functionalizations on the properties of nanoparticles, in which the magnitudes of \(D_M\) for individual nanoparticles were significantly changed in the hybrid structures. As a remarkable conclusion, it could be mentioned that the existence of Si−Si bonds in SiC nanoparticles make the formation of covalent bonds possible for FU tautomers, whereas the existence of C−C bonds only show possibilities for formation of non-covalent interactions. In a very recent work [22], adsorption studies of FU at the surface of original and doped C\(_{60}\) fullerene nanospheres indicated that the interactions are non-covalent for original C\(_{60}\) whereas covalent interactions are observed for doped C\(_{60}\) [28]. In another work [27], the tautomeric structures of FU contribute to non-covalent interactions with original silicon sheets. These results and the results of current research could indicate that the heterogeneous nanostructures show better tendency to interact with FU structures in comparison with original nanostructures. The type of heterogeneous nanostructure is also important, in which the interactions of FU with Si\(_{6}\)C\(_{12}\) are all non-covalent comparing with Si\(_{12}\)C\(_8\) nanostructure.

### 3.2. Atomic chemical shifts

The evaluated chemical shifts (\(\delta\)) for the atoms of optimized individual and hybrid structures of FU, SiC, and FU@SiC (Fig. 1) are listed in Tables 2–4. The chemical shielding (\(\sigma\)) tensors are originated from the electronic sites of atoms; therefore, they could reveal insightful information about the electronic properties of materials [29]. A quick look at the results for atoms of FU counterparts (Table 2) in both individual and hybrid forms indicates that the electronic environment for each atom is changed from the original structure to tautomer or from individual structure to hybrid forms. Moreover, each atom of FU structure detects a different environment in two hybrid systems, based on different components of SiC fullerene-like particles. Two H atoms of FU, H\(_1\) and H\(_3\), are moving through tautomerization processes; but the position for H\(_6\) is kept frozen. Since the magnitudes of \(\delta\) show the discrepancy of electronic properties of the sample atom from the reference atom, these magnitudes could show significant changes of electronic properties of each atom from the reference point to current situation. Although the position of H\(_6\) is kept frozen through tautomers, the electronic properties are still changed in different structures due to indirect side effects, as could be seen by the magnitudes of \(\delta\). In all cases, the effects for H\(_6\) atoms of FU@Si\(_{12}\)C\(_8\) are much more significant than the other hybrid and individual structures.

### Table 2

<table>
<thead>
<tr>
<th>Atom</th>
<th>FU(_1)</th>
<th>FU(_{1\theta})</th>
<th>FU(_2)</th>
<th>FU(_{2\theta})</th>
<th>FU(_3)</th>
<th>FU(_{3\theta})</th>
<th>FU(_4)</th>
<th>FU(_{4\theta})</th>
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</thead>
<tbody>
<tr>
<td>H(_1)</td>
<td>4.995</td>
<td>5.439</td>
<td>5.780</td>
<td>4.986</td>
<td>5.017</td>
<td>4.976</td>
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<tr>
<td>C(_2)</td>
<td>134.621</td>
<td>144.291</td>
<td>139.971</td>
<td>142.662</td>
<td>150.906</td>
<td>140.097</td>
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<td></td>
</tr>
<tr>
<td>C(_4)</td>
<td>146.779</td>
<td>151.802</td>
<td>153.592</td>
<td>143.802</td>
<td>149.995</td>
<td>143.254</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C(_6)</td>
<td>160.498</td>
<td>154.796</td>
<td>154.613</td>
<td>150.177</td>
<td>155.099</td>
<td>143.748</td>
<td></td>
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</tr>
<tr>
<td>N(_1)</td>
<td>117.069</td>
<td>111.918</td>
<td>122.796</td>
<td>130.951</td>
<td>142.045</td>
<td>147.789</td>
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</tr>
<tr>
<td>O(_2)</td>
<td>130.549</td>
<td>118.372</td>
<td>117.580</td>
<td>215.294</td>
<td>230.848</td>
<td>241.019</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O(_4)</td>
<td>154.613</td>
<td>125.641</td>
<td>125.324</td>
<td>149.874</td>
<td>148.893</td>
<td>146.812</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>156.102</td>
<td>220.437</td>
<td>226.799</td>
<td>150.767</td>
<td>213.058</td>
<td>136.042</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The structures are shown in Fig. 1. The results for individual FU are comparable with Ref. [27]. In each column, the free number belongs to individual structure, the number in parenthesis belongs to FU@Si\(_{12}\)C\(_8\) hybrids, and the number in brackets belongs to FU\(_{\theta}\)Si\(_{12}\)C\(_8\) hybrids.*

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However, a clear harmony of changes are not seen for H₁ and H₃ atoms, which are moving through nitrogen and oxygen atomic sites. Interestingly, H₃ from O₄ is moved to S₁₁ atomic site in FU₂@S₁₁C₈ hybrid, which is seen as an unusual observation among the investigated model systems. The small magnitudes of δ for hydrogen atoms are due to existence of weak electronic environment for this atom in comparison with larger magnitudes for other heavier atoms.

The results of Table 2 for carbon atoms also show different electronic environments for different atomic positions. Although the carbon atoms do not directly participate in tautomeration, they can detect effects of these processes as could be seen by their magnitudes of δ. The properties for each atom among these models indicate that the changes of δ are significant due to being in different structural situations. For nitrogen atoms, many more significant effects are seen especially for that atom which is directly participated in the tautomeration. In the original structure, both of N₁ and N₂ are hydrogenated, whereas in the tautomers the hydrogen atoms are removed from one or both of nitrogen atoms. Interesting observations are obtained for FU₂@S₁₁C₈ and FU₄@S₁₁C₈ hybrids, in which N₃ is respectively connected to S₁₂ and S₁₄ atoms through covalent bonds. In comparison with individual structures, the changes of δ for N₃ atoms in two hybrids also indicate that FU₂@S₁₁C₈ and FU₄@S₁₁C₈ are in strong interactions. It seems that the position of N₃ between two types of oxygen atoms, O₂ is urea type and O₄ is amide type, makes it a proper atom to undergo stronger interactions in comparison with N₁. The stability of SIC nanoparticles is also important, in which strong interactions with FU counterparts are seen with S₁₂C₈ (more stability) but not with S₁₄C₁₂ (less stability). Two oxygen atoms of urea type (O₂) and amide type (O₄) show different behaviors in the tautomeric systems and also in interaction with SIC nanoparticles. Parallel to the results for N₃, the interaction for O₄ is strong with S₁₄C₁₂ nanoparticles especially in FU₂@S₁₄C₁₂ hybrids, which covalent bonds with S₁₄ and S₁₂ are formed. Combinations of the results for N₃ and O₄ could reveal that the amide part of FU is more proper for interactions with SIC nanoparticles than the urea part (N₄ and O₂). Moreover, N₃ is the winner of strong interactions, in which O₄ releases its hydrogen in FU₂@S₁₄C₁₂ to make better possibility of strong interactions of N₃ with S₁₂ atoms. The
oxygen atom has two lone pairs of electrons in the electronic site, which could be floated during the interactions to yield different properties. Similar situations of electron lone pairs are observed for the fluorine atom, in which the magnitudes of δ indicate different properties in the investigated individual and hybrid models. Since the F atom does not directly contribute to tautomerization, the magnitudes of changes of δ are not as significant as much as nitrogen and oxygen atoms, but they are still notable. By examining the magnitudes of δ for F atom in FU5 and hybrids, it could be proposed that there is an intramolecular hydrogen bond interaction between H4 and F atoms at individual and FU5@Si12C8 hybrid, whereas this interaction is protected in FU5@Si8C12 hybrid. This result could be more approved by the magnitudes of δ for H1 in FU5 and related hybrids, in which the magnitude is increased in FU5@Si8C12 in comparison with individual FU and FU5@Si12C8 hybrid.

The obtained δ for atoms of optimized Si12C8 and Si8C12 fullerene-like nanoparticles (Fig. 1) in the forms of individual and hybrids are listed in Tables 3 and 4. The tautomeric structures do not similarly interact with the SiC counterparts; therefore, the results for Si12C8 and Si8C12 and also for each SiC counterpart in the tautomeric interacting systems are different. Comparing the atomic parameters between the individual particle and tautomeric interacting counterparts indicate that the properties are significantly highlighted for the atoms of interaction regions. Furthermore, the results of other atoms also show the effects of interactions in other atomic regions are far from the exact interaction regions. Significant effects are observed for the atoms of interaction regions in the FU@Si12C8 hybrids more than the FU@Si8C12 hybrids. As mentioned earlier for the optimized properties, the FU@Si12C8 hybrids were seen more stable than the FU@Si8C12 hybrids with respect to energies. The atomic results for the hybrids and their counterparts also show that there are proper interactions in the FU@Si12C8 hybrids more significant than FU@Si8C12 hybrids. The atomic results for individual nanoparticles also indicated different properties, which could determine their characteristics for desired applications as could be seen by different situations of interactions in the investigated hybrids.

4. Conclusions

Within this work, we have investigated the properties of interactions between FU tautomers and SiC fullerene-like nanoparticles through DFT calculations of molecular and atomic properties. The results indicated that the properties of FU@SiC hybrids and also for each of SiC particles are different. The energetic properties indicated that FU@Si12C8 hybrids are more stable than FU@Si8C12 hybrids, in which the atomic properties also indicated that the interactions between the counterparts of former hybrids are many more significant than the latter ones. Comparing the results for individual SiC particles and hybrids indicated that the most significant effects of interactions could be seen for the atoms of interaction regions, but the effects for other atoms are still notable. In the cases of FU@Si12C8 hybrids, formations of covalent bonds were also detected between the FU tautomers and Si12C8 nanoparticle, in which only non-covalent interactions were seen for FU@Si8C12 hybrids. Distances between the HOMO and LUMO levels for FU@Si12C8 hybrids are smaller than FU@Si8C12 hybrids in agreement with the smaller distance for individual Si12C8 than individual Si8C12 particles. And finally, the stabilities and interactions of FU tautomers could be investigated by SiC fullerene-like nanoparticles, in which Si12C8 fullerene-like nanoparticle could be better than Si8C12 one.

References


