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Interactions of Fluorouracil by CNT and BNNT: DFT Analyses

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ABSTRACT. The effects carbon nanotube (CNT) and boron nitride nanotube (BNNT) have been examined on the properties of fluorouracil (FU) anti-cancer drug in CNT-FU and BNNT-FU complex formations through density functional theory (DFT) calculations. Molecular and atomic scale properties have been evaluated for FU in singular and complex forms to find possible solution for the mentioned problem of this work. Based on the obtained results, BNNT-FU has been seen almost as a chemical complex versus physical CNT-FU complex. Moreover, molecular orbital properties approved such type of complex formations for both CNT-FU and BNNT-FU. Atomic scale properties also indicated many more significant effects for atoms of FU in BNNT-FU than CNT-FU, in which the trend could make a conclusion that the effects on FU are many more significant in BBNT-FU in comparison with CNT-FU. It is worth to note that knowing details of interactions is very much important for molecular consideration in drug delivery systems.

Keywords: BNNT; CNT; Fluorouracil; DFT; Computations; Interactions.

INTRODUCTION

Since the early days of carbon nanotube (CNT) discovery, several works have been dedicated to explore different features of this novel material for specific applications.[1-5] In addition, existence of non-carbon based nanostructures has been also investigated, in which boron nitride nanotube (BNNT) has been introduced as a proper competitor for the already found CNT.[6-10] Moreover, ionic feature has made BNNT much favorable than non-ionic CNT to be dispersed in water media.[11] By vast variety of electronic and structural characteristics of nanotubes, they have been expected to be employed in several types of applications, among which drug delivery purposes have been seen as emerging applications of such novel structures in living systems.[12] Interaction details of medicinal molecules with nanotubes are very much important to be found based on examining the effects of such complex structures on the initial properties of medicinal compounds.[13] To this aim, several attempts have been done to find such effects for different medicinal compounds in both of computational and experimental points of view.[14-16] Since cancer itself is still an unsolved problem and the anti-cancers are not efficient enough yet, investigating advantage of nanostructures applications in such drug delivery systems is an important task to do.[17]

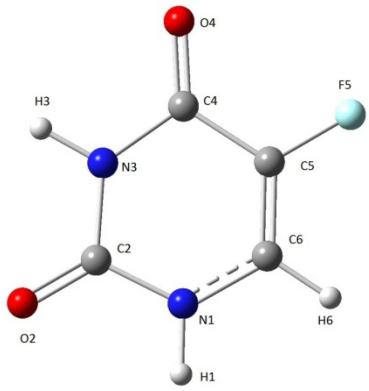

Fig. 1: Fluorouracil (FU).

Fluorouracil (FU) (Fig. 1), or 5-fluorouracil, is a fluorinated derivative of uracil, which has been employed as an anti-cancer for years.[18] Despite its wonderful therapeutic advantages, considerable unwanted side effects are arisen for those patients under

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treatments with FU.[19] Therefore, knowing more about electronic and structural properties of FU may help to improve its capability for more efficient treatments of cancer patients.[20, 21] Earlier works have indicated that FU could bind to nanostructures through physical and chemical interactions making complex systems.[22-26] However, the characters of nanostructure could bring different effects for FU during complex formations. In this work, representative models of CNT and BNNT have been employed as non-ionic and ionic nanotubes to investigate details of interaction of FU with them (Fig. 2). To achieve the purpose, quantum chemical computations have been performed at the molecular scale to find the mechanism of such complex formations between FU and each of CNT and BNNT. The obtained results (Table 1 and 2) have been discussed to evaluate a possible response for the major problem of this work: how are effects of non-ionic CNT and ionic BNNT on the properties of FU?

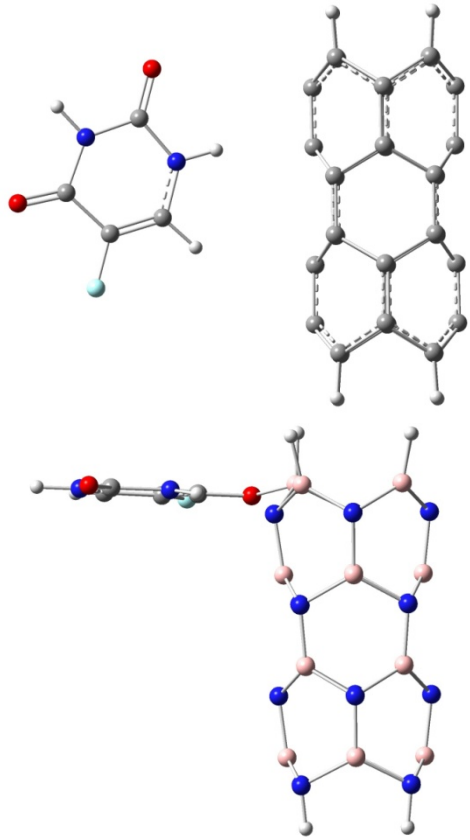

Fig. 2: CNT-FU (top) and BNNT-FU (bottom) complexes; C-H distance: 2.95 Å in , B-O distance: 1.58 Å.

MATERIALS AND METHODS

This work has been done employing density functional theory (DFT) calculations on molecular systems of FU, (4,0) CNT and (4,0) BNNT (Figs. 1 and 2). The B3LYP/6-31G* level of theory has been employed for calculations using the Gaussian 09 program.[27] 3D models of each of three molecules have been optimized first to obtain minimized energy structures. Afterwards, the models of CNT-FU and BNNT-FU have been optimized to explore complex formations of such hybrid systems (Fig. 2). For complex systems, dispersion corrections have been considered by IOp(3/124=30) for interacting systems.[28] Moreover, the basis set superposition error (BSSE) has been examined for the bi-molecular systems showing almost negligible errors to energy values.[29] By these processes, models descriptors including the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO), energy gap (EG), dipole moment (DM) and binding energy (EB) have been evaluated (Table 1). HOMO, LUMO and DM have been directly obtained from the output file whereas eqs. (1) and (2) have been employed to evaluate EG and EB.

$$EG = LUMO - HOMO \quad (1)$$

$$EB = E_{Complex} - E_{FU} - E_{CNT/BNNT} \quad (2)$$

For further analyses at the atomic scales, chemical shielding (CS) descriptors have been calculated for the models of optimized FU in singular and complex forms to explore the effects of nanotube on the properties of attached FU anti-cancer drug (Table 2). To perform such calculation, the gauge included atomic orbital (GIAO) approach has been used.[30] CS properties belong to the NMR technique, which is among the most powerful material characterization techniques.[31] Interestingly, the NMR properties could be reproduced by quantum chemical computations to reveal insightful information about the characteristics of matters at the atomic scale.[32-35]

RESULTS AND DISCUSSION

Within this work, we have explored a possible solution for this problem about the effects of non-ionic CNT and ionic BNNT on the properties of FU, an anticancer drug. To this aim, DFT calculations have been performed to find the optimized geometries for the investigated structures (Figs. 1 and 2) in addition to their atomic and molecular scale properties (Tables 1 and 2). It is indeed an advantage of computational works to investigate the properties of matters at the lowest scale.[36, 37] Hereby, this advantage has been employed here to investigate the characteristic properties of FU in complex with each of CNT and BNNT in comparison with the singular form.

Table 1: Molecular descriptors.

Model	Stoichiometry	HOMO (eV)	LUMO (eV)	EG (eV)	DM (Debye)	EB (kcal/mol)
FU	$C_4H_3FN_2O_2$	-6.79	-1.38	-5.41	3.90	N/A
CNT1-FU	$C_{36}H_{11}FN_2O_2$	-5.49	-3.38	-2.11	6.49	-5.88
BNNT-FU	$C_4H_{11}B_{16}FN_{18}O_2$	-6.21	-2.72	-3.49	9.86	-21.55

See Figs. 1 and 2 for details.

Examining the panels of Fig. 2 indicates that the interacting surface for FU is very much important, in which it interacts with CNT in physical mode but it interacts with BNNT in chemical mode. The importance of non-ionic/ionic surface could be very well seen here by the type of interaction between FU and each of nanotubes. The results of Table 1 also show that the strength of BNNT-FU is four times higher than that of CNT-FU, in which the values of EB are -21.55 and -5.88 kcal/mol. The values of HOMO and LUMO indicate the orbital configurations are changed because of complex formations for FU in both of singular and complex forms. The trend approves the complex formation by changing the orbital configurations. Moreover, the values of EG also indicate that the BNNT-FU could be considered as more stable complex than CNT-FU, in which the absolute value of EG is larger for the former complex than the latter one. The values of DM also indicate the effects of complex formations on molecular properties, in which the BNNT-FU complex could provide better situations of interactions with other molecular systems regarding such ability for the CNT-FU complex. As a concluding remark of this part, chemical complex formation has been occurred for BNNT-FU versus physical complex formation for CNT-FU and the molecular descriptors have approved such formation condition.

Table 2: Atomic CS descriptors for FU.

Atom	Isolated FU	CNT-FU	BNNT-FU
N1	141	134	130
C2	53	52	56
N3	98	98	94
C4	42	42	34
C5	52	53	56
C6	72	69	66
H1	27	25	26
O2	29	35	10
H3	26	26	20
O4	59	49	83
F5	352	356	352
H6	25	25	25

See Figs. 1 and 2 for details. The values are in ppm.

Atomic scale CS descriptors have been obtained (Table 2 and Figs. 1 and 2) for the atoms of FU in singular and complex forms to explore the effects of nanotube on the initial atomic characteristics of FU. A quick look at the results indicates that the atoms of FU detect different electronic environment regarding their position in the pyrimidine heterocyclic ring. In addition, the complex formations have significant effects on FU properties in both of CNT-FU and BNNT-FU complexes, in which the effects are many more significant for the atomic properties of FU of latter complex. Since the CS properties are generated at the electronic sites of atoms, they could very well detect any perturbations to the electronic properties of matters at the atomic scale [38]. Hereby, the atomic effects are very much obvious for FU in the complexes, especially BNNT-FU. O4 is that atom make connection between FU and BNNT, in which its own property detects significant effects of such perturbation. Interestingly, the effects are not only limited to O4 but other atoms of FU also detect significant effects. The trend means that the properties of one atom in a molecule could make different conditions for other molecules, which are very much obvious of atoms of FU in BNNT-FU complex. For example, N1 is in the opposite side of O4 in the FU molecule but it detects notable effects of nanotube existence in BNNT-FU. For CNT-FU, the atoms of FU also detect the effects of nanotube but almost slighter than those of BNNT-FU complex. As a final remark, the atomic scale properties of FU are significantly changed in BBNT-FU but they detect slighter changes in CNT-FU complex meaning that the effects of BNNT are many more significant for the properties of FU in comparison with CNT.

CONCLUSION

Based on performed DFT calculation, molecular and atomic scale properties have been obtained to discuss about possible solution of this problem: how are effects of non-ionic CNT and ionic BNNT on the properties of FU? Based on the results, some trends have been

summarized. First, BNNT-FU is almost a chemical complex versus physical CNT-FU complex. Second, the binding strength of BNNT-FU is much higher than that of CNT-FU. Third, HOMO and LUMO properties of FU detect significant effects of complex formations in both complexes but showing more stability for BNNT-FU than CNT-FU. Fourth, the atomic scale CS properties indicated many more significant effects for atoms of FU in BNNT-FU than CNT-FU. And finally, the properties of FU detect many more significant effects in BBNT-FU in comparison with CNT-Fu meaning the importance of knowing details of interactions for molecular consideration in drug delivery systems.

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REFERENCES

1. Iijima S. Synthetic nano-scale fibrous matrix. Nature 1991;56:354-358.
2. Hoseininezhad-Namin MS, Pargolghasemi P, Alimohammadi S, Rad AS, Taqavi L. Quantum chemical study on the adsorption of metformin drug on the surface of pristine, Si-and Al-doped (5, 5) SWCNTs. Physica E 2017;90:204-213.
3. Mirzaei M, Harismah K, Jafari E, Gülseren O, Rad AS. Functionalization of (n, 0) CNTs (n= 3–16) by uracil: DFT studies. Eur. Phys. J. B 2018;91:14.
4. Harismah K, Mirzaei M, Sahebi H, Gülseren O, Rad AS. Chemically uracil–functionalized carbon and silicon carbide nanotubes: computational studies. Mater. Chem. Phys. 2018;205:164-170.
5. Moghaddam HK, Maraki MR, Rajaei A. Application of Carbon Nanotubes (CNT) on The Computer Science and Electrical Engineering: A Review. Int. J. Reconfig. Embed. Sys. 2020;9:61.
6. Sharma V, Kagdada HL, Jha PK, Śpiewak P, Kurzydłowski KJ. Thermal transport properties of boron nitride based materials: A review. Renew. Sustain. Energy Rev. 2020;120:109622.
7. Huang J, Guo Y, Fan Y, Liang Y. Molecular dynamics investigation of the thermal properties in single-walled boron nitride nanotube. Mater. Res. Exp. 2020;7:025025.
8. Mirzaei M, Yousefi M, Meskinfam M. Chemical shielding properties for BN, BP, AlN, and AlP nanocones: DFT studies. Superlat. Microstruct. 2012;51:809-813.
9. Mirzaei M. The NMR parameters of the SiC-doped BN nanotubes: a DFT study. Physica E 2010;42:1954-1957.
10. Nouri A, Mirzaei M. DFT calculations of B-11 and N-15 NMR parameters in BN nanocone. J. Mol. Struct. THEOCHEM 2009;913:207-209.
11. Yu J, Chen Y, Cheng BM. Dispersion of boron nitride nanotubes in aqueous solution with the help of ionic surfactants. Solid State Commun. 2009;149:763-766.
12. Wong BS, Yoong SL, Jagusiak A, Panczyk T, Ho HK, Ang WH, Pastorin G. Carbon nanotubes for delivery of small molecule drugs. Adv. Drug Deliver. Rev. 2013;65:1964-2015.
13. Mokhtari A, Harismah K, Mirzaei M. Covalent addition of chitosan to graphene sheets: density functional theory explorations of quadrupole coupling constants. Superlat. Microstruct. 2015;88:56-61.
14. Harismah K, Sadeghi M, Baniasadi R, Mirzaei M. Adsorption of vitamin C on a fullerene surface: DFT studies. J. Nanoanalys. 2017;4:1-7.
15. Mirzaei M, Yousefi M. Computational studies of the purine-functionalized graphene sheets. Superlat. Microstruct. 2012;52:612-617.
16. Surya R, Mullassery MD, Fernandez NB, Thomas D. Synthesis and characterization of a clay-alginate nanocomposite for the controlled release of 5-Flurouracil. J. Sci. 2019;4:432-441.
17. Truong NP, Whittaker MR, Mak CW, Davis TP. The importance of nanoparticle shape in cancer drug delivery. Exp. Opin. Drug Deliver. 2015;12:129-142.
18. Malet-Martino M, Martino R. Clinical studies of three oral prodrugs of 5-fluorouracil (capecitabine, UFT, S-1): a review. Oncolog. 2002;7:288-323.
19. Arias JL. Novel strategies to improve the anticancer action of 5-fluorouracil by using drug delivery systems. Molecules 2008;13:2340-2369.
20. Mirzaei M, Gülseren O, Hadipour N. DFT explorations of quadrupole coupling constants for planar 5-fluorouracil pairs. Comput. Theor. Chem. 2016;1090:67-73.
21. Mirzaei M. 5-Fluorouracil: computational studies of tautomers and NMR properties. Turk. Computat. Theor. Chem. 2017;1:27-34.
22. Mirzaei M. Effects of carbon nanotubes on properties of the fluorouracil anticancer drug: DFT studies of a CNT-fluorouracil compound. Int. J. Nano Dimens. 2013;3:175-179.
23. Yaraghi A, Ozkendir OM, Mirzaei M. DFT studies of 5-fluorouracil tautomers on a silicon graphene nanosheet. Superlat. Microstruct. 2015;85:784-788.
24. Kouchaki A, Gülseren O, Hadipour N, Mirzaei M. Relaxations of fluorouracil tautomers by decorations of fullerene-like SiCs: DFT studies. Phys. Lett. A 2016;380:2160-2166.
25. Yousefvand H, Mirzaei M, Tabbakhian M. Investigating chitosan–curcumin nanorings for containing fluorouracil. Turk. Comput. Theor. Chem. 2017;1:6-12.
26. Mirzaei M, Ahangari RS. Formations of CNT modified 5-(halogen) uracil hybrids: DFT studies. Superlat. Microstruc. 2014;65:375-379.
27. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. Gaussian 09 A.01. Gaussian Inc., Wallingford; 2013.
28. Dobson JF, Gould T. Calculation of dispersion energies. J. Phys. 2012;24:073201.
29. Simon S, Duran M, Dannenberg JJ. How does basis set superposition error change the potential surfaces for hydrogen-bonded dimers? J. Chem. Phys. 1996;105:11024-11031.
30. Chesnut DB, Rusiloski BE. Ab initio in the gauge including atomic orbital method. Chem. Phys. 1991;157:105-110.

31. Paul T. Callaghan. Principles of nuclear magnetic resonance microscopy. Oxford University Press. UK; 1993.
32. Mirzaei M, Meskinfam M. Computational studies of effects of tubular lengths on the NMR properties of pristine and carbon decorated boron phosphide nanotubes. Solid State Sci. 2011;13:1926-1930.
33. Mirzaei M. A computational NMR study of boron phosphide nanotubes. Z. Naturforsch. A 2010;65:844-848.
34. Mirzaei M. The NMR parameters of the SiC-doped BN nanotubes: a DFT study. Physica E 2010;42:1954-1957.
35. Mirzaei M. Calculation of chemical shielding in C-doped zigzag BN nanotubes. Monatsh. Chem. 2009;140:1275-1278.
36. Mirzaei M. Science and engineering in silico. Adv. J. Sci. Eng. 2020;1:1-2.
37. Ozkendir OM. Electronic structure study of Sn-substituted InP semiconductor. Adv. J. Sci. Eng. 2020;1:7-11.
38. Mirzaei M, Meskinfam M. Computational NMR studies of silicon nanotubes. Comput. Theor. Chem. 2011;978:123-125.

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