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Investigation of the Adsorption Properties of Hydroxyurea Drug on Functionalized Fullerene as an Anticancer Drug Carrier

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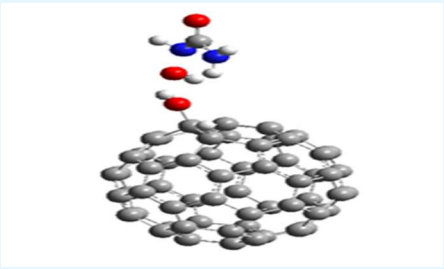
Abstract: A theoretical examination of hydroxyurea adsorption capabilities toward the Fullerene C60-OH for fit drug delivery systems occurred by using DFT simulations. The research goal is to assess the efficacy of Fullerene in increasing its stableness and efficiency in optimized interactions, hence facilitating optimal hydroxyurea drug delivery hydroxyurea, also known as Hydroxycarbamide is a medication used for many health complications, including gastric, intestinal, and breast cancer. Fullerene has remarkable properties such as high stability, which can be used as a drug carrier in targeted drug delivery systems. This study is focused on the characteristics of the combination of hydroxyurea with Fullerene, which can have a good effect on the anti-cancer effects of the drug. Based on this, the adsorption reaction of hydroxyurea on C60-OH was performed using DFT by B3LYP/6-311+G method along with the calculation of adsorption energy. Information of The HOMO (-7.251 ev) and LUMO (-0.0209 ev) energy level data show four regions for hydroxyurea, confirming that it is thermodynamically stable while the entropy-consisting features (+301.34 J/mol- Kelvin) Gibbs free energy (-788.75 kJ), enthalpy (-788.66 kJ), and thermodynamic capacity (77.74J/mol-kelvin), along with effective electronic components such as ω(23.903 ev), μ(-3.63 ev), σ(0.276 ev), η(3.61 ev) and χ(3.63 ev) were calculated. The reduction of chemical potential in the combination of hydroxyurea with C60-OH fullerene is proof of its better reactivity.



Keywords: DFT, Hydroxyurea, Fullerene, Anti-cancer drug, Nanocarrier

1. Introduction

Hydroxyurea (HU) is a medication used for many health complications, including gastric, intestinal, and breast cancer.[1] Anyway, common side effects are also apparent. The side effects of the drug include loss of appetite, fever, headache, shortness of breath, and increased risk of subsequent cancers.[2] Like anti-cancer drugs, it is believed to work by disrupting the structure of DNA and most clearly acts in the S phase of the cell cycle.[3] It is believed that this drug works by inhibiting the enzyme ribonucleotide reductase.[4]

Among the various targeted drug delivery methods, nanostructures can be used effectively and efficiently[5], and the process of treating diseases has an effective effect. nano particles are sized particles with diameters ranging between 1 and 100 nanometer, in which drugs may be adsorbed, dispersed, or encapsulated.[6] In the last few decades, buckyballs have been introduced as carbon-based carriers for drug delivery applications. buckyballs, also known as Fullerenes, are carbon's new allotrope.[7] Fullerenes have a specific structure, and it helps in the treatment of some diseases.[8] Fullerenes consist out of 12 pentagons and 20 hexagons with a carbon atom on each edge of this lattice structure. What makes Fullerene good for delivering the drug is the ability to, deliver to the targeted cells. buckyballs are used to deliver anti-cancer medications for therapy.[9-12]

2. MATERIALS & METHODS

Quantum chemical calculations were done using Gaussian 09W software run on a computer. This process was carried out in Gaussian 09W software using DFT with the B3LYP method and 6-311+G basis along with the calculation of absorption energy, and it was performed with no solvent and no specific temperature. Electrical parameters and thermal dynamic properties of all of them were investigated using parameter DFT with the B3LYP method.[13,14] In this research, fullerene C60-OH was used as an absorbent material, whose absorption energy is as follows:

$$E(ads) = E(Fullerene–HU) – (E(hydroxyurea) + E(Fullerene))$$

3. RESULTS AND DISCUSSION

The most important point about the targeted drug delivery system is that the studied system should be designed in such a way that it can be formed and stable when its components are connected. Because the stability of any system depends on its energy level and the lower the energy level, the more stable it is. The stability of this system can be checked by the

value of its energy level. The second most influential factor in the design of a targeted drug delivery system is to check the solubility of the designed system in water. The system must have enough polarity to be soluble in polar solvents. To achieve this goal, a functional group (OH) was first bonded with Fullerene, the optimized structure of which can be observed in Figure 1. According to the results obtained by the current study All parameters were checked using the DFT with the B3LYP/6-311+G method.[15,16] It can be seen, that there are four active sites for hydroxyurea, covering two oxygen (O) atoms and two nitrogen (N) atoms, as shown in Figure 2.

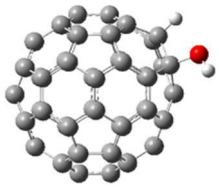
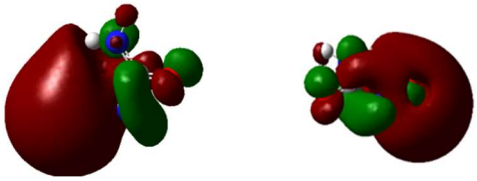


Figure 1. Fullerene C60-OH the optimized.

It can be said that HOMO is the highest energy molecular orbital that has electrons, while LUMO is the next level energy orbital that has no electrons. It can be said that the larger the energy gap of HOMO-LUMO orbitals of a compound, it has a direct effect on its stability and that compound is more stable. HOMO energy indicates the ability of a molecule to donate an electron. From the previous statement, it can be inferred that as the energy levels of HOMO increase, the likelihood of the molecule donating electrons also increases. On the other hand, considering the LUMO energy, lower energy levels suggest a higher probability for the molecule to accept electrons. It can be concluded that a higher parameter IP leads to an increase in stability. HOMO-LUMO Energy Gap States that hard molecules have a large energy gap and soft molecules have a small energy gap (Figure 3). Let us first clarify the correct definition of hard molecules and soft molecules. These terms refer to the polarizability of electrons in an atom or a molecule. The ionization potential (IP) is a significant descriptor of chemical reactivity, where higher IP values are associated with increased stability. "Hard" molecules (η) exhibit larger energy gaps, while "soft" molecules (σ) are more reactive, readily offering electrons for acceptance. The electrophilicity (ω) index is used to describe a molecule's capability to accept electrons. For Hydroxyurea, its HOMO energy level suggests strong engagement in chemical reactions due to the presence of electronegative atoms (Oxygen, Nitrogen) in its chemical structure.

Figure 2. Different active places in hydroxyurea.

Table 1 shows the data related to the orbitals (HOMO and LUMO) of the hydroxyurea compound. Based on the data in this table, the dipole moment of hydroxyurea is 3.9061 D moreover, parameters including enthalpy (-788.66 kJ), Gibbs free energy (-788.75 kJ), heat capacity (77.74 J/mol-kelvin) as well as entropy (+301.34 J/mol-kelvin) has been prepared. Based on these, the chance of participation is equal for all different positions of fullerene C60-OH. Figure 5 shows all active positions of hydroxyurea for fullerene C60-OH acceptance (Figure 4).



HOMO **LUMO**

Figure 3. The HOMO and LUMO for hydroxyurea.

Table 1. Hydroxyurea energy data and dipole momentum

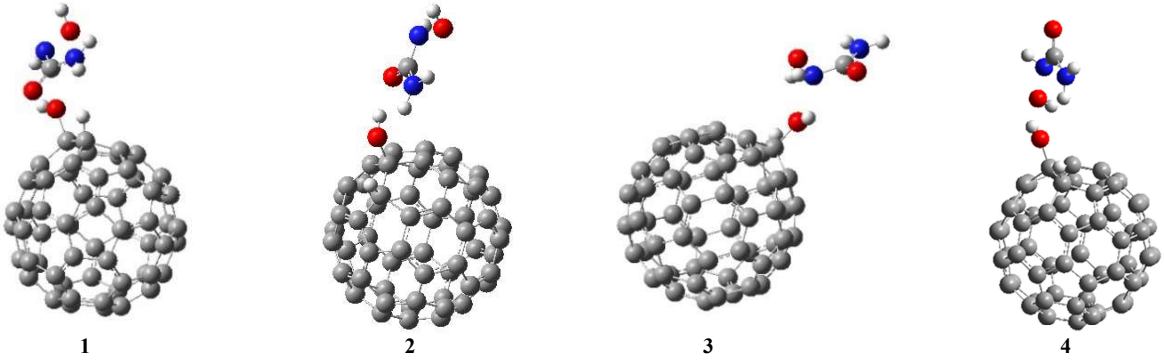
Parameters	Values
Energy	-788.85 kJ
Gibbs free energy	-788.75 kJ
Enthalpy	-788.66 kJ
Entropy	301.34 J/mol-kelvin
Heat capacity	77.74 J/mol-kelvin
Dipole moment	3.9061 Debye
HOMO	-7.2518 ev
LUMO	-0.0209 ev

In making compounds, atoms tend to move in the direction of decreasing energy. Figure 5 shows the optimized and most stable structures of hydroxyurea-C60 Complex (no.4). A better reaction product favors the formation of a more stable substance. In this way, we are looking for the most absorbed and released energy.[17-23] According to the results obtained by hydroxyurea had significant reactivity and stability within chemical reactions. Table 2 shows hydroxyurea reactivity parameters. Therefore the positions of different hydroxyurea parts have other angles and chemical spaces; which can affect the adsorption product and the composition energy. The adsorption energy data is given in Table 3.

Table 2. Hydroxyurea electronic parameters in the gas phase with B3LYP/6-311+G

Parameter	IP[a] (ev)	EA[b] (ev)	X[c] (ev)	μ[d] (ev)	η[e] (ev)	σ[f] (ev)	ω[g] (ev)
Value	7.2518	0.0209	3.6363	-3.6363	3.6154	0.2765	1.8286

[a]IP = -E_{HOMO} [b]EA = -E_{LUMO} [c]χ = (IP+EA)/2 [d]μ = -χ [e]η = (IP-EA)/2 [f]σ = 1/η [g]ω = χ2/2η



1 2 3 4

Figure 4. Structure of Fullerene_Hydroxyurea Compounds.

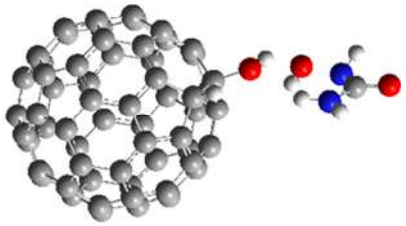


Figure 5. Hydroxyurea-C60 Complex optimized structure.

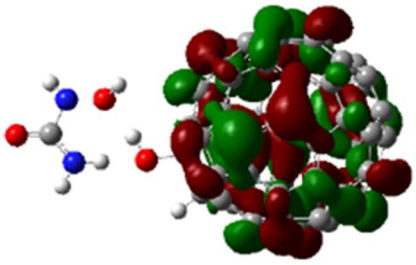


Figure 6. The HOMO of hydroxyurea-C60 Complex.

Table 3. Adsorption energy in hydroxyurea-fullerene-OH complexes

HU-C60 complexes	E (ads) (kJ)
1	0.25502
2	0.25499
3	0.25670
4	0.25692

According to the obtained data, it was found that all four compounds of hydroxyurea with fullerene C60-OH have good stability, and among them, the fourth compound is more stable than the others (Figure 6). Chemical potential (μ) can be employed to compute thermodynamic parameters for different materials under specific pressure and temperature conditions. Additionally, it aids in assessing the stability of substances, chemical compounds, and solutions when considering constant pressure and temperature. Hydroxyurea show that in the product resulting from their combination the two mentioned parameters are less compared to, exhibits a chemical potential (μ) of -3.6363 ev, affirming its data values of ΔE and (μ) for hydroxyurea and complex hydroxyurea, which leads to more reactivity for the combination (Table 4).

4. CONCLUSION

Utilizing DFT with the B3LYP method and a 6-311+G basis set, the study examined hydroxyurea's adsorption on C60-OH fullerene adsorbent. Analyzing the HOMO (-7.251 ev) and LUMO (-0.0209 ev) energy data revealed four distinct regions for hydroxyurea. All combinations of hydroxyurea with fullerene C60-OH demonstrated strong stability, with the fourth combination being the most stable. This investigation, conducted in the gas phase, employed DFT (B3LYP/6-311+G) to assess the adsorption process's energy calculations between hydroxyurea and fullerene C60-OH adsorbent. While the properties include entropy (+301.34 J/mol-K), Gibbs free energy (-788.75 kJ), enthalpy (-788.66 kJ), and thermodynamic capacity (77.74 J/mol). It is along

Table 4. Chemical data of hydroxyurea, fullerene-OH, and hydroxyurea-fullerene-OH complex in ev (complex no. 4)

Molecular parameters	Hydroxyurea	C60	Hu-C60
E_{HOMO}	-7.2518	-6.3647	-6.5007
E_{LUMO}	-0.0209	-3.7143	-3.8476
ΔE	7.2309	2.6504	2.6531
IP	7.2518	6.3647	6.5007
EA	0.0209	3.7143	3.8476
χ	3.6363	5.0395	5.1742
μ	-3.6363	-5.0395	-5.1742
σ	0.2765	0.7546	0.7538
η	3.6154	1.3252	1.3265
ω	1.8286	9.5821	10.0913

with chemical potentials such as ω (23.903 ev), μ (-3.63 ev), (0.276 ev), η (3.61 ev) and χ (3.63 ev) were calculated. The reduction of chemical potential in the combination of hydroxyurea with C60-OH fullerene is proof of its better reactivity. It can be expected that the use of carriers to transfer the hydroxyurea drug has a good effect on the properties and stability of the drug.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

Author Contributions

A.P. designed the experiments, performed experiments, and collected data; S.A.A. discussed the results and strategy, directed and managed the study, Visualization Critical Revision or Editing of the Article, Final Approval of the Version to be Publish.

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References

1. S. E. Alavi, M. K. Esfahani, F. Alavi, F. Movahedi, A. Akbarzadeh, *Indian J. Clin. Biochem.*, **2013**, *28*, 299-302.
2. S. Jinna, P. B. Khandhar, Hydroxyurea Toxicity, StatPearls Publishing, **2023**.
3. A. Singh, Y. J. Xu, *Genes (Basel)*, **2016**, *7*, 99.
4. M. M. Salmani, M. Hashemian, H. J. Yekta, M. Ghadiri Nejad, S. Saber-Samandari, A. Khandan, *J. Supercond. Nov. Magn.*, **2020**, *33*, 2809-2820.
5. S. Sahmani, A. Khandan, S. Saber-Samandari, M. M. Aghdam, *Mater. Sci. Eng.*, **2020**, *111*, 110835
6. A. Kordjamshidi, S. Saber-Samandari, M. Ghadiri Nejad, A. Khandan, *Ceram. Int.*, **2019**, *45*, 14126-14135.
7. D. Nagda, K. S. Rathore, M. Bharkatiya, S. S. Sisodia, R. K. Nema, *J. Chem. Pharm. Res.,* **2010**, *2*, 240-248.
8. R. Bakry, R. M. Vallant, M. Najam-ul-Haq, M. Rainer, Z. Szabo, C. W. Huck, G. K. Bonn, *Nanomed.*, **2007**, *2*, 639-649.
9. K. Raza, N. Thotakura, P. Kumar, M. Joshi, S. Bhushan, A. Bhatia, V. Kumar, R. Malik, G. Sharma, S. K. Guru, O. P. Katare, *Int. J. Pharm.*, **2015**, *495*, 551-559.
10. H. Xu, X. Tu, G. Fan, Q. Wang, X. Wang, X. Chu, *J. Mol. Liq.*, **2020**, *318*, 114315.
11. W. Li, T. Zhao, *J. Mol. Liq.*, **2021**, *340*, 117226.
12. G. J. Ogunwale, H. Louis, T. E. Gber, A. S. Adeyinka, *J. Environ. Chem. Eng.*, **2022**, *10*, 108802.
13. N. Tagmatarchis, H. Shinohara, *Mini. Rev. Med. Chem.*, **2001**, *1*, 339-348.
14. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, H. Nakatsuji, Gaussian DV, revision H. 10 (2010).
15. L. Ye, L. Kollie, X. Liu, W. Guo, X. Ying, J. Zhu, S. Yang, M. Yu, *Mol.*, **2021**, *26*, 3252.
16. F. Yahyazadeh, S. A. Ahmadi, D. Ghazanfari, M. R. Akhgar, *J. Org. Chem. Res.,* **2021**, *7*, 200-205.
17. J. T. Muya, M. T. Nguyen, A. Ceulemans, *Chem. Phys. Lett.*, **2009**, *483*, 101-106.
18. Z. NazarAli, S. A. Ahmadi, D. G hazanfari, E. Sheikhhosseini, *Nanochem. Res.,* **2022**, *7*, 22-27.
19. R. Razavi, H. Beitollahi, S. A. Ahmadi, M. Salajegheh, *J. Indian Chem. Soc.*, **2023**, *100*, 101090.
20. N. Jafari, S. A. Ahmadi, R. Razavi, *Nanochem. Res.*, **2023**, *8*, 40-49.
21. Y. Najibzadeh Vameghabadi, E. Sheikhhosseini, M. R. Akhgar, S. A. Ahmadi, *Iran. J. Chem. Chem. Eng.*, **2022**, *41*, 2628-2634.
22. S. Tavakoli, S. A. Ahmadi, D. Ghazanfari, E. Sheikhhosseini, *J. Indian Chem. Soc.*, **2022**, *99*, 100561.
23. Y. Najibzadeh Vameghabadi, E. Sheikhhosseini, M. R. Akhgar, S. A. Ahmadi, *Pak. J. Pharm. Sci.*, **2022**, *35*, 815-818.