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Interaction of carbon nanotubes (CNT) with Amoxicillin antibiotic by computational analysis

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ABSTRACT: In this research, the performance of Carbone nanotubes (CNT) as a sensing material and adsorbent for the detection and removal of Amoxicillin was investigated. at the first, the structures of Amoxicillin and CNT were optimized with Gaussian program. Then, using the molecular docking strategy and its grading system, they were computed the arrangement of 10 structures with more negative binding energy than other . Finally, for the best arrangement of Amoxicillin with CNT, molecular orbitals evaluations and depedents parameters , binding energy and other thermodynamic parameters evaluated, the results indicated that the adsorption of Amoxicillin antibiotic on CNT was an exothermic. This procedure was carried out at 298 K and 1 atm. Finally, the QTAIM calculations were performed to evaluate the type of interaction and bonds created between amoxicillin and CNT.

Keywords: *Amoxicillin antibiotic, Carbone nanotubes (CNT), Molecular docking, QTAIM*

INTRODUCTION

Carbon nanotubes are one of type the allotropes of carbon, intermediate among fullerene cages and flat CNT, in the range of a nanometer [1]. They can be visualized as cutouts from a two-dimensional hexagonal lattice of carbon atoms. they can exhibit remarkable electrical conductivity [2], as a semiconductors. They also have special tensile strength and thermal conductivity because of their nanostructure and rigidity of the bonds between carbon atoms. we examined the interaction of amoxicillin with Carbone nanotubes to investigate the thermodynamic variables and evaluate the extent of heat from the absorption of antibiotic amoxicillin from these calculations [3], to see is nanotube suitable sensor for the amoxicillin . it was employed Gauss View software to develop the nano tube [4] with amoxicillin. To minimize the energy of systems, the explored systems were initially geometrically optimized by the software using B3LYP/6-31G set [5]. Then they were examined using the Autodock Tools program [6], and finally, the nature of the resulting bonds was calculated utilizing quantum theory of atoms in the molecule [7]. The purpose of this research is to investigate the ability of this nanostructure as a sensor, which is determined according to the amount of energy parameters such as binding energy and Gibbs free energy, etc. This has not been done so far by computational and molecular docking. So it is completely new Fig. 1.

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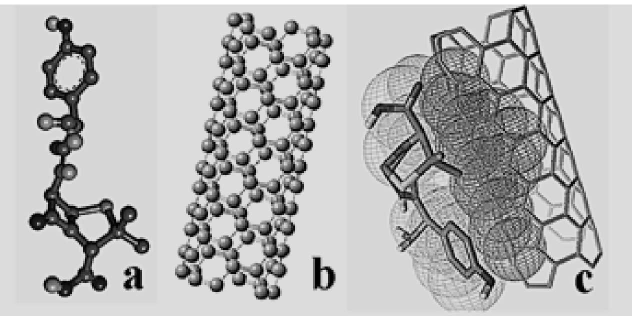

Fig. 1. Chemical structure of Amoxicillin (a), the structure of single walled Carbon nanotubes (CNT) (b) and Interactions of CNT with the antibiotic Amoxicillin (c) (Carbon: gray, nitrogen: blue, oxygen: red, hydrogen: white, sulfur: yellow).

EXPERIMENTAL

Computational techniques

Initially, Amoxicillin and CNT structures were extracted by nanotube modeler 1.3.0.3 [8], and GaussView 5.0 software [9]. In the next step, geometric optimization were conducted via the density function hypothesis technique and computational level: B3LYP/6-31G(d). This computational level was chosen since its findings were in good line with empirical data in previously conducted studies. All computations were conducted at a temperature and a pressure of 298 K and 1 atmosphere, respectively, utilizing Gaussian software [10]. Afterwards it was used from Auto Dock software (Auto Dock, version 4.2) [6]. Auto Dock created a sequence of ten conformation designs, indicating the ten greatest anticipating models about the way the antibiotic could possibly cooperate with the CNT [2]. Auto Dock generated a sequence of energy values (binding energy [11], ligand proficiency, Van der Waals [12], hinderance constant, intermolecular energy., electrostatic and overal inner energy) utilizing a program. The process under investigation were expressed as the following formula:

$$\text{Amoxicillin} + \text{CNT} \rightarrow \text{Amoxicillin} - \text{CNT} \qquad (1)$$

RESULTS AND DISCUSSION

To detect the most steady arrngement of Amoxicillin with CNT, as can be seen in Fig.2 , we employed the docking technique via Auto dock software. Docking is the process of determining the orientation and binding energy of two compound. In this work, the interaction was researched between amoxicllin and graphen as a Receptor in its active site. Docking is a Molecular mechanic computation [13]. That is an automated molecular algorithm that connects a smaller compound, Specifies the (ligand) to the active site of the larger molecule (target). This method includes determining the orientation of the composition, the geometric structure of the conformation (formulation) and the ranking. Ranking can be a measure of connection energy, free energy or a numerical qualitative measure. Each automatic docking algorithm attempts to put the combination in active position in different orientations and formulations and calculate a score for each. Some programs store all the data obtained from the tested orientations, but some of them keep only the best scores in memory [14].

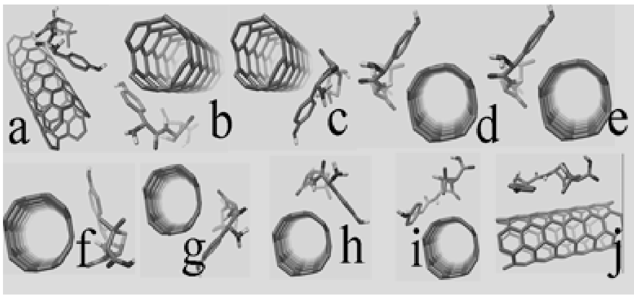

Fig. 2. Ten steady complexes (AG) created from molecular docking computations, Amoxicillin with CNT.

Table 1. In normal circumstancse (T= 298.15 K, p=1 atm). The Structures Computed by Docking method for adsobtion Amoxicillin on CNT.

Results of Docking for A SWCNT						
Rank	ki	BE	IME	IE	TE	UEE
1	234.61	-4.95	-7.04	-1.89	2.09	-1.89
2	300.71	-4.80	-6.89	-2.50	2.09	-2.50
3	319.30	-4.77	-6.86	-2.44	2.09	-2.44
4	357.38	-4.70	-6.79	-2.32	2.09	-2.32
5	328.96	-4.75	-6.84	-2.51	2.09	-2.51
6	336.13	-4.74	-6.83	-2.59	2.09	-2.59
7	356.32	-4.70	-6.79	-2.59	2.09	-2.59
8	361.78	-4.70	-6.78	-2.57	2.09	-2.57
9	511.50	-4.49	-6.58	-2.62	2.09	-2.62
10	644.56	-4.35	-6.44	-2.38	2.09	-2.38

BE (kcal/mol): Binding Energy; IME (kcal/mol): Intermolecular Energy; IE (kcal/mol): Internal Energy; TE (kcal/mol): Torsional Energy; UEE (kcal/mol): Unbound Extended Energy; Ki: Inhibition Constant.

More details about the parameters of Table 1 :
All energy values possess units of kcal/mol
BE: It is obtained from this Equation [= (IME) + (IE) + (TE)- (UEE)]
Notice: IME= [(a) + (b)]
(a): VDW + H_{bond} + desolv
Abbreviations: VDW: It is Van Der Waals energy; H_{bond}: It is Hydrogen Bonding; Desolv: It is Desolvation Energy.
(b) Electrostatic Energy (kcal/mol)

Table 1 and Fig. 3 evidently indicate the results of Amoxicillin derivatives with CNT, suggesting that the energy changes were not positive, so it reflects the exothermic of the adsorption procedure in these arrangements. Hence, we expect the physical adsorption of Amoxicillin to occur in the interplay of CNT with Amoxicillin; further, this nanostructure can be utilized for producing novel thermal sensors to calculate Amoxicillin. These sensors generally measure the temperature variations resulting from the development of a procedure using an extremely precise and sensitive thermistor that is used as an indicator to calculate the volume of analytes.

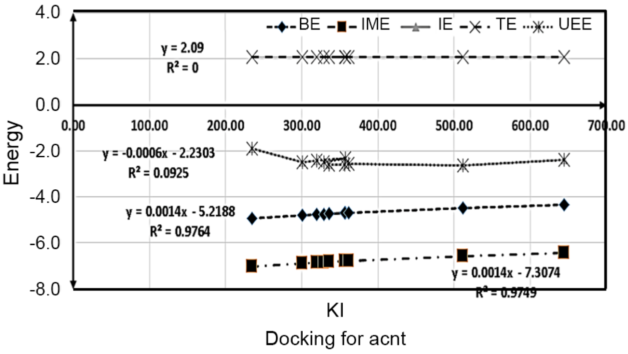

Fig. 3. The results of docking for ACNT.

HOMO, in Chemistry, refers to the greatest involved molecular orbital, while LUMO indicates the least unoccupied or vacant molecular orbital. Further, energy gap refers to the energy differenciation between the two orbitals, which is generally characterized by the HLG sign, and formula (2) is applied to measure it [15]. In this formula, E_H and E_L refer to the HOMO and LUMO orbital energies, respectively. The energy gap is straightly associated with th molecules electric conductivity. Indeed, mixtures with little energy gaps can transfer electrons more effortlessly via the prohibited band into the conduction band. For this reason, compunds with smaller energy gaps exhibit greater electric onductivity compared to materials with greater energy gaps. The findings illustrated in Table 2 and Fig. 4 evidently demonstrate that the level

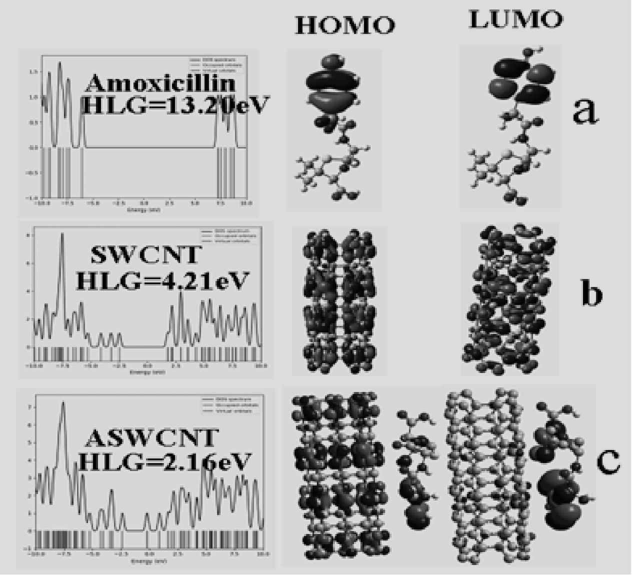

Fig. 4. HOMO and LUMO molecular orbitals and DOS diagrams for Amoxicillin (a), Carbon nanotube: CNT (b) complex of carbon nanotubes with the antibiotic Amoxicillin: ACNT (c).

Table 2. Energy levels of HOMO and LUMO orbitals, chemical potential, electrophilicity, chemical stiffness, energy gap, highest load transmitted to the system and dipole time for Amoxicillin, CNT and ACNT.

Compound	HOMO	LUMO	gap	μ	η	S	ω	ΔNmax	DM
Amoxicilin	-6.02	7.18	13.20	0.58	6.60	0.15	0.03	-0.09	1.981858
CNT	-2.43	1.78	4.21	-0.32	2.11	0.47	0.02	0.15	0.00947
ACNT	-2.35	-0.19	2.16	-1.27	1.08	0.93	0.75	1.18	8.898318

E_{HOMO}(eV), E_{LUMO} (eV), GE: Gap Energy (eV), μ: Chemical Potential(eV), η:Hardness(eV), S: softness (eV), ω: Electrophilicity(eV), ΔN_{max} (eV), DM:Dipole Moment (debye).

of energy gap after absorbing Amoxicillin on the CNT surface reduced dramatically. Indeed, the conductivity of Amoxicillin enhanced sharply after interplay with CNT. Another noteworthy issue is that we can utilize the rise in conductivity induced by the absorption of explosives on the CNT surface to detect and calculate them. Otherwise stated, CNT will be employed to produce novel electrochemical sensors for calculating Amoxicillin. The next explored variable is chemical stiffness (η), the amount of which can be drawn from Equation (3). Chemical stiffness can be a reliable account of the reactivity of a novel material since molecules with softer structures and lower chemical stiffness can more effortlessly alter their electron thickness. Consequently, transfer of electron, which is necessary for chemical interactions, takes place easier and more suitable in soft matetrials. The results of Table 2 demonstrate that the reactivity of Amoxicillin enhanced after being absorbed on CNT since all derivatives extracted via interaction with CNT posses less chemical stiffness compared to intact Amoxicillin. The value of chemical potential (μ) utilized for obtaining the other variables was also measured based on Equation (4). Electrophilicity (ω) and highest charge transnitted to the system (ΔN_{max}) are both acceptable features that show the inclination of a material to attract electrons. These two features were measured via Equations (5) and (6), respectively. When two molecules start reacting with each other, one molecule plays the role of an electrophile whereas the other functions as a nucleophile. Moreover, a molecule with greater electrophile capacity and charge potential is tended to serve as a receptor electron. However, a compound with little electrophile capacity and charge potential will be more inclined to deliver electrons to the system. According to the results illustrated in the table, Amoxicillin is inclined to act as an electron donor in reaction with the nanostructure as its electrophile potential amounts to 0 electron volts. Conversely, intact CNT acts as an electron receiver since its electrophile capacity amounts to 0.01 electron volts. Hence, we can conclude that CNT is able to be involved in electrochemical reactions with Amoxicillin. Furthermore, the results of Table 2 reveal that the electrophilicity of Amoxicillin rised after being absorbed on the CNT surface. Consequently, we may come to the conclusion that the tendenacy of Amoxicillin towards adsorbing electron has enhanced after reaction with nanostructure. Bipolar time of the investigated structures was examined, too. This feature is a suitable benchmark for measuring the solvency level of molecules in polar solvents. Compounds with greater dipole time will have superior solvency in water, while molecules with less dipole time would have less solvency in polar solvents. As it was observed, the dipole time of Amoxicillin rises after being absorbed on the CNT surface. Accordingly, CNT derivatives with Amoxicillin will manifest greater solvency in water compred with Amoxicillin [16].

$$\mathrm{HLG} = E_L - E_H \tag{2}$$

$$\eta = (E_L - E_H)/2 \tag{3}$$

$$\mu = (E_L + E_H)/2 \tag{4}$$

$$\omega = \mu^2 / 2\eta \tag{5}$$

$$\Delta N_{max} = -\mu / \eta \tag{6}$$

In the Fig. 4. Contour diagrams of the molecular electrostatic potential (ESP) of Amoxicillin and AG in its ground state. Every panel includes a plot in the plane . Contours of places shadowed in dark gray indicate places of negative ESP, while the bright places indicate the positive state of ESP. Calculations were done at the B3LYP/6-31G* level of hypothesis). Due to the shapes of electron surfaces, contour diagrams of the molecular ESP and the positions of the HOMO and LUMO orbitals on the surface of the drug, it appears that at the position of the benzene and the Oxygen ring on the ring, a higher electron cloud density is located,

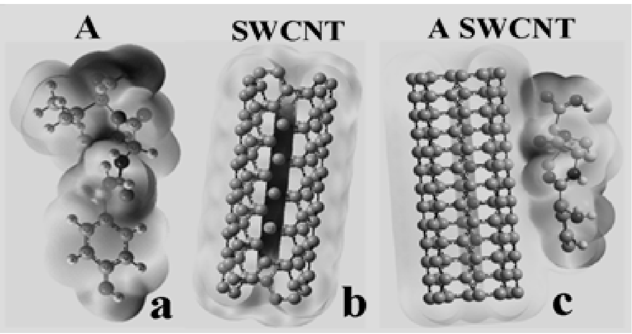

Fig. 5. Diagram of the surface of a molecule or electrostatic potential (ESP).

so in electrophilic reactions from this position are occured. On the other hand illustrations of more stable structures produced from molecular docking calculations, and the theoretical findings derived from this research are in great congruence with each other [17-20].

Quantum theory of atoms in molecules (QTAIM)

We applied the AIM analysis to identify the existence of bond critical points (BCPs) of the intramolecular bonds and to calculate their energies Table 3. These features for the intramolecular bonds in the explored molecules are presented in Table 2. A significant relationship was found between the values of (r_c) and L(r_c). The positive Laplacian $\nabla^2\rho(r_c)$ values in Table 2 demonstrate electronic charge draining along the bond way, which could characterize closed shell interactions bonds. Table 3 illustrates the measured bonds energies as follows: where, Vc indicates the density of nearby potential electron energy , and Gc denotes the density of nearby kinetic electron energy. Moreover, the ratio of Gc/Vc where, Vc denotes the density of nearby potential electron energy, and Gc refers to the density of nerby kinetic electron energy. In the end, we utilized the ratio of Gc/Vc as an indicator of the nature of bonds: for Gc/Vc>1, the bond is noncovalent,while for 0.5<Gc/Vc<1, it is somewhat covalent. In addition, for Gc/Vc<0.5, the bond is covalent (EA. . .B, kcal mol^{-1}), and bond critical position data (in a.u.) from quantum theory of atoms in molecules analysis [4].

Quantum theory of atoms in molecules

The AIM analysis was used to determine the presence of bond critical points (BCPs) of the intramolecular bonds and to evaluate their energies. The most often used criteria of the existence of bonding interactions are the electron density $\rho(r_c)$ and the Laplacian of the electron density $\nabla^2\rho(r_c)$ at the BCPs. These parameters for the intramolecular bonds in the studied molecules are given in Table 3. There is a good correlation between the $\rho(r_c)$ and $\nabla^2\rho(r_c)$ values. The positive values of Laplacian $\nabla^2\rho(r_c)$ in Table 3 are indicative of depletion of electronic charge along the bond path, which is a characteristic of closed shell interactions bonds. Table 2 shows the bonds energies calculated similar to the following:

$$E_{A....B} = 12V_c \tag{7}$$

$$V_c = 1/4\nabla^2\rho(r_c)2G_c \tag{8}$$

where, Vc is the local potential electron energy density and Gc is the local kinetic electron energy density. Finally, the ratio of Gc/Vc where, Vc is the local potential electron energy density and Gc is the local

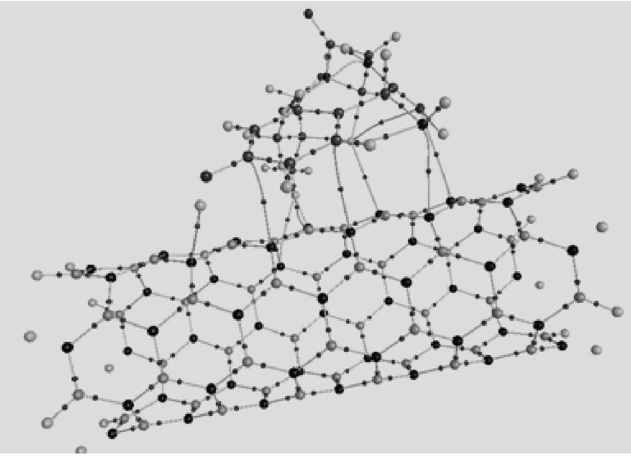

Fig. 6. Critical points of the intramolecular bonds.

Table 3. Bond critical points (BCPs) of the intramolecular bonds and to calculate their energies for ACNT.

Number	$\rho(r_c)$	L(r_c)	Ñ$^2\rho$ (r_c)	E(A…B)=v/2	Gc/Vc	Bond type
163 (3,-1)	0.013375	-0.013529	0.054116	-3.669201	1.078434	non-covalent
104 (3,-1)	0.004942	-0.007080	0.028320	-1.045603	1.562235	non-covalent
92 (3,-1)	0.014315	-0.012303	0.049212	-3.307697	1.083508	non-covalent
36 (3,-1)	0.007100	-0.006405	0.025621	-1.531675	1.156029	non-covalent
165 (3,-1)	0.010551	-0.008421	0.033685	-2.367246	1.058072	non-covalent
164 (3,-1)	0.019133	-0.017597	0.070390	-5.291909	1.021670	non-covalent
133 (3,-1)	0.006985	-0.008187	0.032748	-1.290886	1.494941	non-covalent
175 (3,-1)	0.007197	-0.008135	0.032542	-1.206932	1.557449	non-covalent

kinetic electron energy density. Finally, the ratio of Gc/Vc, was used as a criterion of the nature of bonds : for Gc/Vc>1, the bond is noncovalent, whereas for 0.5<Gc/Vc<1, it is partially covalent and Gc/Vc<0.5 it is covalent. bonds (EA. . .B, kcal mol-1), and bond critical point data (in a.u.) from quantum theory of atoms in molecules analysis equations 7-8.

CONCLUSION

Adsorbing Amoxicillin on the CNT surface was examined utilizing the molecular docking and density function theories. The computed binding energy indicated the exothermic and spontaneous absorption procedure of this drug and this procedure was measured at room temperature. In addition, molecular orbitals' analysis suggested that complex CNT with amoxicillin had more electrophile potential and were more conductive and reactive compared to intact Amoxicillin. It was also found that CNT could be used to create novel electrochemical sensors for identifying and measuring Amoxicillin. CNT is a chemical sensor to detect compounds that structurally bear a close resemblance to Amoxicillin. Based on the measured results, it is recommended that the function of CNT in removing and measuring Amoxicillin and impact of these nanostructures on their energy qualities be explored empirically. And since the molecular bond between amoxicillin and CNT is weak, we can look at CNT as a suitable sensor for amoxicillin.

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