ABSTRACT

The removal and detection of nalidixic acid (NA) as an emerging environmental contaminant and a medicine are of great importance. In this respect, the performance of fullerene (C$_{20}$) as a sensing material and an adsorbent for NA was investigated by infrared-red (IR), frontier molecular orbital (FMO), and natural bond orbital (NBO) computations. The calculated adsorption energies, Gibbs free energy changes, enthalpy changes, and thermodynamic constants showed that NA interaction with C$_{20}$ was experimentally feasible, exothermic, and spontaneous. The NBO results indicated that NA interaction with C$_{20}$ was physisorption and no bond was created among the adsorbent and adsorbate. Moreover, findings on the effect of the temperature indicated that the adsorption process was more favorable at lower temperatures. The computed bandgap values showed that when NA was adsorbed on the surface of C$_{20}$, the bandgap of fullerene experienced a sharp increase (+298.462%) from 1.950 to 7.770 (eV). Hence, this nanostructure is a suitable sensing material for the development of novel electrochemical sensors for the determination of NA.

Keywords: Nalidixic acid, Fullerene, Density Functional Theory, Adsorption, Sensor.
**Introduction**

In the last few years, pharmaceuticals have caused a growing concern due to their presence in environmental samples. Among these compounds, it should be highlighted that, the antibiotics which are used in large quantities for several decades as human infection medicine, veterinary medicine, and husbandry growth promoters. Due to incomplete metabolization of these compounds in human and animal body, a portion of administered antibiotic is excreted as the parent compound or as metabolites via urine and feces. As a result of the agricultural application of manure and sewage sludge containing unmetabolized drugs, wastewater irrigation, and the disposal of domestic and hospital waste, they are eventually released into soils, sediments, and aquatic environments through different pathways [1–3]. Nalidixic acid (NA) (1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3 carboxylic acid), as shown in Figure 1, is the first synthetic quinolone antibiotic that was introduced in therapy in the 1960s [4].

![NA and Fullerene (C<sub>20</sub>)](image)

**Figure 1.** The optimized structures of fullerene (C<sub>20</sub>) and NA (oxygen: red, nitrogen: blue, carbon: gray, hydrogen: white)

NA is effective against both gram-positive and gram-negative microbes. It acts as a bacteriostatic agent in lower concentrations, but can be bactericidal at higher concentrations. Nalidixic acid has been selected in the present study because of its presence in hospital wastes, wastewater treatment plants effluents, environmental waters and soils [5-7]. It has serious effects on human health, such as chronic toxicity and carcinogenicity effect [8]. Various methods for removing nalidixic acid from aqueous solutions were used, including an embedded MBR-ozonation scheme [9], powdered activated carbon [10], adsorption on to anion-exchange and
neutral polymers [11] and UV and UV/H2O2 processes [12]. Adsorption, as a simple and relatively economic method, is widely utilized in the removal of pollutants. On the other hand, fullerene (C\textsubscript{20}, Figure 1) is the smallest nanomaterial with a dodecahedral cage structure [13-18]. The structure of this fullerene is highly curved and it is composed of pentagonal rings. C\textsubscript{20} has unique traits that make it an eminent sensing material like high conductance, great surface area/volume ratio and excellent reactivity [19-31]. In this respect, the goal of this study is to evaluate the sensing performance of C\textsubscript{20} for electrochemical detection and removal of NA by density functional theory simulations.

**Computational Details**

Software versions GuassView 6 and Nanotube modeler 1.3.0.3 were used to design the structures of C\textsubscript{20}, NA, and their complexes [18-19]. Each of the structures that were designed first underwent geometric optimization. After that, computations for IR, FMO, and NBO were performed on designed structures. The density functional theory method was used throughout the computations by Gaussian 16 software at the B3LYP/6-31G (d) level of theory [20]. This level was selected since the findings obtained from earlier studies were acceptable and were consistent with experimental results. The densities of states (DOS) spectrums were obtained using the GuassSum 3.0 software [21]. All computations were performed in the vacuum between 298 and 398 K at intervals of 10°.

The following processes were investigated [22]:

\[ \text{NA + Adsorbent} \rightarrow \text{NA-Adsorbent} \]  

(1)

Adsorption energy values (E\textsubscript{ad}) and thermodynamic parameters, such as thermodynamic equilibrium constant (K\textsubscript{eq}), Gibbs free energy changes (\Delta G\textsubscript{ad}), entropy changes (\Delta S\textsubscript{ad}), and adsorption enthalpy changes (\Delta H\textsubscript{ad}), were calculated using equations 2–6 [23-25].

\[
E_{ad} = \left( E_{(\text{Complex})} - (E_{(\text{NA})} + E_{(\text{Adsorbent})} + E_{(\text{BSSE})}) \right)
\]  

(2)

\[
\Delta H_{ad} = \left( H_{(\text{Complex})} - (H_{(\text{NA})} + H_{(\text{Adsorbent})}) \right)
\]  

(3)

\[
\Delta G_{ad} = \left( G_{(\text{Complex})} - (G_{(\text{NA})} + G_{(\text{Adsorbent})}) \right)
\]  

(4)
\[ \Delta S_{\text{ad}} = \left( S_{(\text{Complex})} - \left( H_{(\text{NA})} + H_{(\text{Adsorbent})} \right) \right) \] (5)

\[ K_{\text{th}} = \exp\left(-\frac{\Delta G_{\text{ad}}}{RT}\right) \] (6)

In the equations above, \( E \) stands for the total electronic energy for every structure, \( E_{\text{BSSE}} \) stands for the basis set superposition correction, and \( H \) represents the total energy of the evaluated materials plus the thermal correction of enthalpy. For each structure under study, the \( G \) denotes the total energy plus the thermal correction of the Gibbs free energy [22]. \( R \) represents the constant of the ideal gas, \( S \) is the thermal correction entropy for the studied structures, and \( T \) stands for temperature [26-28].

Equations 7–12 were used to calculate the bandgap (\( E_g \)), chemical hardness (\( \eta \)), chemical potential (\( \mu \)), maximum charge capacity (\( \Delta N_{\text{max}} \)), and the electrophilicity (\( \omega \)) of frontier molecular orbitals [29-31].

\[ E_g = E_{\text{LUMO}} - E_{\text{HOMO}} \] (7)

\[ \%\Delta E_g = \frac{E_{g2} - E_{g1}}{E_{g1}} \times 100 \] (8)

\[ \eta = \frac{(E_{\text{LUMO}} - E_{\text{HOMO}})}{2} \] (9)

\[ \mu = \frac{(E_{\text{LUMO}} + E_{\text{HOMO}})}{2} \] (10)

\[ \omega = \frac{\mu^2}{2\eta} \] (11)

\[ \Delta N_{\text{max}} = -\frac{\mu}{\eta} \] (12)

\( E_{\text{LUMO}} \), in the equations above, is the energy of the lowest unoccupied molecular orbital, and \( E_{\text{HOMO}} \) is the energy of the highest occupied molecular orbital. The bandgaps of the Nano-adsorbent and NA-Adsorbent complexes are shown as \( E_{g1} \) and \( E_{g2} \), respectively [29].

**Results and Discussion**

NA interaction with \( C_{20} \) was scrutinized at three various configurations to achieve the conformer with the highest stability. The initial structures and the optimized versions of those are presented in Figure 2. It demonstrates that the carbonyl and carboxylic acid functional groups of
NA was inserted near the C$_{20}$ at A-Conformer. In B-Conformer, the adsorbate was located near the adsorbent towards its aliphatic substitutions, and in C-Conformer, the NA molecule was placed adjacent to C$_{20}$ towards its naphthyridine ring. As seen from the provided optimized structures in Figure 2, after geometrical optimizations, the NA molecule only come closer to fullerene, and no tangible structural deformations occurred in the adsorbate and adsorbent molecules. Both findings indicate that NA interaction with C$_{20}$ is relatively weak. Table 1 displays the determined adsorption and total electronic energies. As shown, all of the scrutinized conformers have negative adsorption energy values, which shows experimentally possibility of the adsorption of NA on the C$_{20}$ surface at all of the studied configurations. Also, according to this table, fullerene nanocage is an effective adsorbent for NA removal [25-30].

<table>
<thead>
<tr>
<th>Initial Structures</th>
<th>Optimized Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-Conformer</td>
<td><img src="image1.png" alt="Image" /></td>
</tr>
<tr>
<td>B-Conformer</td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td>C-Conformer</td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
</tbody>
</table>

**Figure 2.** Initial and optimized structures of NA-C$_{20}$ complexes (oxygen: red, nitrogen: blue, carbon: gray, hydrogen: white)
The optimized structures were also subjected to IR computations, and Table 1 provides the highest and lowest obtained IR frequencies. According to this table, all the structures that were investigated are true local minimums since there is obviously no negative vibrational frequency. Dipole moment values were also computed. These values revealed that with NA adsorption on the surface of fullerene, the dipole moment increases remarkably, indicating that with the formation of NA-C_{20} complexes, their reactivity becomes higher than pure NA. The optimized structures were also subjected to NBO computations to learn more about the adsorption mechanism. The outcomes demonstrated that the formation of a chemical bond between NA and nanostructure was prevented in all the examined conformers [26-34].

**Table1.** The values of total electronic energy, adsorption energy, zero-point energy (ZPE), the maximum and minimum IR frequencies and dipole moment for NA, C_{20} and their complexes.

<table>
<thead>
<tr>
<th></th>
<th>Total electronic energy (a.u)</th>
<th>Adsorption energy (kJ/mol)</th>
<th>ZPE (kJ/mol)</th>
<th>ν_{min} (cm^{-1})</th>
<th>ν_{max} (cm^{-1})</th>
<th>Dipole Moment (Debye)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>-784.860</td>
<td>---</td>
<td>692.680</td>
<td>9.707</td>
<td>4093.279</td>
<td>0.880</td>
</tr>
<tr>
<td>C_{20}</td>
<td>-747.196</td>
<td>---</td>
<td>325.260</td>
<td>261.392</td>
<td>1690.640</td>
<td>0.000</td>
</tr>
<tr>
<td>A-Conformer</td>
<td>-1532.088</td>
<td>-84.150</td>
<td>1040.350</td>
<td>3.682</td>
<td>4241.622</td>
<td>4.250</td>
</tr>
<tr>
<td>B-Conformer</td>
<td>-1532.100</td>
<td>-115.656</td>
<td>1040.510</td>
<td>1.800</td>
<td>4242.268</td>
<td>5.310</td>
</tr>
<tr>
<td>C-Conformer</td>
<td>-1532.091</td>
<td>-92.026</td>
<td>1040.630</td>
<td>1.948</td>
<td>4242.409</td>
<td>4.660</td>
</tr>
</tbody>
</table>

The thermodynamic parameters calculated for the process of NA adsorption are shown in Figure 3 as a function of temperature, including ΔH_{ad}, ΔG_{ad}, ΔS_{ad}, and the logarithm of K_{th}. Clearly, all the conformers under investigation have negative ΔH_{ad} values. These values show the exothermic nature of the adsorption process. The NA adsorption process is spontaneous, two-sided
and equilibrium as shown by the low quantities of thermodynamic constants and the negative amounts for $\Delta G_{\text{ad}}$. The drop-in chaos is shown by the negative values of $\Delta S_{\text{ad}}$ in the NA adsorption process. Also, these negative values exhibit that the entropy of the NA interaction with C$_{20}$ is unsuitable. According to the results of the investigation into how temperature affects all of the thermodynamic parameters, the temperature fluctuations did not significantly impact the adsorption process, and NA interaction with fullerene is somewhat more favorable at lower temperatures [25-28].

**Figure 3.** Thermodynamic parameters of NA adsorption process including $\Delta H_{\text{ad}}$, $\Delta G_{\text{ad}}$, $\Delta S_{\text{ad}}$, and the logarithm of $K_{\text{th}}$ in the temperature 298-398 K at 10° intervals

The difference between the HOMO and LUMO orbital energies is the band gap, which is inversely related to the electrical conductivity of materials. The electrical conductivity of materials with a narrow band gap is higher than the materials with a wide one [29]. Therefore, to assess the efficiency of C$_{20}$ as an electrochemical sensor for measuring NA, this parameter was computed.
for each of individual structures. According to the data presented in Table 2, the $E_g$ of fullerene nanocage is 1.950 (eV). When NA is adsorbed on its surface, this parameter tangibly increases to 7.770, 7.740, and 7.730 (eV), respectively, for A, B, and C conformers. It appears C$_{20}$ can be used as an appropriate material for developing electrochemical sensors for NA detection, as this nanostructure bandgap variation is only about 298% for all three investigated configurations [30]. Equations 9–12 were used to calculate the electrophilicity, chemical hardness, maximum transferred charge capacity, and chemical potential. Table 2 shows the results. It reveals that the NA chemical hardness for the A, B, and C conformers decreases from 5.443 (eV) to 3.885, 3.870, and 3.865 (eV), respectively, when NA is adsorbed on the surface of fullerene. As a result, NA-C$_{20}$ complexes are softer and more reactive than pristine NA that does not contain a nano adsorbent [28]. All investigated structures have a negative measured chemical potential, suggesting that they all have thermodynamic stability [29]. Following its interaction with C$_{20}$, NA becomes more electrophilic and has a higher maximum transferred charge capacity, indicating that NA-C$_{20}$ complexes have higher electrophilicity and, compared to pristine NA, are more likely to absorb electrons [24-31].

Table 2. The calculated FMO parameters for NA, C$_{20}$ and their complexes.

<table>
<thead>
<tr>
<th>NO</th>
<th>$E_{\text{HOMO}}$ (eV)</th>
<th>$E_{\text{LUMO}}$ (eV)</th>
<th>$E_g$ (eV)</th>
<th>$%\Delta E_g$</th>
<th>$\eta$ (eV)</th>
<th>$\mu$ (eV)</th>
<th>$\omega$ (eV)</th>
<th>$\Delta N_{\text{max}}$ (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>-5.821</td>
<td>5.066</td>
<td>10.887</td>
<td>5.443</td>
<td>-0.377</td>
<td>0.013</td>
<td>0.069</td>
<td></td>
</tr>
<tr>
<td>C$_{20}$</td>
<td>-5.060</td>
<td>-3.110</td>
<td>1.950</td>
<td>---</td>
<td>0.975</td>
<td>-4.085</td>
<td>8.558</td>
<td>4.190</td>
</tr>
<tr>
<td>A-Conformer</td>
<td>-4.100</td>
<td>3.670</td>
<td>7.770</td>
<td>298.462</td>
<td>3.885</td>
<td>-0.215</td>
<td>0.006</td>
<td>0.055</td>
</tr>
<tr>
<td>B-Conformer</td>
<td>-4.580</td>
<td>3.160</td>
<td>7.740</td>
<td>296.923</td>
<td>3.870</td>
<td>-0.710</td>
<td>0.065</td>
<td>0.183</td>
</tr>
<tr>
<td>C-Conformer</td>
<td>-4.230</td>
<td>3.500</td>
<td>7.730</td>
<td>296.410</td>
<td>3.865</td>
<td>-0.365</td>
<td>0.017</td>
<td>0.094</td>
</tr>
</tbody>
</table>

Conclusion

This study used density functional theory computations to examine NA adsorption on the surface of fullerene (C$_{20}$). The negative values for $E_{\text{ad}}$, $\Delta G_{\text{ad}}$, and $\Delta H_{\text{ad}}$, as well as little values for $K_{\text{th}}$, showed that the NA interaction with fullerene was experimentally possible, exothermic,
spontaneous, and reversible. The NBO results showed that NA and C\textsubscript{20} did not form any chemical bond; hence, according to a physisorption adsorption process. The computed FMO parameters revealed that whereas C\textsubscript{20} bandgap increased by +298.462\% during the adsorption process. Because of the sharp variation of electrical conductivity during the adsorption process, it is clear that C\textsubscript{20} makes a great sensing material for the development of cutting-edge electrochemical sensors for NA measurement. In this respect, the performance of the fullerene (C\textsubscript{20}) as an adsorbent and sensing material for the removal and detection of NA is recommended to be evaluated by analytical chemist.

References


**HOW TO CITE THIS ARTICLE**