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THEORETICAL INVESTIGATION OF GUANETHIDINE ADSORPTION ON GRAPHENE: A DFT STUDY

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ABSTRACT

Graphene based nanocarriers are of interesting studying issues due to their unique physiochemical properties such as small size, high drug loading capacity and large surface area. In this paper, computational studies were conducted for the interaction between Graphene and Guanethidine. All investigations were obtained by means of density functional theory (DFT). Optimization and frequency calculations were carried out at B3LYP/6-311G (d) basis set and vibrational frequencies were allocated. The structures of individual counterparts and hybrids were firstly optimized and the molecular properties have been evaluated. The Density of States (DOS) Plots and Nuclear Magnetic Resonance spectroscopy (NMR) are two main proofs of changes of electronic properties of Guanethidine when attached to Graphene surface. Guanethidine molecule was embedded onto the surface of pure Graphene with adsorption energies of approximately -580.14, -580.18 and -580.31 kj/mol respectively. As the results indicate, good linear dependencies exist between E_{ad} and orbital energy values of studied Graphene. This study facilitates a deeper insight on how the attachment of Guanethidine to Graphene leads to a more efficient drug delivery.

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Introduction

Guanethidine is a hypotensive agent which decreases blood pressure due to decline in release of norepinephrine. In fact Guanethidine has actions which exclusively deal with peripheral nervous system. The selectivity comes out of the fact that the drug is a substrate for the pump which transports norepinephrine into the nerve endings. Guanethidine is transported into the neuron through this pump. The distinguishing function of Guanethidine deals with inhibition of responses to stimulation of adrenergic nerves but this action is not assisted by the blockade of exogenous norepinephrine. Guanethidine is considered as an adrenergic neuron blocking agent due to its potentiality of blocking transmission at adrenergic nerve terminals and evacuates tissue storage of norepinephrine [1]. Unlike ganglionic blocking agents, Guanethidine equally restrains the responses moderated by alpha-and-beta-adrenergic receptors, whereas parasympathetic blockade is not produced. Guanethidine decreases blood pressure due to slight decline in peripheral resistance as a result of sympathetic blockade. Some of the common side effects of Guanethidine include unusual fatigue or drowsiness, depression, slow heartbeat, sexual problems in male and diarrhea.

Within the recent years, the growing progress of groundbreaking drug delivery devices for various therapeutic agents has drawn the attention of many researchers. In fact several studies, were carried out on the design, synthesis, and characterization of novel materials to be applied as delivery systems with the purpose of improving the efficiency of a selected drug [2]. In this study adsorption of Guanethidine on Graphene is surveyed with the aid of density functional theory (DFT).

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Creating effective targeted drug delivery strategies leads to improvement of bio-availability, bio-compatibility and safety of therapeutic agents [3]. Targeted therapy is considered as a specific interaction between a drug and its receptor at the molecular level. Hence with the aid of drug delivery the efficiency of drug would be improved; moreover, side effects are minimized [4, 5]. As a matter of fact, nanocarriers increase the accumulation of drug in targeted cells using both active and passive targeting strategies, while toxicity in normal cells is prevented. The term "active targeting" is defined as interactions between drug/drug-carrier and the targeted cells, normally via particular ligand-receptor interactions [6]. On the other hand passive targeting is considered as enhanced permeability and retention(EPR) effect which assists targeted delivery of specific ligand-drug and drug carries into areas with lower accessibilities [6,7]. Although the active targeting strategy seems interesting nanodrugs which are presently approved for clinical usages are fairly simple and normally require active targeting or triggered drug delivery elements. Therefore for investigating the application of targeted drug delivery, we may need to figure out the properties of therapeutic drugs as well as their sites and mechanisms of action in order to achieve the desired results. Graphene sheet as a promising drug carrier is appealing due to accessibility of both sides of a single sheet [8]. The major question of this work is to investigate the adsorption of Guanethidine on Graphene surface to determine whether Guanethidine can be applied as a targeted nanodrug or not.

2- Computational details:

In this study, we have employed density functional theory (DFT) calculations to optimize the structural models of Guanethidine (Gu) and Graphene (Gr), supercell (5 × 5), which contains 72 carbon atoms and was selected as the basic model for the calculations. The Si- and Al- doped Graphene structures were then modeled by replacing a single Silicon or Aluminum atom with one Carbon atom on the surface. Interaction of Guanethidine molecule with Graphene systems has been conducted in gas due to reduction of computational cost compared with regarding each molecule individually. All the structures were optimized at 6-311G (d) level of theory. The B3LYP exchange-correlation functional and the 6-311G standard basis set have been applied to perform all computations through the Gaussian 03 package [9]. It is worth noting that the values of NMR parameters calculated by B3LYP levels are all in good agreement. The adsorption energy of the adsorbate Guanethidine with the doping Graphene is calculated based on the following formula.

$$\Delta E_{ads} = E_{Gu-Gr} - (EGr + E_{Gu}) \qquad (1)$$

According to the formula EGr-Gu, EGu and EGr are the total energies of the adsorbate-substrate (Gr-Gu) system, the substrate (Gu) and adsorbate (Gr), respectively. Nuclear Quadrupole Resonance and Nuclear Magnetic Resonance analysis were conducted at the B3LYp/6-311G (d) level. The molecular systems consist of individual Graphene, individual Guanethidine and Guanethidine-Graphene hybrid (Fig.1).

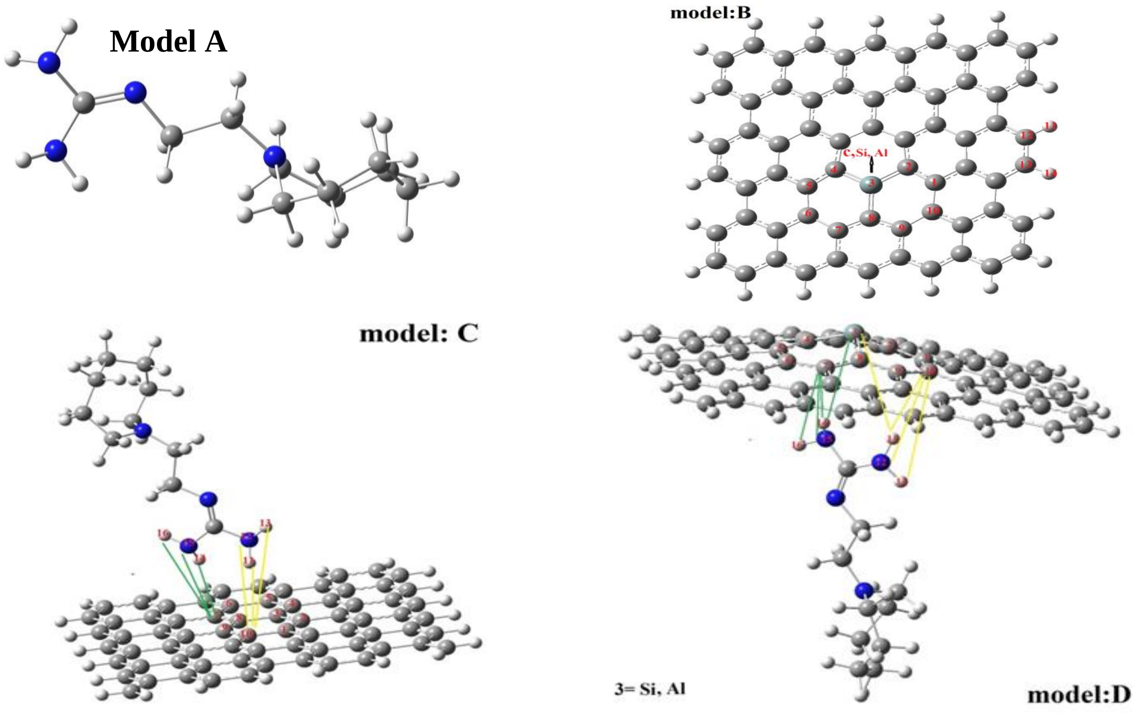


Fig1. The optimized structures a) Guanethidine b) Graphene with doping Al and Si c) Graphene with Guanethidine d) Al and Si doped Graphene with Guanethidine

3- Results and Discussion

3-1- Optimized structures of Al and Si-doped Graphene

At first, it is crucial to study the geometric structure and electronic features of optimized Al- and Si-Graphene sheets in comparison to pristine Graphene. Figure 1 (model B) indicates the geometric structure of the isolated Al- and Si-Graphene sheets after geometry optimization. The values of dipole moments (DM) are zero for them due to symmetry of electronic distributions; however, changes of these symmetric situations in the doping Al/Si models raise the magnitudes of dipole moments. Various magnitudes of energies for HOMO and LUMO levels of Graphene and doping models were observed. The magnitudes of energy gap (Egap), which demonstrate the energy differences between HOMO and LUMO levels, slightly declined for Al/ Si structures compared with their corresponding Graphene structures. However, the magnitudes of EGr for Al/ Si structures are equal to the magnitudes of corresponding Al/ Si structures confirming the role of Al/ Si in electronic conductivity of Graphene. In addition, the energy differences between HOMO and LUMO levels have declined for pristine model (table 1).

As illustrated in Figure 1(model B), doping of Graphene sheet by Al atom leads to a remarkable change in Graphene structure. The larger bond lengths accompanied by the difference in bond angles force Al to stick out from the sheet, replacing the positions of the first- and second- neighbors out of the plane as well. The average bond length between the central C (Al) atom and the adjacent C atoms vary from 1.74 Å in the pristine Graphene to 1.42 Å in Al-Graphene together with the deformity of hexagonal structure of Graphene sheet. In case of Si-Graphene, due to possessing larger atomic radius than Al, the Si dopant is pushed outside from the Graphene plane and this results in the average expansion of three newly formed Si-C bonds (1.68 Å) in comparison to the C-C bond of the pure Graphene.

Table 1. Optimized properties of model B, C and D

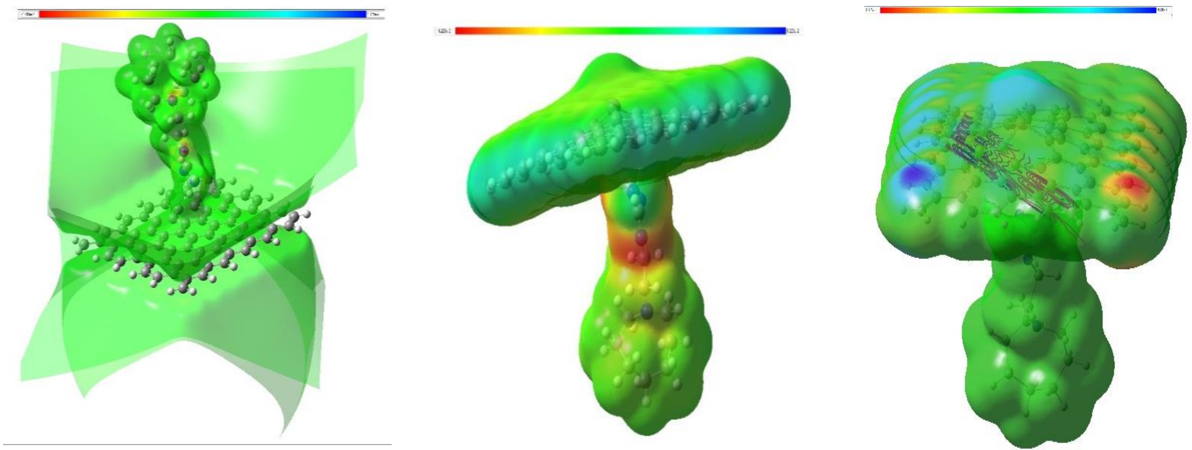
Atoms (length bond (A^0)	**Gr**	**Gr-Al**	**Gr-Si**	**Atoms (length bond (A^0)**	**Gu-Gr**	**Gu-Gr-Al**	**Gu-Gr-Si**
H11-C12	1.08	1.08	1.08	C2-C1	1.42	1.41	1.42
C12-C13	1.38	1.39	1.39	X3-C2	1.43	1.84	1.75
C13-H14	1.08	1.09	1.08	C4-X3	1.42	1.84	1.76
C1-C2	1.42	1.37	1.40	C5-C4	1.43	1.40	1.41
C2-X3	1.43	1.75	1.68	C7-C6	1.43	1.49	1.48
X3-C4	1.43	1.75	1.68	C8-X3	1.44	1.84	1.76
C4-C5	1.42	1.37	1.40	C9-C8	1.43	1.42	1.48
C5-C6	1.44	1.52	1.48	C10-C9	1.42	1.41	1.46
C6-C7	1.41	1.49	1.46	H13-C10	4.68	4.40	4.39
C7-C8	1.42	1.39	1.41	N12-C10	4.09	3.85	3.91
C8-C9	1.42	1.39	1.41	H11-C10	3.09	2.95	3.91
C8-X3	1.43	1.75	1.69	H14-C7	3.03	2.91	2.96
C9-C10	1.41	1.49	1.46	N15-C7	4.00	3.92	3.96
C10-C1	1.44	1.52	1.48	H16-C7	4.48	4.35	4.49
DM (Debye)	0.0001	1.0905	0.3157	-	3.48	4.58	2.64
E_{HOMO} (ev)	-0.13673	-0.16	-0.13605	-	-0.141	-0.160	-0.141
E_{LUMO} (ev)	-0.12534	-0.11	-0.12456	-	-0.132	-0.109	-0.132
E_{gap} (ev)	-0.0114	-0.0547	-0.0115	-	-0.008	-0.05105	-0.009
E_{Ads} (kj/mol)	-	-	-	-	-580.14	-580.31	-580.18
E (kev)	-68.81	-74.36	-75.64	-	-91.75	-97.31	-98.59

*DM= dipole moment

3-2- Guanethidine adsorption over Al and Si-doped Graphene

As shown in Fig.1, adsorption of Guanethidine on Graphene surface increases the bond length between doping Al/Si atom and C atom. Hence with regard to decrease in bond angles, which is approximately 109,hybridation of doping Al/Si changes from sp2 to sp3.Therefore Al-C and Si-C bond lengths change to 1.84 A and 1.75 A respectively. Adsorption energy of Gu-Gr,Gu-Gr-Si and Gu-Gr-Al are -580.14, -580.18 and -580.31 kj/mol respectively. According to the investigated results, it can be conceived that the adsorption energy of nanodrug Guanethidine-Graphene-Aluminum has the highest value. All energies are more than 8 kj/mol, therefore they are considered as adsorption (chemisorption) energies in which strong van der Waals force is made between the drug and Graphene and as mentioned previously the strongest London force exists between

Guanethidine-Graphen-Aluminium. Due to increase of dipole moment after adsorption of Guanethidine on Graphene surface it can be concluded that solubility of nanodrug Guanethidine-Graphene rises, hence it may have the function of targeted drug in body (table 1). As Fig.2 exhibits, molecular electric charge of atom no.3 in nanodrug Guanethidine-Graphene is 0.028e which has reduced in comparison to Graphene (0.037e). Molecular charge of Al in nanodrug Guanethidine-Graphene-Aluminium is 0.028e which has reduced in comparison to Graphene (0.037e). Molecular electric charge of Al in nanodrug Guanethidine-Graphene-Aluminium is 0.201e which has increased compared to Graphene-Aluminium. Moreover, molecular electric charge of nanodrug Guanethidine-Graphene-Silicon is 0.210e which has declined compared to Graphene-Silicon (0.265).



Gu- Gr

Gu-Gr-Si

Gu-Gr-Al

Fig 2. Optimized structures of four Guanethidine molecules over Al-/Si-Graphene along with their corresponding electron density difference maps. In the EDD maps, the charge depletion and accumulation sites are displayed in red and blue, respectively.

3-3- Nuclear Quadrupole Resonance

Nuclear Quadrupole Resonance (NQR) is one of the promising chemical techniques for identifying the composite of the elements which collaborates with nuclear magnetic resonance. Unlike NMR, the NQR analysis can be detected even in the absence of magnetic field in nuclear conversion. In simpler terms, the NQR spectroscopy functions the same as NMR with zero magnetic field. In fact the NQR resonance is a connection between electric field gradient (EFG) and Nuclear Quadrupole Resonance in which the charge distribution takes place. The EFG, demonstrates the total transformation of an element, furthermore a location of a nuclei in material in which the linked valance electrons of the atoms which are altered is shown as well. Indeed, this frequency is in good agreement with Nuclear Quadrupole Resonance, nuclei properties and EFG of neighbor nuclei in a composite or a crystal.

As well as the optimized properties, Quadrupole Coupling constants (C_Q) have been calculated for the atoms of optimized structures in order to distinguish the properties of investigated models at the atomic levels (Table 2). Electric field gradient (EFG) tensors have been evaluated as well and they have been changed into C_Q parameters using equation C_Q (MHz) = $e^2Qq_{zz}h^{-1}$, in which e, Q, q_{zz}, and h respectively stand for electronic charge, nuclear electric quadrupole moment, EFG tensors main eigenvalue, and Planck's constant [10]. Due to sensitivity of EFG tensors to electronic sites of atoms, they are able to reveal any perturbations employed to these sites demonstrating insightful information about the electronic features of matters [11]. The magnitudes of C_Q could be evaluated by means of Nuclear Quadrupole Resonance (NQR) spectroscopy, furthermore they could take the advantage of being accurately reproduced through quantum computations by means of computational chemistry for predication and analysis of experimental investigations [12-15]. The standard Q values are (C_{11}) =33.27 mb, H_2= 2.86 mb and Al_{27}=146.6 mb which are reported by Pyykkö [16].

Table2. NQR parameters for Gu-Gr, Gu-Gr-Al and Gu-Gr-Si

atom	Gu-Gr		atom	Gu-Gr-Al		Gu-Gr-Si	
	η_Q	C_Q		η_Q	CQ	η_Q	C_Q
C4	0.00	1.75	C2	0.00	3.99	0.00	3.99
C8	0.00	1.75	C4	0.00	3.99	0.00	3.99
H13	0.00	0.00	C5	0.00	3.99	0.00	3.99
			C7	0.00	3.99	0.00	3.99
			C8	0.00	3.99	0.00	3.99
			C9	0.00	3.99	0.00	3.99
			C10	0.00	3.98	0.00	3.98
			H11	0.00	0	0.00	0
			H13	0.00	0	0.00	0
			X3	0.00	196.13	0.00	-
average	0.00	1.75		0.00	6.87	0.00	3.99

Mirzaeie and colleagues have reported the value of C_Q for Graphene atoms (5x5) 1.7-2.3. The value has decreased as a result of attaching Guanethidine on Graphene surface [14].In other words, the electric charge value is not along the z-z axis. By doping the central atom of Graphene with Al and Si and attaching Guanethidine on its surface, the value of C_Q increases in all carbon atoms and the C_Q of Al atom changes to 196.1 which demonstrates the highest impact in comparison to pristine Graphene.

3-4- Nuclear Magnetic Resonance

In this computational study, the properties of the electronic structure and chemical shielding parameters of Graphene derivatives were evaluated through density functional theory (DFT) calculations of the Nuclear Magnetic Resonance (NMR) parameters. The chemical shielding (CS) tensors were calculated according to the gauge consist of atomic orbital (GIAO) approach [17]. The calculated CS tensors in principal axis system (PAS) (d33> d22> d11) were converted to measurable NMR parameters, chemical shielding isotropic (CSI) and chemical shielding anisotropic (CSA) by using Eqs. (1) and (2), respectively [18]. The evaluated NMR parameters are exhibited in Table 3.

$C_{SI} = 1/3(\sigma_{11} + \sigma_{22} + \sigma_{33})$ Equation (1)

$C_{SA} = \sigma_{33} - ½(\sigma_{22} + \sigma_{11})$ Equation (2)

Table3. Nuclear Magnetic Resonance parameters

Gu-Gr-Si					**Gu-Gr-Al**				**Gu--Gr**			
atoms	Isotropy	Anisotropy	C_{SI}	C_{SA}	Isotropy	Aniotropy	C_{SI}	C_{SA}	Isotropy	Aniotropy	C_{SI}	$\mathbf{C_{SA}}$
C1	68.3	156.2	68.3	137.7	68.9	156.6	68.9	101.8	-	-		-
C2	73.6	151.0	73.6	126.3	74.5	149.8	74.7	99.8	73.6	149.5	73.6	60.7
C4	67.5	166.1	67.5	89.9	60.9	152.1	60.9	48.4	-	-		-
C5	62.1	176.0	62.1	127.6	54.1	170.8	67.4	65.9	-	-		-
C6	73.6	150.4	73.6	107.5	72.8	152.1	72.8	91.4	-	-		-
C7	63.3	170.1	63.3	162.7	55.1	174.9	56.4	166.3	-	-		-
C8	71.8	152.0	71.8	67.6	72.8	152.2	72.8	51.2	71.5	152.2	71.5	63.6
C9	71.8	152.0	71.8	115.1	72.6	151.0	72.6	113.9	73.4	149.5	73.4	58.2
C10	74.2	149.7	74.2	125.9	72.3	156.0	72.3	123.6	67.7	157.0	67.7	60.7
H11	30.8	11.2	30.8	9.4	30.2	8.3	30.2	4.1	29.7	8.1	29.7	3.1
H13	30.8	12.3	30.8	7.5	32.7	17.1	32.7	9.2	30.7	11.1	30.7	1.4
X=Al	-	-	-	-	325.8	162.2	325.8	103.2	--	-	-	-

In table 3, the evaluated C_{SA} parameter for C_{11} is 58.2-63.24 ppm and the maximum anisotropic effect accounts for C_{24} while for hydrogens in nanodrug Guanethidine-Graphene the C_{SA} is 1.4-4.5 ppm. In Guanethidine-Graphene-Aluminium CSA for carbon atoms is 51.2-166.3 ppm in which the doping Al has caused C_{24} to be deshielded and C_{41}, C38, C33 have the highest anisotropic effect and became shielded. In nanodrug Guanethidine-Graphene-Silicon CSA is in range of 67-162.7 and C_{38}, C41 have the highest values which are 160.8-162.7, respectively.

3-5- HOMO and LUMO parameters and density of state (DOS)

In Fig.3, the electronic density of states (DOS) of individual Graphene derivatives were presented. The following figures indicate the molecular orbitals of each element per to hole system that were calculated using the Gauss view software.

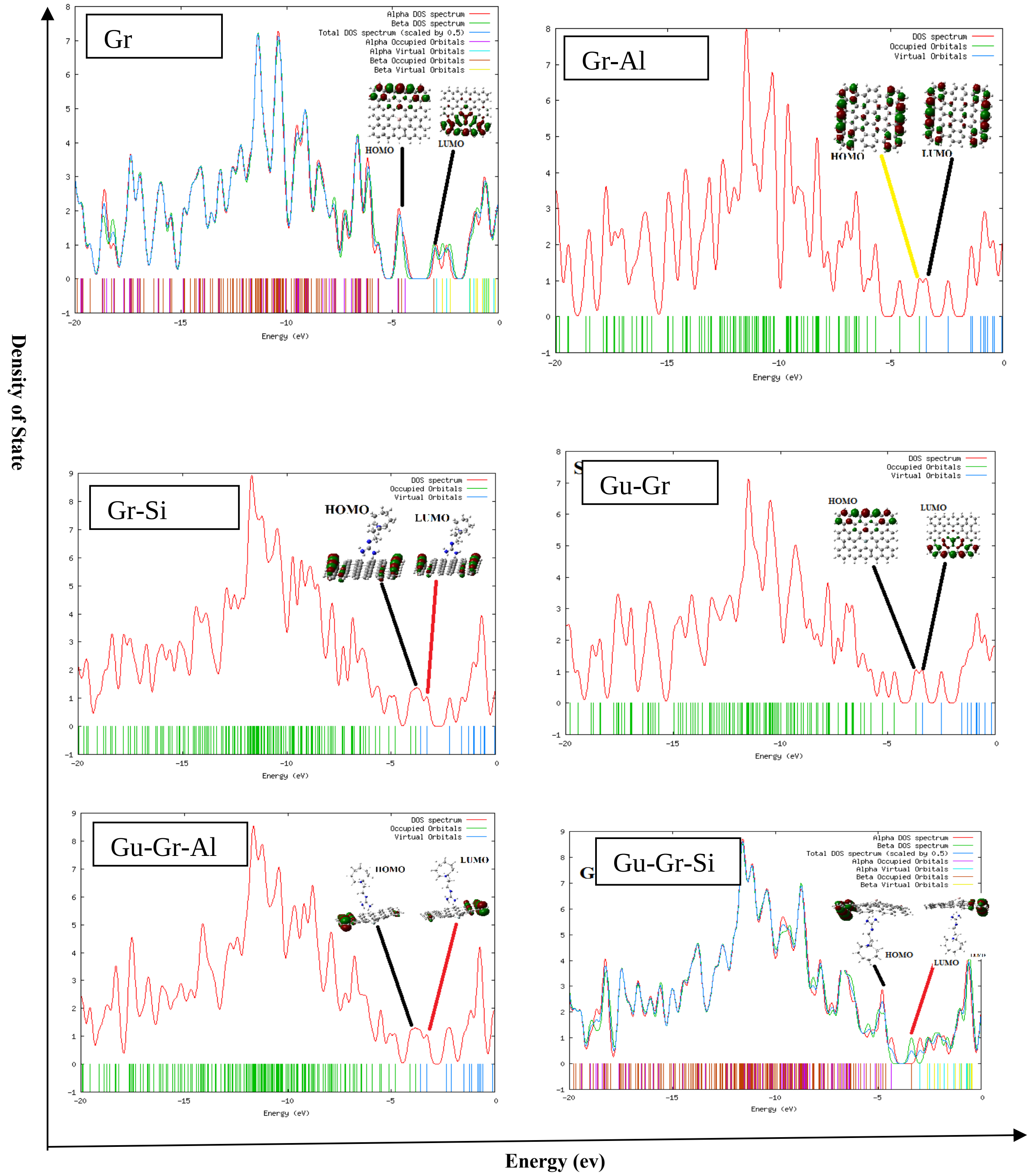


Fig 3. Diagram of the density of state per energy for Graphene-Al/Si and Guanethidine-Graphene-Al/Si

HOMO and LUMO energies and the corresponding energy gap (Egap in ev) are two main parameters which are used for characterizing the electronic properties of Graphene derivatives. The distribution patterns of the frontier molecular orbitals; Highest Occupied Molecular orbitals (HOMOs) and Lowest Unoccupied Molecular orbitals (LUMOs) [19] were presented in Fig. 1 and Table 1. As Figure 1 indicates, the variance between HOMO and LUMO in Guanethidine- Graphene is -0.008 eV which is less than other Graphene derivatives in this study. The energy gaps in four modeled samples vary as below:

Egap (Gr-Si) > Egap (Gr) > Egap (Gr-Al) > Egap (Gu-Gr-Al) > Egap(Gu-Gr) > Egap(Gu-Gr-Si)

As indicated energy gaps of all Graphene derivatives follow the above trend. According to these results as the energy gap decreases, the electrical conductivity increases. Hence nanodrug Guanethidine-Graphene-Si has the minimum energy gap while possessing maximum electrical conductivity.

3- 6- Natural Bonding Orbitals

In Fig.4 graph of atomic charge to atom type in different models is shown. In Guanethidine-Graphene and Guanethidine-Graphene-Si no significant change was observed in atomic charge of Graphene and doped Graphene by Silicon due to interaction of Guanethidine on Graphene and doped Graphene by Silicon and this confirms the adsorption. However, in Guanethidine-Graphene-Al there is a noticeable change in comparison to Graphene-Al and it demonstrates a strong interaction between Graphene-Al and Guanethidine. The atomic charge values of C_{10},C_8,C_5 and Al_3 in Graphene-Al are 0.02,-0.17,0.03 and 0.17 respectively while in Guanethidine-Graphene-Al model the atomic charge values of the above atoms are 0.19,0.17,-0.12,0.09 respectively.

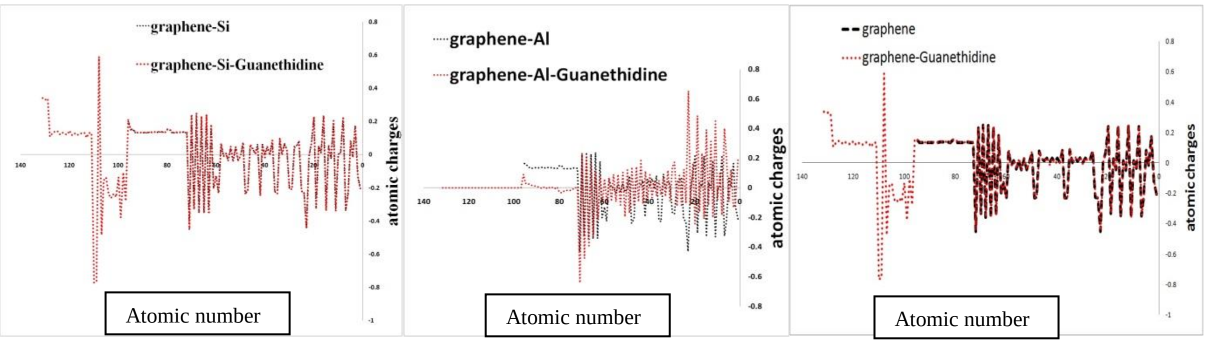


Figure4. Graph of atomic charge to atomic number in Graphene and Guanethidine-Graphene (model A), Graphene-Al and Guanethidine-Graphene-Al (model B), Graphene-Si and Guanethidine-Graphene-Si (model C)

Table 4 demonstrates that bonds in Graphene and its derivatives are π and has almost hybridization of SP^2.Furthermore the average value of occupancy of orbital is 1.98 .In doped Graphene by Aluminum no common bond with hybridized Aluminum was observed. However, hybridization of atoms bonded to Aluminum is almost $SP^{1.75}$ and occupancy rate is 1.98 In Graphene doped by Silicon the hybridization of Silicon is $SP^{2.6}$ .A very tiny difference in atom hybridization and occupancy rate is observed which can be ignored.

Table 4. Comparison of hybridization properties of various models A-D

Model	Gr	Gu-Gr	Gr-Al	Gu-Gr-Al	Gr-Si	Gu-Gr-Si
Orbital atomic	Hybrid (Occupancy)	Hybrid (Occupancy)	Hybrid (Occupancy)	Hybrid (Occupancy)	Hybrid (Occupancy)	Hybrid (Occupancy)
BD(1) C1-C2	$SP^{1.97}$- $SP^{1.97}$ (1.96816)	$SP^{1.97}$- $SP^{1.97}$ (1.96807)	$SP^{1.94}$- $SP^{1.57}$ (0.98410)	$SP^{1.94}$- $SP^{1.57}$ (0.98376)	$SP^{1.93}$ -$SP^{1.86}$ (1.96834)	$SP^{1.99}$- $SP^{1.87}$ (1.96809)
BD(1) C1-C10	$SP^{2.03}$- $SP^{2.03}$ (1.96738)	$SP^{2.03}$- $SP^{2.03}$ (1.96723)	$SP^{2.00}$- $SP^{1.94}$ (0.98589)	$SP^{2.00}$- $SP^{1.94}$ (0.98576)	$SP^{1.93}$- $SP^{1.94}$ (1.97122)	$SP^{1.93}$- $SP^{1.94}$ (1.97101)
BD(1) C2-C3	$SP^{1.99}$- $SP^{2.00}$ (1.96803)	$SP^{1.99}$- $SP^{2.00}$ (1.96798)	-	-	$SP^{2.57}$- $SP^{2.13}$ (1.91562)	$SP^{2.53}$- $SP^{2.14}$ (1.91813)
BD(1) X3-C4	$SP^{1.96}$- $SP^{1.96}$ (1.96826)	$SP^{1.96}$- $SP^{1.96}$ (1.96826)	-	-	$SP^{2.30}$- $SP^{2.08}$ (1.94314)	$SP^{2.61}$- $SP^{2.08}$ (1.81329)
BD(1) C3-C8	$SP^{2.04}$- $SP^{2.04}$ (1.96734)	$SP^{2.05}$- $SP^{2.04}$ (1.96727)	-	-	$SP^{2.54}$- $SP^{2.11}$ (1.91503)	$SP^{2.29}$- SP2.11 (1.94728)
BD(1) C4-C5	$SP^{2.00}$- $SP^{2.01}$ (1.96876)	$SP^{2.00}$- $SP^{2.01}$ (1.96880)	$SP^{1.57}$- $SP^{1.93}$ (0.98407)	$SP^{1.57}$- $SP^{1.93}$ (0.98399)	$SP^{2.03}$- $SP^{1.93}$ (1.96845)	$SP^{1.87}$ -$SP^{2.04}$ (1.96606)
BD(1) C5-C6	$SP^{2.01}$- $SP^{2.01}$ (1.96785)	$SP^{2.01}$- $SP^{2.01}$ (1.96835)	$SP^{1.97}$- $SP^{2.06}$ (0.98639)	$SP^{1.97}$- $SP^{2.06}$ (0.98637)	$SP^{1.91}$- $SP^{1.93}$ (1.97148)	$SP^{1.91}$- $SP^{1.93}$ (1.97139)
BD(1) C6-C7	$SP^{2.01}$- $SP^{1.99}$ (1.96883)	$SP^{2.01}$- $SP^{1.99}$ (1.96786)	$SP^{1.92}$- $SP^{2.02}$ (0.98638)	$SP^{1.92}$- $SP^{2.02}$ (0.98635)	$SP^{1.96}$- $SP^{1.98}$ (1.97109)	$SP^{1.96}$- $SP^{1.98}$ (1.97121)
BD(1) C7-C8	$SP^{1.96}$- $SP^{1.96}$ (1.96838)	$SP^{1.97}$- $SP^{1.96}$ (1.96873)	$SP^{1.99}$- $SP^{1.62}$ (0.98403)	$SP^{1.99}$- $SP^{1.61}$ (0.98392)	$SP^{2.05}$- $SP^{1.93}$ (1.96760)	$SP^{2.05}$- $SP^{1.94}$ (1.96805)
BD(1) C8-C9	$SP^{2.00}$- $SP^{1.99}$ (1.96811)	$SP^{2.00}$- $SP^{2.00}$ (1.96795)	$SP^{1.49}$- $SP^{1.87}$ (0.98460)	$SP^{1.49}$- $SP^{1.87}$ (0.98444)	$SP^{1.94}$- $SP^{1.85}$ (1.96945)	$SP^{1.94}$- $SP^{1.86}$ (1.96933)
BD(1) C9-C10	$SP^{1.97}$- $SP^{1.97}$ (1.96820)	$SP^{1.97}$- $SP^{1.97}$ (1.96801)	$SP^{2.08}$- $SP^{2.00}$ (0.98579)	$SP^{2.09}$- $SP^{2.00}$ (0.98571)	$SP^{2.03}$- $SP^{2.02}$ (1.97011)	$SP^{2.02}$- $SP^{2.02}$ (1.97018)

In table 5 orbital interactions between acceptor and donor atoms of electronic transfer is demonstrated. A significant increase in E_2 occurs as a result of doping in Graphene which shows a stronger resonance compared with pure Graphene. Due to adsorption of drug on Graphene and doped Graphene orbital energy interaction increases significantly in comparison to Graphene and doped Graphene which verifies the adsorption of drug on Graphene and doped Graphene.

Table 5. Energies of some interactions between Acceptor and donor NBO in Graphene models

		Gr-Al	Gu-Gr-Al			Gu-Gr	Gr
Donor	Acceptor	E(2)	E(2)	Donor	Acceptor	E(2)	E(2)
π C9-C8	π *C10-C1	5.33	5.34	π C2-C3	π*C4-C5	22.11	20.84
π C1-C10	π *C9-C8	10.84	10.84	π C2-C3	π*C7-C8	19.87	17.9
π C9-C10	π *C1-C2	11.88	11.99	π C7-C8	π*C2-C3	18.93	17.9
LP(1)C8	LP*(1)Al3	97.11	96.1	π C7-C8	π*C9-C10	20.56	18.25
LP(1)C8	LP*(2)Al3	32.33	30.17	π C9-C10	π*C7-C8	21.01	20.81
LP(1)C8	LP*(4)Al3	25.97	11.67	σ C7-C8	π*N12-H11	0.36	-
LP(1)C4	LP*(1)Al3	97.88	95.41	σ C9-C10	π*N15-H14	0.21	-
LP(1)C4	LP*(2)Al3	24.19	26.77			Gr-Si	Gr-Gu-Si
LP(1)C4	LP*(3)Al3	6.29	9.14	Donor	Acceptor	E(2)	E(2)
LP(1)C4	LP*(4)Al3	30.37	11.61	π C6-C5	π *(2)C4-Si3	14.65	216.14
LP(1)C2	LP*(1)Al3	95.62	89.63	π C9-C8	π (2)C4-Si3	16.84	98.25
LP(1)C2	LP*(3)Al3	46.36	39.85	π C4-Si3	σ * C4-Si3	7.08	147.97
LP(1)C2	LP*(4)Al3	15.41	9.96	π C2-Si3	π * C4-Si3	4.18	7.71
π C2-C1	σ *(1)N12-H11		0.31	π C1-C10	σ * N12-H11		0.33

4- Conclusion

In this study impacts of Guanethidine on Graphene and Si-and Al-doped Graphene were surveyed. Based on the investigations it was revealed that due to the adsorption on Graphene surface bond length and bond angles of doped atoms change when doped to Al and Si and the hybridization will change into sp3. Herein the adsorption is chemisorption and among all Guanethidine-Graphene-Al has the maximum value. Dipole moment increases as a result of Guanethidine adsorption on Graphene surface, hence the solubility of drug rises and it could be applied as a targeted drug. The comparison of calculated energy gap indicates that Guanethidine-Graphene has the lowest energy gap and thus possesses the highest conductivity. In surveying nucleic magnetic resonance it can be conceived that in nanodrug due to anisotropic effect Graphene atoms bear more changes compared to Graphene individually. Moreover, Nuclear Quadrupole Resonance (NQR) on Graphene surface changes due to this adsorption.

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