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Electronic Properties of InPNT Drug Carrier

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ABSTRACT

Stability and electronic properties of Cisplatin anti-cancer drug, single well –zigzag (4,0) Indium phosphide nanotube (SWInPNT) and SWInPNT-Cisplatin (complex) have been analyzed by employed density functional theory using the Gauss view and Gaussian 09 by B3LYP (beck three-parameter hybrid functional combined with Lee-Yang-Parr correlation functional) method and lanl2dz standard basis set. The optimized structures, total energies, energy gaps, highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO) energy, ionization potentials, electron affinities, chemical potential, global hardness, softness, and electrophilicity index have been investigated. Diameter and length of SWInP nanotube are about 7.50 and 10 Å, respectively. Structural stability (zinc blende) for the SWInP nanotube that is useful for drug carriers.

KEY WORDS: Density functional theory (DFT), SWInPNT, Drug-carrier, Cisplatin.

1. INTRODUCTION

Through the past few years, there has been a rapid development in the field of nanotechnology to diagnose many diseases and their treatments. Nanoparticles of fullerenes and some of their derivatives like nanotube can overcome the resistance of certain diseases to certain drugs, thus serving as drug delivery carriers (Pabitra and Kalyan, 2016). The employ of nanocarriers becomes a major interest in the field of nanomedicine. Indeed, they can incorporate chemotherapeutics drug in their inner free volume while specific cancer cell ligands could be chemically attach on their outer surface to target cancer cell receptors (El Khalifi, 2016). The molecular size and the biodegradability of nanocarriers are two very important factors since the eventual nanocarrier clearance from the body, after delivering the drug, will depend on these two parameters essentially. Nanotubes are a very important geometric class of nanomaterials that are using in biotechnology and medicine (El Khalifi, 2016). Because of the unique physicochemical and biological properties of nanotubes attracted a wide attention as carriers for biologically relevant molecules,. Indeed, their very large surface area is a real asset that makes them able to be modified with functional groups of various complexities. More, their ability to enhance cellular internalization of poorly permeable drugs, compared to the free drug, increases the drug action near the disease cell (El Khalifi, 2016). Since discovery carbon nanotube (CNT) has opened up new scope in science and technology because of its unique properties (Davood and Samereh, 2003). The binary compounds of groups III - V are always semiconductors and suggested as suitable alternative materials for the CNTs (Mahmoud Mirzaei, 2012) and periodic table exhibited preferable optical properties for applications in areas such as biology and medicine. The presence of covalent bonds, little toxicity to the environment, specific features of excitation, radiative mission taking place in the visible and near IR range, resistance to degradation, high extinction coefficients, as well as the great possibility of bio-conjugation, make the III-V nano- compounds ideal candidates for the development and expansion of new luminescent biomarkers (Yousif Abid Al Shaabani, 2016). Among these materials, the tubular structure properties of the group III-nitrides, e.g., boron nitride (BN), aluminum nitride (AlN), gallium nitride (GaN), and indium nitride (InN) are more study (Mahmoud Mirzaei, 2012). At present, indium phosphide (InP) is one of the most promising compounds in this context .The InP nanotubes have the zinc blende structure(stable structure) and therefore represent a new class of tube materials (Erik, 2003). Indium phosphide (InP) is a binary semiconductor consists of indium and phosphorus with direct band gap of 1.34eV at (300^{o}K) (Fikrat Jasim, 2016). Many medications are being using as individual or in combination as anti-cancer; one of the most commonly used medicines is Cisplatin. Cisplatin was discovered in 1845 and licensed for medical use in 1979 (Cisplatin Fischer, 2016). It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system (WHO Model List of Essential Medicines). Cisplatin is a drug usually used to treat different kinds of tumor cells (Alia Mejri, 2014). It's a highly effective chemotherapeutic agent used to treat solid tumors, including ovary, testis, bladder, and head and neck solid tumors (Angela Callejo, 2015). To increase the therapeutic efficacy and improved, Cisplatin was already transport by several carriers such as nanotubes (Alia Mejri, 2014). In this study, a theoretical study, we reported types of drug delivery system such as InP nanotube. The structural stabilities of Indium phosphide nanotube (InPNTs) is examined by performing density functional theory (DFT) calculations on the representative (4, 0) zigzag models as shown in figure.1. The atomic geometries are given the relax by optimization.

2. MATERIALS AND COMPUTATIONAL DETAIL

The calculations were carried out using a personal computer has name Toshiba which has processor Intel® core (TM) i7-3610 QM CPU 2.30 GHz 2.30 GHz with 8-GB RAM. The representative zigzag model of the single-walled InPNTs is considered within this work. The diameter and length of the pristine (4, 0) SWInPNT are about 7.5 and 10 Å, respectively. SWInPNTs consisting of 32 atoms (12 Indium atoms, 12 Phosphorus atoms, and 8 hydrogen atoms). Used hydrogen atoms to saturated the Indium and Phosphorus atoms in the open edges to avoid dangling bonds at their open edges by keeping three covalent bonds for each In and P atoms of nanotubes (Mahmoud Mirzaei, 2012) as shown in figure.1. A nanotube is forming by using a nanotube modeler package (Frey & Doren, 2011). The selected drug (Cisplatin) was made using Gauss View. The structures (complexes of the single-walled nanotube with cisplatin) are optimize by employing DFT/ B3LYP exchange-functional and the standard basis set lanl2dz because there is a platinum atom in the compound, by Gauss View and Gaussian 09 program package (Frisch & Schlegel, 2009) as see in figure.1. The total energy and HOMO/LUMO investigated in the models. Binding energy (E_B) of SWInPNTs and complexes obtained from Equation (1) (Anurag Srivastava, 2014).

$$E_B = [(I\ E_{In} + J\ E_P) - E_{InPNT}]/I + J \ldots\ldots\ldots\ldots 1$$

Where, E_{InPNT} stands for the total energy considered for single wall nanotube (SWInPNT), E_{In}, E_P energy of In and P atoms respectively. I and J are the number of In and P atoms present in the tube respectively. The quantum molecular descriptors for nanotubes were determined as follows (Bahjat, 2017):

Chemical potential (μ) which shows escape tendency of an electron from equilibrium defined as follows:

$$\mu = -(IP + EA)/2 \ldots\ldots\ldots\ldots 2$$

Electronegativity (χ) is a measure of the tendency of an atom to attract a bonding pair of electrons (Abbas Shwya Alwan).

$$\chi = -\mu \ \ldots\ldots\ldots\ldots 3$$

The global hardness (η) shows the resistance of one chemical species against the change in its electronic structure equation (4) and the softness given as in equation (5) (Bahjat, 2017):

$$\eta = (IP - EA)/2 \ldots\ldots 4$$

$$S = 1/2\eta \ldots\ldots\ldots\ldots 5$$

Electrophilicity index (Ω) defined as follows:

$$\Omega = (\mu^2/2\eta) \ldots\ldots\ldots\ldots\ldots 6$$

The amount of charge transfer between the drug and the SWNT, as calculated using the ΔN method:

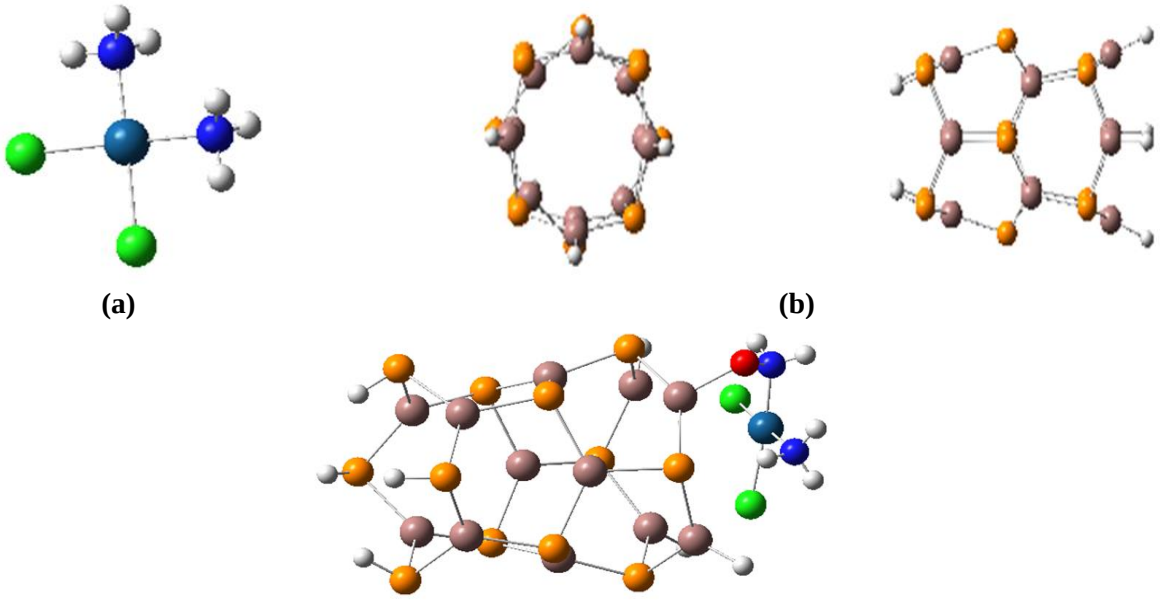
$$\Delta N = (\mu_B - \mu_A)/2(\eta_A + \eta_B) \ldots\ldots\ldots\ldots\ldots 7$$

Where IP ($-E_{HOMO}$) is the ionization potential and EA ($-E_{LUMO}$) the electron affinity of the molecule. μ_A, $\mu_B$and η_A, η_B are the chemical potential and the chemical hardness of the systems A and B. A positive value of ΔN denoted that charge flows from nanotube to the drug and the drug act as an electron acceptor, while a negative value of ΔN means that charge flows from the drug to nanotube and the drug acts as an electron donor (Bahjat, 2017).

3. RESULTS AND DISCUSSION

In the equilibrium geometries the relaxed structural of pristine zigzag (4, 0) SWInPNTs, Cisplatin drug, and complex (cisplatin-InPNT) computed using DFT calculations at the lanl2dz method, in gas phase as shown in figure.1 (a, b and c), its shown the optimized of anticancer drug Cisplatin, SWInPNT (4, 0) and complex (SWInPNT-Cisplatin), respectively. The computed average bond lengths of the zigzag In–P bonds are 2.55 Å. In this work, the zigzag (4, 0) open-ended single-walled InPNT with 7.5 Å diameter and 10 Å length was considered. The total energy, electronic states for the analyzed structures, energy gap and the values of the Ionization potential (IP), electron affinity (EA), Chemical potential (μ), Electronegativity (χ), hardness (η), Softness (S),Electrophilicity index (Ω) and ΔN for the Cisplatin, (4, 0) SWInPNT, and (4, 0) SWInPNT– Cisplatin (complex) are summarized in Table 1. The final total energy of the product is the collection of total energy of all small atoms, which build the product nanotube –drug. The binding energy is defined as the amount of energy which is required pulling the tube apart into a set of free atoms and obtained it is from equation (1). That nanotube with lowest total energy and highest binding energy value that is an indication of high stability of the nanostructure and this is a good agreement with (Yousif Abid Al Shaabani, 2016). From the table (1) the values of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) energy levels are negative ,that shows neither adding nor removing electrons from SWInPNT are energetically favorable. This reflects high stability and inertness of the SWInPNT structure, which is useful for drug carriers. The three dimensions plots of the (HOMO) and (LUMO) for SWInPNT and the complex are shows in Figure (2). From figure (2.a) can be seen that the majority of the molecular orbital density in the HOMO is distributed on all the tube(InP) and a highly localized at the one end of tube while a small amount is distributed on the other end of tube. The HOMO is distribute on the terminals phosphorus atoms, which is due to unequal charge distribution along the atoms. Whereas the LUMO is highly localized inside one of the end the

tube(InP) and over the same end of the tube, which distributed on the In atoms and a small amount is distributed on the P atoms as show in figure (2.b).



(a) **(b)**

(c)

Figure.1. The structures of optimized molecular by B3LYP/lanl2dz method. (a) Cisplatin, (b) SWInP Nanotube (4, 0), (c) Complex (SWInP-Cisplatin)

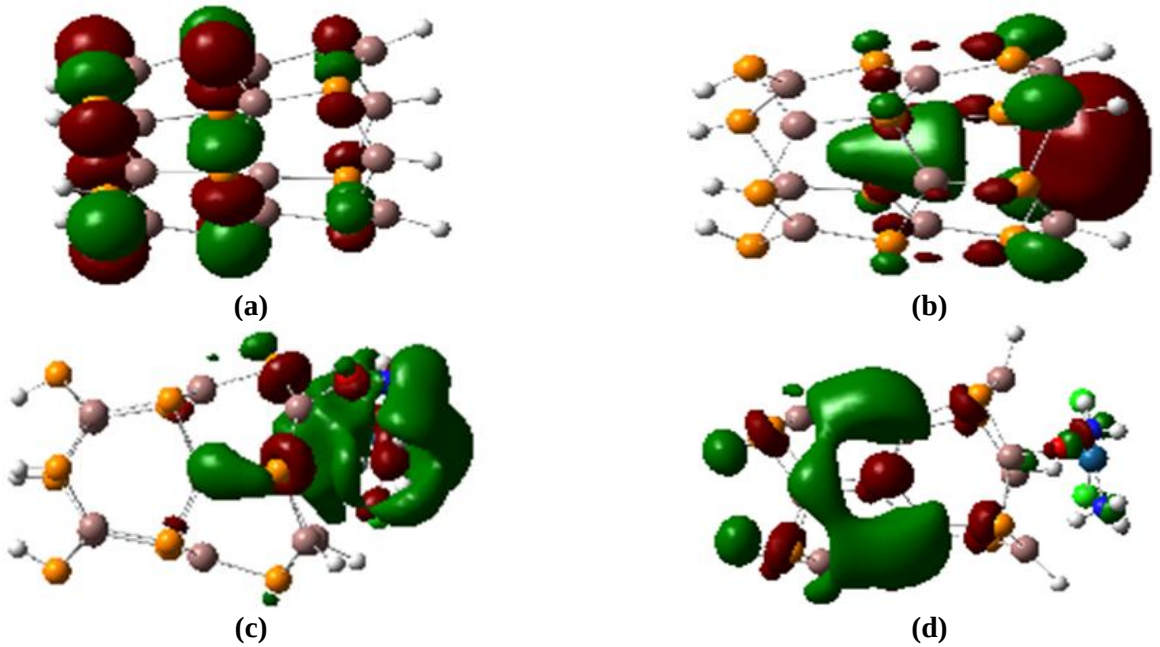
After conjugation Cisplatin with SWInPNT, HOMO plot indicated that the electron density (the electronic cloud) are localized on the structure of Cisplatin drug with an energy value -5.735ev while the LUMO orbitals at -3.689 are delocalized on the far end of SWInPNT and a small amount distributed on the N and O atoms of the drug as clear from figure 2 (c and d).The LUMO energy of molecules is lower than that of the original drug molecule, with decreasing energy gap from (4.370ev)for drug to (2.046ev) for complex. Thus, electrons can be easily excited from the ground state.

Table.1. Quantum molecular descriptors in B3LYP/lanl2dz level for optimized geometries of Cisplatin, (4, 0) SWInPNT and (4, 0) SWInPNT - Cisplatin/complex. Values in units of ev.

Property	Cisplatin	SWInPNT	Complex
E	-7137.397	-2880.770	-12033.463
E_B	3.647	2.920	3.232
HOMO	-6.272	-6.106	-5.735
LOMO	-1.902	-3.774	-3.689
Eg	4.370	2.331	2.046
IP	6.272	6.106	5.735
EA	1.902	3.774	3.689
μ	-4.087	-4.940	-4.712
X	4.087	4.940	4.712
η	2.185	1.166	1.023
S	0.229	0.429	0.489
Ω	3.821	10.467	10.851
ΔN			-0.097

The ionization potential for the Cisplatin -SWInPNT is lower than that for Cisplatin drug molecule; this indicates that the INP Cisplatin molecules not need more energy to become cation comparing with Cisplatin molecule alone. As it shown in table 1, the resulting Cisplain-SWInPNT structure is highly reactive because of its tendency to capture electrons from environment and this is due to increasing E.A value, this large number indicates that it forms a stable negative ion; i.e. it is an electrophilic structure. An important application of electronegativity is the prediction of polar nature of the resulting structure after conjugation with InP nanotube and this is convinced with a lower hardness, a higher softness and much higher electrophilicity index. Electronegativity value reflects the enable of nanotube to be more reactive toward electron to accept and exchange reactions. Hardness is an important property to measure the molecular stability and reactivity, the decreasing of hardness is the main feature as a sign for the band gap that goes to be rather soft and lowering the resistance of species to lose an electron. The behavior of softness shows that binding of the drug give the nanotube more softness. Increased electrophilicity Ω due to increase in charge

transfer from drug to nanotube. From the results ΔN value is negative, indicated that (4, 0) SWInPNT act as electron acceptors.



(a) **(b)**

(c) **(d)**

Figure.2. HOMO and LUMO level of. (a) HOMO of SWInPNT. (b) LUMO of SWInPNT (c) HOMO of Complex, (d) LUMO of complex

4. CONCLUSION

Using density functional theory to study the electronic properties and effects of the coupled of Cisplatin anti-cancer drug with (4, 0) zigzag single wall Indium Phosphide nanotube (SWInPNT). That nanotube with lowest total energy and highest binding energy have been consider that structure is more stable. Decrease in hardness, energy gap, and ionization potential and also, increase in electron affinity, electrophilicity and negative value ΔN of the complexes shows a charge transfer from the Cisplatin drug molecule to the nanotube model. In addition, the negative values of (HOMO) and (LUMO) energy levels denote to high stability and inertness of the SWInPNT structure, which is useful for drug carriers.

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