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Original Research

A Facile Adsorption of Fluorouracil Anticancer by the Assistance of a Boron Nitride Nanoflake: DFT Insights

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Abstract: Density functional theory (DFT) calculations were performed to provide insights into a facile adsorption of fluorouracil (FU) anticancer by the assistance of a representative boron nitride (BN) nanoflake. The singular models were optimized to prepare the minimized energy structures and their combinations were re-optimized to obtain the models of FU@BN complexes. Three complexes were found with different levels of adsorption strengths based on the orientation of molecular site of FU towards the BN surface. In this case, the models were achievable based on the structural energies and additional electronic features evaluations showed possibility of distinguishing the models by their frontier molecular orbitals (FMO) features. As a consequence, the models of FU@BN complexes were achievable and their electronic features indicated both of sensing and distinguishing features for confirming a facile adsorption of FU anticancer by the assistance of a boron nitride (BN) nanoflake.

Keywords: Adsorption; Anticancer; DFT; Fluorouracil; Interaction.

Introduction

The issue of drug design and delivery is very important by the need of novel treatments protocols for those earlier wild diseases or newly appeared ones [1-3]. In this case, several efforts have been always dedicating to the exploration of new drugs or treatments for the patients [4-7]. Not only the drug related issues, but also dealing with the biological media is always a challenging area of research [8-10]. To this aim, further investigations are still required to provide further insights especially for those materials which want to be involved in the biological related systems [11-13]. In a general note, exploring the topics of biological and biomedical applications is an essential work of several researchers to reveal new insights on the maintenance of health systems [14-16]. Accordingly, the drug design and delivery issues are also very important for approaching novel treatments for an enhanced health maintaining level [17-20]. Among the known diseases, cancer is indeed a wild disease without any certain treatment for years and several people around the world are affected by the serious adverse effects of cancer and even its treatments [21]. To this point, learning details of cancer and anticancer are very important for developing novel treatments for the patients with fewer symptoms of adverse effects [22]. In this case, modifications of chemical structures of anticancers or combining them with other substances are two

main methods of current drug enhancements [23-25]. To combine with other substances, nanostructures have been seen useful for working as carriers of drugs in managing the processes of drug delivery [26]. Indeed, nanostructures have been become very famous very soon after their pioneering innovation because of showing unique features such as wide surface areas and electronic behaviors [27]. Additionally, several types of nanostructures including both of carbon and non-carbon compositions have been characterized to approach brighter information for developing nano applications [28-30]. Combined compositions of boron and nitrogen atoms yielded boron nitride (BN) nanostructures with excellent electronic features in addition to their heteroatomic surface [31]. In the case of drug delivery, BN nanostructures have been also proposed as useful carriers of drugs in a targeted process, but further information are still required to approach a successful process [32]. Within the current work, a representative model of BN nanoflake was employed for adsorbing the very well-known fluorouracil (FU) anticancer along with performing density functional theory (DFT) calculations. Due to the complexity of investigating such models, employing DFT tools could help to provide detailed information for analyzing such a complex FU@BN system [33-35].

Fluorouracil or 5-fluorouracil (FU) (Figure 1) is among the most prescribed anticancers for various types of cancers with single-standing treatment or in conjugation with other complimentary anticancers [36]. In this case, several efforts have been done to enhance the treatment level of FU for approaching a more successful medication of cancer patients [37]. Employing the nanostructures as carriers has been also examined with several works for providing a targeted drug delivery platform [38]. To this aim, the current work was done to investigate the adsorption process of FU by the assistance of a BN nanoflake for providing more insights into the drug delivery processes of FU in the form of FU@BN complex formation (Figure 2). DFT calculations were performed for optimizing the structures and evaluating their features, details were summarized in Table 1 and Figures 1-3.

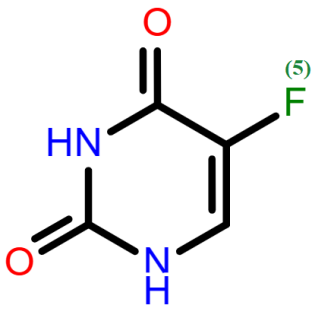

Figure 1: Fluorouracil or 5-fluorouracil (FU).

Materials and Methods

The models of this work included the 3D structures of FU and a representative model of BN nanoflake, which were obtained from ChemSpider [39]. For preparing the BN nanoflake, the original model of coronene was obtained and it was decorated by the combinations of B and N atoms (Figure 2). Then, the formula of employed BN nanoflake was $B_{12}N_{12}H_{12}$, in which the roles of H atoms were as edge saturators. The formula of employed FU was the original one as $C_4H_3FN_2O_2$. The singular models were first optimized to obtain their minimized energy geometries. Next, their combinations were investigated by re-optimizing the bimolecular models of FU@BN complexes to explore the adsorption processes. Besides the minimized energy structures, additional structural and electronic features were evaluated to analyze details of the investigated systems, especially in the cases of singular and complex models. The obtained results were included in Table 1 to show the characteristic features of the models. Since the frontier molecular orbitals (FMO) are essential for recognition of the chemical systems, the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO) were evaluated for the

investigated models in both terms of quantitative values (Table 1) and qualitative representations of distribution patterns (Figure 3). All calculations of current work including geometries optimizations and properties evaluations were performed employing the B3LYP-D3/6-31G* level of DFT calculations as implemented in the Gaussian program [40].

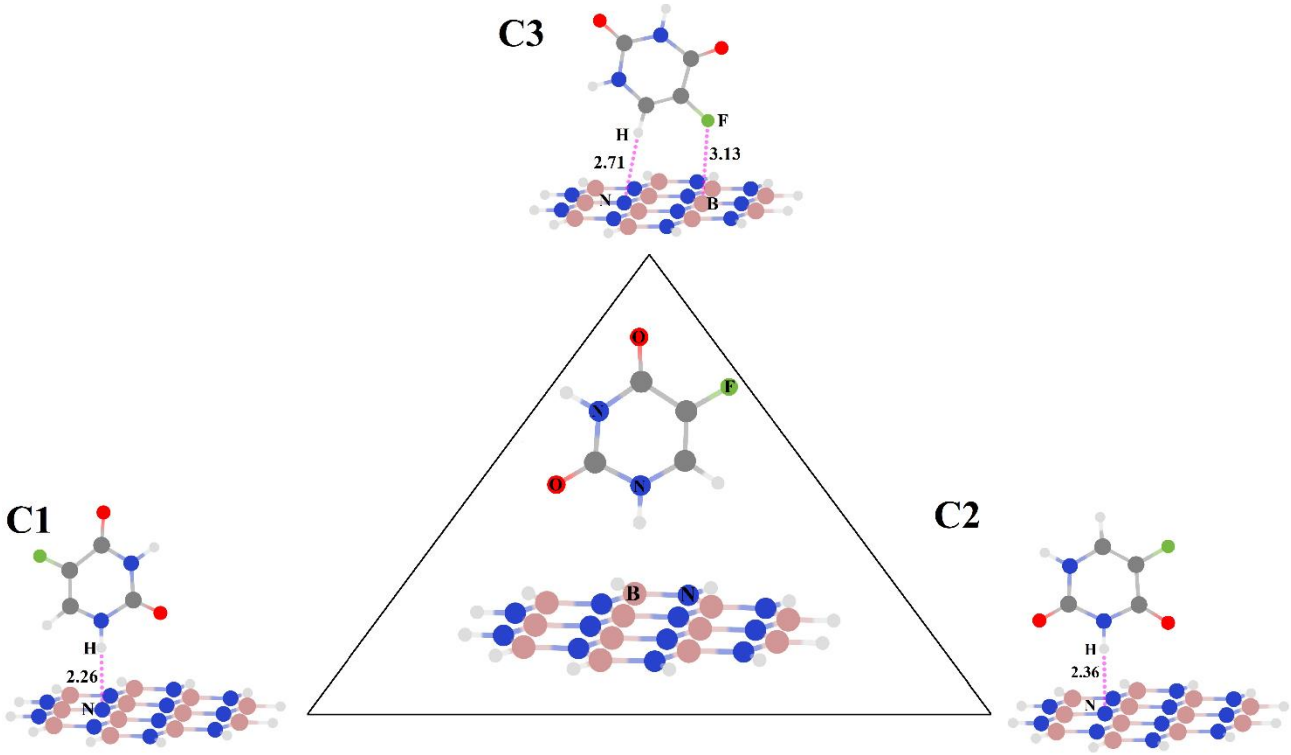

Figure 2: Models of FU@BN complexes.

Results and Discussion

The main goal of this work was the investigation of FU adsorption by the assistance of BN nanoflake. To this aim, the models of this work (Figure 2) were optimized to obtain the minimized energy systems. The models were in two sets of the singular state including FU and BN models and the complex state including FU@BN complexes, in which three complexes were obtained for the interacting systems; C1, C2, and C3. The models were recognized based on their calculated minimized energy level among all possibilities of energies variations. In this case, the singular models were easier to obtain than the complex models with various possibilities of interacting configurations. By examining the possible starting configurations, three complexes were found regarding the orientation of FU molecular sites towards the BN surface. After performing optimization calculations, the complex models were obtained and their features were evaluated. By comparing the values of adsorption energy (E_{ads}) for the complexes, it was found that the models were in different strengths of adsorption processes with such order: C1 > C2 > C3. The results were based on the comparing energies of each complex and its singular counterparts, in which the results indicated changes of such adsorption strengths in the models. Accordingly, the optimized geometrical configurations indicated the shortest distance of two interacting molecules in C1 and the longest one in C3. In this regard, the models were recognized and their features indicated benefits of performing such DFT calculations to learn details of interacting FU@BN complexes. The models of C1 and C2 were in similar H…N interaction from the FU counterpart to the BN surface, but the involving molecular site of FU towards the BN surface indicated a different chemical environment for managing the adsorption process. For the case of C3, H…N and F…B interactions were found from the FU counterpart to the BN counterpart and this model was found at the lowest level of adsorption strength among the obtained complexes.

Table 1: Evaluated features of minimized singular and complex models.

Model	E_{ads} kcal/mol	HOMO eV	LUMO eV	E_{gap} eV
FU	n/a	-6.79	-1.38	5.41
BN	n/a	-6.73	0.20	6.93
C1	-4.19	-6.55	-1.16	5.38
C2	-3.60	-6.61	-1.29	5.33
C3	-2.79	-6.66	-1.27	5.39

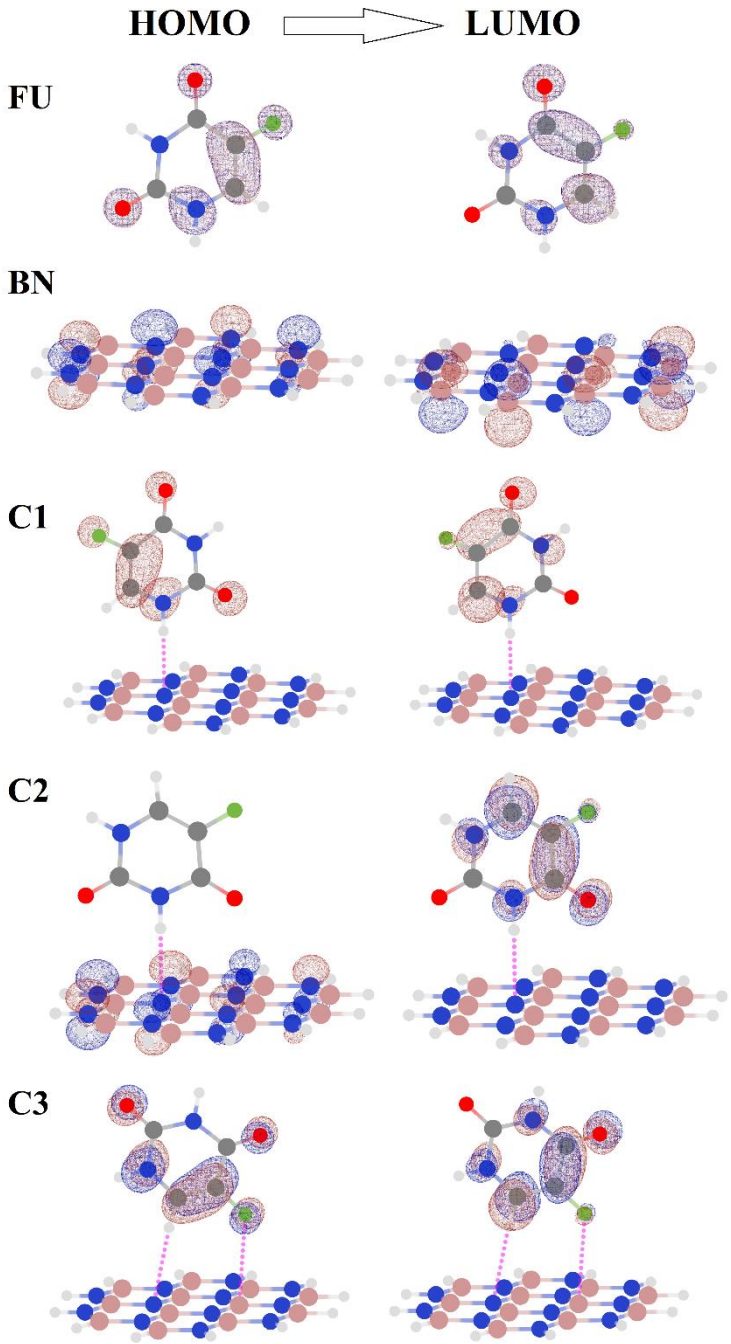

Figure 3: HOMO-LUMO patterns of singular FU and BN models and their FU@BN complexes; C1, C2, and C3.

in addition to the obtained structural features, the FMO features were evaluated to recognize the electronic systems of investigated models. As could be found by the quantities of Table 1 and representative patterns of Figure 3, the models were distinguishable by such features. Although the molecular counterparts of complexes were the same, but it was found that the adsorption strengths were different. In this regard, the patterns of HOMO-LUMO were distributed in different models of

localizations by sharing the patterns among the counterparts such as C2 or by a single standing localization of patterns at the site of only one counterpart such as C1 and C3. Changes of energy levels of HOMO and LUMO for the complexes in comparison with the singular models were obvious and their differences were also meaningful. Energy gap (E_{gap}) stands for the energy distance of HOMO and LUMO levels, in which its value could help to make a sensing possibility for the occurrence of adsorption process. On the other hand, the models were also achievable by examining the variations of such features of electronic systems. In this case, formations of complexes and their recognitions were found suitable to manage a facile adsorption process of FU be the assistance of a BN nanoflake.

Conclusion

An idea of exploring a facile adsorption of FU by the assistance of BN nanoflake was investigated within this work along with performing DFT calculations. The results were evaluated to show possibility of managing a targeted drug delivery platform of FU anticancer by the employed BN nanoflake. The singular models were optimized to obtain the minimized energy structures and their combinations were subsequently investigated. Three models of FU@BN complexes were found for the interacting FU and BN counterparts, in which the orientation of FU towards the BN surface was dominant of such complex formations. The adsorption strengths of the models were different and their evaluated features were also different. Based on the achievements, formations of FU@BN complexes were achievable to manage the adsorption processes of FU by the assistance of BN nanoflake. The models were also suitable for being recognized by their electronic features, in which their FMO features were distinguishable by changes from the singular to the complex state. In this case, a promising sensing function was also considerable for the investigated models. As a consequence, the idea of managing a facile adsorption process of FU by the BN nanoflake was achievable by both of structural and electronic features.

Disclosure Statement

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

References

1. Wang M, Wang Z, Sun H, Wang J, Shen C, Weng G, Chai X, Li H, Cao D, Hou T. Deep learning approaches for de novo drug design: an overview. Current Opinion in Structural Biology. 2022; 72: 135.
2. Aghili SS, Pourzal A, Mosaddad SA, Amookhteh S. COVID-19 risk management in dental offices: a review article. Open Access Macedonian Journal of Medical Sciences. 2022; 10: 763.
3. Ranjbar R, Shahreza MH. Prevalence, antibiotic-resistance properties and enterotoxin gene profile of Bacillus cereus strains isolated from milk-based baby foods. Tropical Journal of Pharmaceutical Research. 2017; 16: 1931.
4. Mashak Z, Jafariaskari S, Alavi I, Sakhaei Shahreza M, Safarpoor Dehkordi F. Phenotypic and genotypic assessment of antibiotic resistance and genotyping of vacA, cagA, iceA, oipA, cagE, and babA2 alleles of helicobacter pylori bacteria isolated from raw meat. Infection and Drug Resistance. 2020; 13: 257.
5. Mosaddad SA, Abdollahi Namanloo R, Ghodsi R, Salimi Y, Taghva M, Naeimi Darestani M. Oral rehabilitation with dental implants in patients with systemic sclerosis: a systematic review. Immunity, Inflammation and Disease. 2023; 11: e812.
6. Saliminasab M, Jabbari H, Farahmand H, Asadi M, Soleimani M, Fathi A. Study of antibacterial performance of synthesized silver nanoparticles on streptococcus mutans bacteria. Nanomedicine Research Journal. 2022; 7: 391.
7. Hasanpour Dehkordi A, Khaji L, Sakhaei Shahreza MH, Mashak Z, Safarpoor Dehkordi F, Safaee Y, Hosseinzadeh A, Alavi I, Ghasemi E, Rabiei-Faradonbeh M. One-year prevalence of antimicrobial susceptibility pattern of methicillin-resistant staphylococcus aureus recovered from raw meat. Tropical Biomedicine. 2017; 34: 396.

8. Ranjbar R, Shahreza MH, Rahimi E, Jonaidi-Jafari N. Methicillin-resistant Staphylococcus aureus isolates from Iranian restaurant food samples: panton-valentine leukocidin, SCCmec phenotypes and antimicrobial resistance. Tropical Journal of Pharmaceutical Research. 2017; 16: 1939.
9. Darestani MN, Houshmand B, Mosaddad SA, Talebi M. Assessing the surface modifications of contaminated sandblasted and acid-etched implants through diode lasers of different wavelengths: an in-vitro study. Photobiomodulation, Photomedicine, and Laser Surgery. 2023.
10. Ebadian B, Fathi A, Khodadad S. Comparison of the effect of four different abutment screw torques on screw loosening in single implant-supported prosthesis after the application of mechanical loading. International Journal of Dentistry. 2021; 2021: 3595064.
11. Torkan S, Shahreza MH. VacA, CagA, IceA and OipA genotype status of Helicobacter pylori isolated from biopsy samples from Iranian dogs. Tropical Journal of Pharmaceutical Research. 2016; 15: 377.
12. Mosaddad SA, Namanloo RA, Aghili SS, Maskani P, Alam M, Abbasi K, Nouri F, Tahmasebi E, Yazdanian M, Tebyaniyan H. Photodynamic therapy in oral cancer: a review of clinical studies. Medical Oncology. 2023; 40: 91.
13. Fathi A, Giti R, Farzin M. How different influential factors affect the color and translucency of y-ztp: a review of the literature. Annals of Dental Specialty. 2018; 6: 338.
14. Ren X, Chen D, Wang Y, Li H, Zhang Y, Chen H, Li X, Huo M. Nanozymes-recent development and biomedical applications. Journal of Nanobiotechnology. 2022; 20: 92.
15. Mosaddad SA, Rasoolzade B, Namanloo RA, Azarpira N, Dortaj H. Stem cells and common biomaterials in dentistry: a review study. Journal of Materials Science: Materials in Medicine. 2022; 33: 55.
16. Mosharraf R, Molaei P, Fathi A, Isler S. Investigating the effect of nonrigid connectors on the success of tooth-and-implant-supported fixed partial prostheses in maxillary anterior region: a finite element analysis (FEA). International Journal of Dentistry. 2021; 2021: 5977994.
17. Giordano D, Biancaniello C, Argenio MA, Facchiano A. Drug design by pharmacophore and virtual screening approach. Pharmaceuticals. 2022; 15: 646.
18. Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it?. Acta Pharmaceutica Sinica B. 2022; 12: 3049.
19. Esfahani S, Akbari J, Soleimani-Amiri S, Mirzaei M, Ghasemi Gol A. Assessing the drug delivery of ibuprofen by the assistance of metal-doped graphenes: insights from density functional theory. Diamond and Related Materials. 2023; 135: 109893.
20. Malik MK, Bhatt P, Kumar T, Singh J, Kumar V, Faruk A, Fuloria S, Fuloria NK, Subrimanyan V, Kumar S. Significance of chemically derivatized starch as drug carrier in developing novel drug delivery devices. The Natural Products Journal. 2023; 13: 40.
21. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA: A Cancer Journal for Clinicians. 2023; 73: 17.
22. Paprocka R, Wiese-Szadkowska M, Janciauskiene S, Kosmalski T, Kulik M, Helmin-Basa A. Latest developments in metal complexes as anticancer agents. Coordination Chemistry Reviews. 2022; 452: 214307.
23. Ghamsari PA, Samadizadeh M, Mirzaei M. Halogenated derivatives of cytidine: Structural analysis and binding affinity. Journal of Theoretical and Computational Chemistry. 2020; 19: 2050033.
24. Zhang H, Fan T, Chen W, Li Y, Wang B. Recent advances of two-dimensional materials in smart drug delivery nano-systems. Bioactive Materials. 2020; 5: 1071.
25. Mu W, Chu Q, Liu Y, Zhang N. A review on nano-based drug delivery system for cancer chemoimmunotherapy. Nano-Micro Letters. 2020; 12: 1.
26. Zong TX, Silveira AP, Morais JA, Sampaio MC, Muehlmann LA, Zhang J, Jiang CS, Liu SK. Recent advances in antimicrobial nano-drug delivery systems. Nanomaterials. 2022; 12: 1855.
27. Kumar N, Chamoli P, Misra M, Manoj MK, Sharma A. Advanced metal and carbon nanostructures for medical, drug delivery and bio-imaging applications. Nanoscale. 2022; 14: 3987.
28. Nyholm N, Espallargas N. Functionalized carbon nanostructures as lubricant additives–a review. Carbon. 2023; 201: 1200.
29. Antunes JM, Pereira AF, Sakharova NA. Overview on the evaluation of the elastic properties of non-carbon nanotubes by theoretical approaches. Materials. 2022; 15: 3325.
30. Sun Q, Li XH, Wang KX, Ye TN, Chen JS. Inorganic non-carbon supported Pt catalysts and synergetic effects for oxygen reduction reaction. Energy & Environmental Science. 2023.
31. Han N, Wang S, Rana AK, Asif S, Klemeš JJ, Bokhari A, Long J, Thakur VK, Zhao X. Rational design of boron nitride with different dimensionalities for sustainable applications. Renewable and Sustainable Energy Reviews. 2022; 170: 112910.

32. Cheng Y, Han Y, Zhang W, Zeng L, Long Y, Wang S, Weng Q. Gram-scale synthesis of boron nitride nanosheets by salt-template method for anticancer drug delivery. Chemical Engineering Journal. 2022; 437: 135304.
33. Sheikhi M, Kaviani S, Azarakhshi F, Shahab S. Superalkali X3O (X= Li, Na, K) doped B12N12 nano-cages as a new drug delivery platform for chlormethine: a DFT approach. Computational and Theoretical Chemistry. 2022; 1212: 113722.
34. Hosseinzadeh E, Foroumadi A, Firoozpour L. A DFT study on the transition metal doped BN and AlN nanocages as a drug delivery vehicle for the cladribine drug. Journal of Molecular Liquids. 2023; 374: 121262.
35. Saadh MJ, Harismah K, Ruiz-Balvin MC, Da M, Arias-Gonzales JL, Cotrina-Aliaga JC, Mohany M, Mirzaei M, Akhavan-Sigari R. Computational assessments of sensing functions of an oxygen-decorated silicon carbide nanocage for the adsorption of mesalazine drug. Computational and Theoretical Chemistry. 2023; 1224: 114125.
36. Pinedo HM, Peters GF. Fluorouracil: biochemistry and pharmacology. Journal of Clinical Oncology. 1988; 6: 1653.
37. Entezar-Almahdi E, Mohammadi-Samani S, Tayebi L, Farjadian F. Recent advances in designing 5-fluorouracil delivery systems: a stepping stone in the safe treatment of colorectal cancer. International Journal of Nanomedicine. 2020; 15: 5445.
38. Valencia-Lazcano AA, Hassan D, Pourmadadi M, Behzadmehr R, Rahdar A, Medina DI, Díez-Pascual AM. 5-Fluorouracil nano-delivery systems as a cutting-edge for cancer therapy. European Journal of Medicinal Chemistry. 2023; 246: 114995.
39. Ayers M. ChemSpider: the free chemical database. Reference Reviews. 2012; 26: 45.
40. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. Gaussian 09 program. Gaussian Inc. Wallingford, CT. 2009.

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