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Graphene Scaffold for Tioguanine Delivery: DFT Approach

Esmaeil Moezi
Department of Chemistry, Faculty of Pharmaceutical Chemistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Mahmoud Mirzaei✉
Department of Biomaterials, Nanotechnology and Tissue Engineering, School of Advanced Technologies in Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

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ABSTRACT. Density functional theory (DFT) approach was used to perform molecular scale calculations to examine the capability of graphene scaffold for delivery of tioguanine anticancer drug. To achieve the purpose, singular models were optimized to provide required components for bimolecular tioguanine@graphene complex formation in re-optimization processes. The calculation results indicated favorable perpendicular localization of tioguanine to the graphene surface, in which evaluated molecular descriptors approved such achievement of bimolecular complex formation. Each of frontiers molecular orbitals (HOMO and LUMO) distribution patterns and electrostatic potential (ESP) surfaces showed the existence of tioguanine@graphene complex. Finally, the obtained results of this work made sense the starting hypothetic idea of graphene scaffold application for delivery of tioguanine to be examined more by future practical works.

KEYWORDS. Graphene; Scaffold; Tioguanine; Anticancer; DFT.

INTRODUCTION. Since the early days of carbon nanotube (CNT) introduction by Iijima, considerable attempts have been dedicated to explore various features and applications for this novel material.[1-3] Soon after, existence of other types of nanostructures have been proposed in both of atomic components of geometrical shapes.[4-6] One of the important goals of such typical scientific activity was to develop applications of nanostructure in biological media especially for drug delivery purposes.[7-9] To this aim, several other features were investigated to evaluate such activity of nanostructures regarding the purposes of targeted drug delivery systems and biomedical applications.[10] Such nano-scaffolds have been seen to work as carriers for drugs to increase the efficacy and to decrease the unfavorable side effects.[11-13] Graphene, as a well-known, carbon nanostructure, has been expected to play dominant roles in the fields of such biomedical applications to deliver drugs up to correct targets.[14-16] Graphene-based scaffold could work as proper surface for adsorption of medicinal substances to carry them inside different media.[17-19] Tioguanine is an example of anti-cancer drugs, in which its improvement regarding the targeted drug delivery processes of saving the health of patients is almost a crucial issue.[20-22] This drug, which has been also known as thioguanine or 6-thioguanine, is a guanine nucleobase derivative for medication of several types of cancers.[23-25] Within this work, employing a representative graphene scaffold was explored for tioguanine to examine the features of drug before/after such complexation process (Fig. 1). To achieve this goal, molecular scale calculations were performed to optimize model systems to obtain

✉ Corresponding author: M. Mirzaei; *E-mail address*: **mdmirzaei@pharm.mui.ac.ir**, *ORCiD*: **0000-0001-9346-4901**.

required information for discussing the research topic. It is an important point that the computer-based works could provide insightful information before or after experiments to make sense the ideas properly.[26-30]

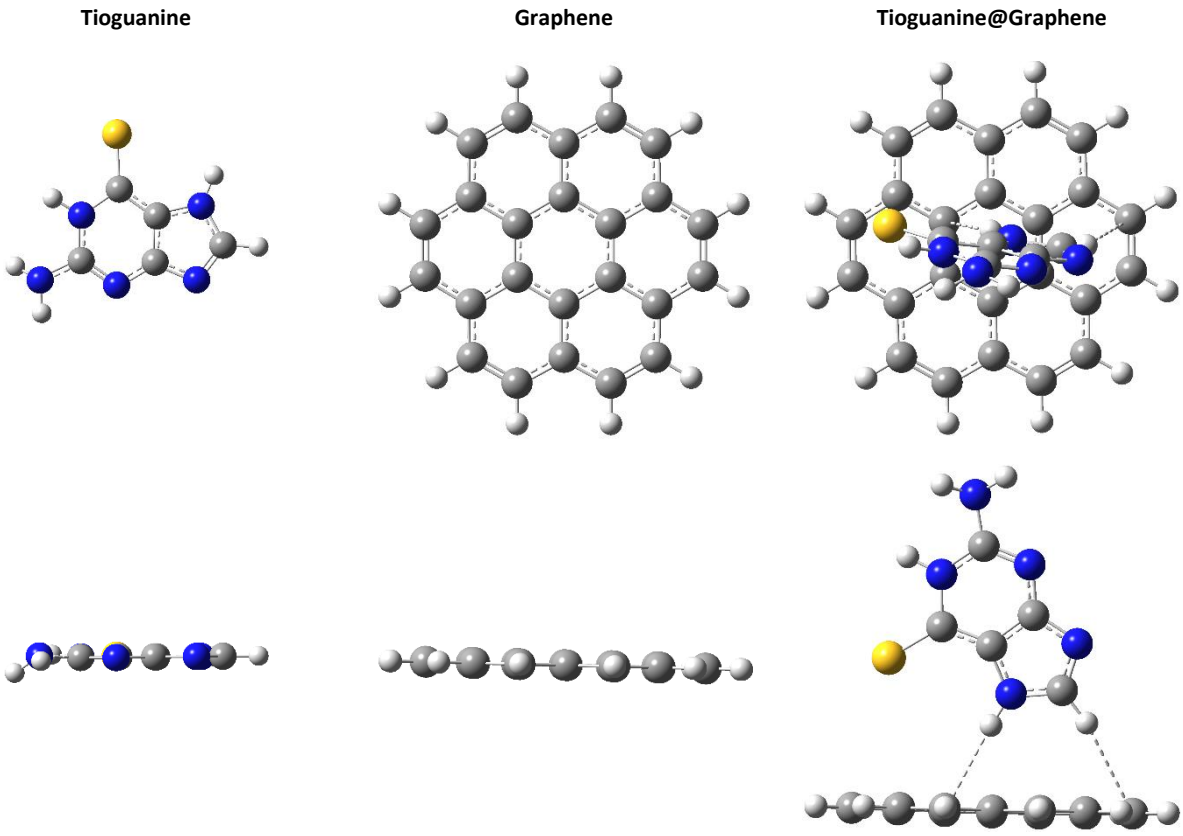

Fig. 1: Molecular models of singular and complex systems in different views.

METHODOLOGY. Density functional theory (DFT) calculations were performed to obtain required information to achieve the goal of this work. The B3LYP exchange-correlation functional and the 6-31G* basis set were employed for performing DFT calculations using the Gaussian program.[31] First, singular models of tioguanine and graphene (Fig. 1) were optimized to achieve the minimum energy structures. It is important to mention here that coronene ($C_{24}H_{12}$) could be designated for a single-standing structural reprehensive of graphene, which was used in this work.[32-34] Those hydrogen atoms are important for the planar sheets in molecular calculations avoiding the dangling effects.[35] Next, complexation of tioguanine and graphene scaffold were done by re-optimizing the available singular models in new bimolecular mode. As a result, optimized bimolecular complex of tioguanine@graphene was achieved regarding the obtained minimum energy structure (Fig. 1). Subsequently, molecular descriptors of optimized models including energy levels of the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO), dipole moment (DM), adsorption energy (AE) and adsorption distance (AD) were evaluated (Table 1). Furthermore, HOMO/LUMO distribution patterns and electrostatic potential (ESP) surfaces were evaluated for better examining the structural features (Fig. 2).

Table 1: Molecular descriptors for the optimized systems.*

Descriptor	Tioguanine	Graphene	Tioguanine@Graphene
HOMO /eV	-5.662	-5.452	-5.298
LUMO /eV	-1.516	-1.411	-1.581
DM /Debye	1.935	0	1.613
AE /eV	N/A	N/A	-0.042
AD /Å	N/A	N/A	2.498
			2.751

*See Figs. 1 and 2 for the models description. AE = $E_{Complex}$ – Sum of $E_{Components}$.

RESULTS & DISCUSSION. Within this work, a representative graphene scaffold was investigated for tioguanine delivery using DFT approach. The model systems of this work and the obtained results were all summarized in Table 1 and Figs. 1 and 2. It has been already mentioned that the molecular scale computational works could provide insightful information for careful examination of matters at the lowest possible scales.[36-40] In the first step of this work, singular models including tioguanine and graphene were optimized to achieve the minimum emery structures. Next, parallel optimization calculations were performed to achieve the bimolecular tioguanine@graphene complex. By doing such steps, the models were provided for further analyzing in order to reach the goal of this work. As in important point shown in Fig. 1, the initial position of tioguanine was parallel to the graphene surface; however, the optimization processes yielded a complex system with tioguanine perpendicular to the surface. Another important point was localization of tioguanine almost at the center of the surface showing the validity of such representative graphene model for examining such capability of scaffold for drug delivery processes. The energy values of HOMO and LUMO for singular and complex models show deviations of level in order to employed perturbation of such complex formation processes. The changes of each level detected such deviations when comparing the results in to singular and complex models. Therefore, it could be expected that such tioguanine@graphene complex was existed regarding the obtained molecular descriptors. The values of DM showed deviations of electric charge distributions at the molecular system models.

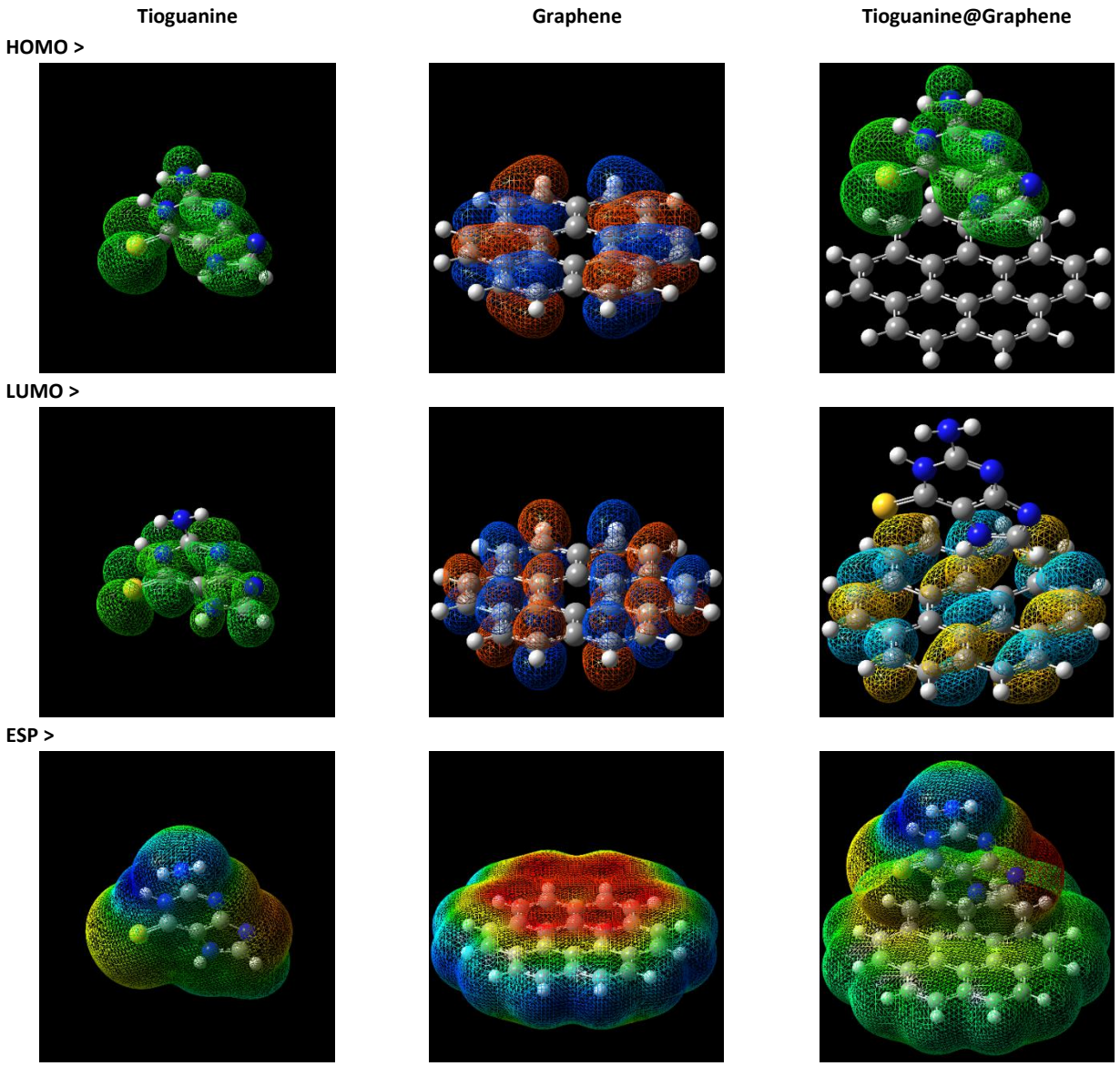

Fig. 2: HOMO/LUMO distribution patterns and ESP surface representations.

The visual exhibitions of HOMO and LUMO distribution patterns and ESP surfaces (Fig. 2) also approved such complex formation to make sense the starting hypothetic idea. Indeed, frontier orbitals are very much important for describing chemical features, in which the changes of their level could show the employed perturbations to such systems.

Bimolecular formation of tioguanine@graphene complex was investigate more by obtained values of AE and AD, in which the results indicated a reasonable strength for such complex system regarding the obtained value of AE energy and AD distances. Both values could indicate physical loading of tioguanine at the surface of graphene, as an important factor for reversible drug delivery processes. Although the physical interactions are weaker than those of chemical ones, but their strength are still appropriate for adsorption of matters especially in the reversible processes. Within the obtained results of this work, the perpendicular adsorption of tioguanine to the graphene surface was appropriate to achieve the minimum energy system of bimolecular complex formation.

CONCLUSION. Within this DFT work, application of graphene scaffold for delivery of tioguanine was investigated at the molecular scale calculations. Based on the obtained results, some remarks could be summarized. First, the results indicated that the bimolecular tioguanine@graphene complex formation was achieved. Second, the favorable localization of tioguanine was perpendicular to the graphene surface. Third, HOMO and LUMO related molecular descriptors approved such complex formation in addition to their visual representation and ESP. Fourth, values of AE and AD indicated that such complex formation was achievable. Fifth, the surface size was appropriate for such investigation as the localization of tioguanine was optimized to the center of surface. Finally, graphene scaffold could be supposed for using in delivery process of tioguanine for performing further examinations to achieve practical results about confirmation of this idea within experiments.

DISCLOSURE STATEMENT. The author(s) did not report any potential conflict of interest.

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