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Original Research Article

$B_{12}N_{12}$ Nanocluster as a Sensor for Flurazepam: A DFT Study

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ABSTRACT

The research conducted in this study focused on examining the potential use of boron nitride nanocluster as a sensor for electrochemical detection of flurazepam. Through the use of IR, FMO, and NBO computations, the feasibility of flurazepam interaction with the nanostructure was thoroughly analyzed. The obtained negative values of adsorption energy and thermodynamic parameters indicate that the interaction is not only experimentally possible, but also exothermic and two-sided in nature. Furthermore, the investigation into the effects of solvent and temperature revealed that flurazepam adsorption is feasible in an aqueous phase and is more favorable at lower temperatures. The NBO results provided valuable insights by indicating that the interactions between flurazepam and the boron nitride nanocluster have a non-covalent nature. Additionally, the FMO calculations yielded significant findings, showing that the bandgap of the BN nanocage experiences a sharp decline of 44.6% when flurazepam adsorbs on its surface. This suggests that the nanocage has the potential to be utilized for the sensitive detection of flurazepam. Overall, the findings of this research underscore the promising applicability of boron nitride nanocluster as a sensor for electrochemical detection of flurazepam. The thorough computational analyses have provided valuable insights into the nature of the interaction, as well as the potential impact of solvent and temperature on the adsorption process.

Keywords: Flurazepam, Adsorption, DFT, $B_{12}N_{12}$, Sensor

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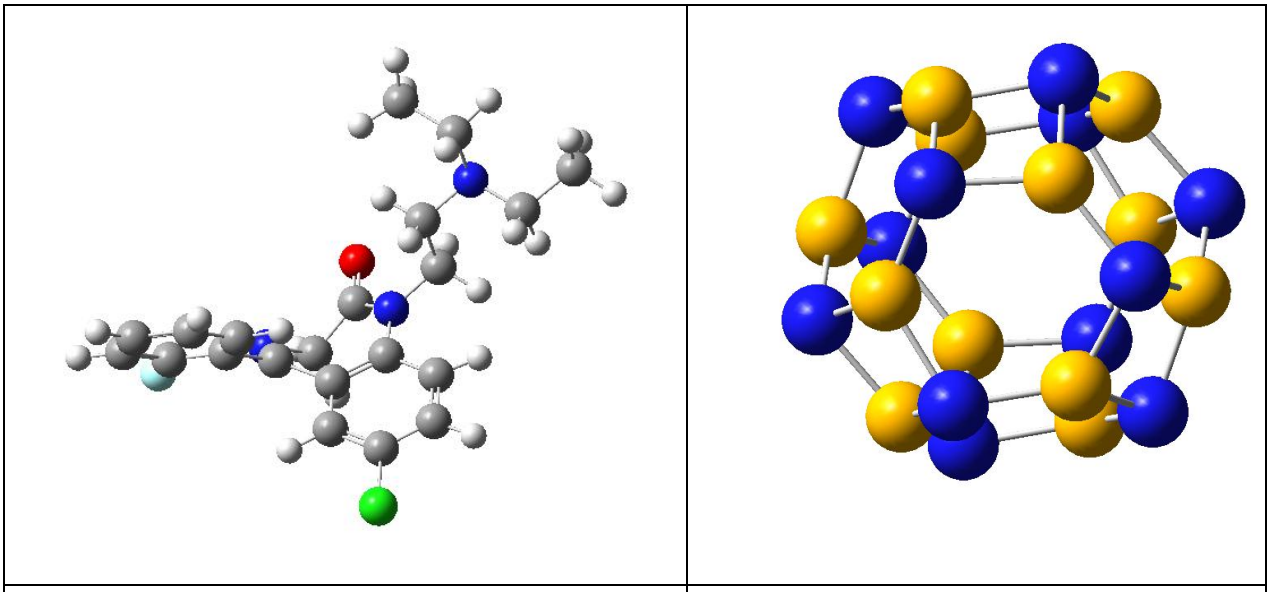
Introduction

Flurazepam (Flurazepam) is a benzodiazepine derivative that exerts its pharmacological effects by enhancing the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the central nervous system. This results in sedative, hypnotic, anxiolytic, and muscle relaxant properties. Flurazepam is primarily used for the short-term treatment of insomnia, as it helps to induce and maintain sleep. Despite its therapeutic benefits, flurazepam also carries the potential for toxicity and severe side effects. Overdose or misuse of flurazepam can lead to central nervous system depression, manifested by symptoms such as drowsiness, confusion, respiratory depression, and coma. It is important to note that the risk of toxicity is heightened when flurazepam is combined with other central nervous system depressants, such as alcohol or opioids. Moreover, the long-term use of flurazepam is linked to the development of tolerance, dependence, and addiction. Tolerance occurs when higher doses of the medication are required to achieve the same therapeutic effect, while dependence is characterized by the emergence of withdrawal symptoms upon discontinuation. Addiction, on the other hand, involves the compulsive use of flurazepam despite its adverse consequences. In this respect, rapid, accurate and precise detection of flurazepam is of great importance. On the other hand, electrochemical sensors offer a promising solution as they are rapid, sensitive, portable devices capable of measuring analytes even in opaque and colored specimens [13]. However, the initial and fundamental step in developing a novel electrochemical sensor is identifying an appropriate sensing material modifier that can selectively interact with the desired analyte [14].

The $B_{12}N_{12}$ nanocluster, depicted in Figure 1, is a structure of great interest due to its potential applications across various fields [22-24]. Comprising 12 boron and 12 nitrogen atoms, this nanocluster forms a distinct and stable arrangement [25-27]. Its unique properties render it a compelling subject for scientific inquiry and technological progress [28]. Within the realm of nanotechnology, the $B_{12}N_{12}$ nanocluster stands out for its exceptional characteristics [29]. Its stability, electronic configuration, and reactivity present promising prospects for applications in catalysis, electronics, and material science [30]. The exploration and manipulation of these properties hold the key to significant advancements in this field [31]. In this respect, we examined the effectiveness of the $B_{12}N_{12}$ nanocage in adsorption and sensing of flurazepam using Density Functional Theory (DFT) simulations. Our goal was to assess its potential for

addressing challenges in flurazepam removal and detection to contribute to advanced materials for environmental and analytical applications. Through rigorous simulations, we aimed to understand its adsorption and sensing capabilities, providing valuable insights for environmental remediation and chemical sensing practices. Our findings offer new possibilities for addressing issues related to flurazepam contamination and detection.



Flurazepam	$B_{12}N_{12}$

Figure 1. The optimized structures of flurazepam and BN nanocage

Computational Methods

The structures of $B_{12}N_{12}$, flurazepam, and their complexes were created using GuassView 6 [21] and Nanotube Modeler 1.3.0.3 [22]. The calculations were performed with the density functional theory (DFT) method in Gaussian 16 [23] software at the B3LYP/6-31G (d) level of theory [23]. The parameters were determined following a method outlined in [20].

Results and Discussion

Structural Analysis

The investigation of the interaction between adsorbate and adsorbent was conducted to determine the most stable conformer. Two different configurations, A-Conformer and B-Conformer, were studied. In A-Conformer, the drug approached adsorbent through its aliphatic chain, while in B-Conformer, the nanostructure was located near the aromatic rings of the drug molecule in a parallel form. The optimized structures showed no significant structural deformations, indicating that no chemical bonds were formed between the adsorbate and adsorbent molecules [15]. Table 1 presents the calculated adsorption energies and other structural properties. The adsorption energy for B-Conformer were more negative than those for A-Conformer in both vacuum and aqueous phases, indicating that the formation of B-Conformer was more energetically favorable [16]. The negative adsorption energies suggest that the interaction between flurazepam and BN nanocage is experimentally possible in both phases. In addition to geometric optimizations, IR calculations were performed on the structures, and no negative frequencies were observed, confirming that all structures were true local minimums [17]. The dipole moment of flurazepam increased significantly after its adsorption on the surface of $B_{12}N_{12}$, suggesting that flurazepam-$B_{12}N_{12}$ complexes are more soluble in polar solvents compared to the pure drug without the nanostructure [18]. Furthermore, the reactivity and bioavailability of flurazepam improved noticeably after its interaction with B12N12, indicating that nanocluster can serve as a suitable nanocarrier for this drug. NBO computations were also conducted to gain further insights into the adsorption mechanism, and the results showed that no bonds were formed between the adsorbate and adsorbent, confirming that the adsorption mechanism is physisorption [29].

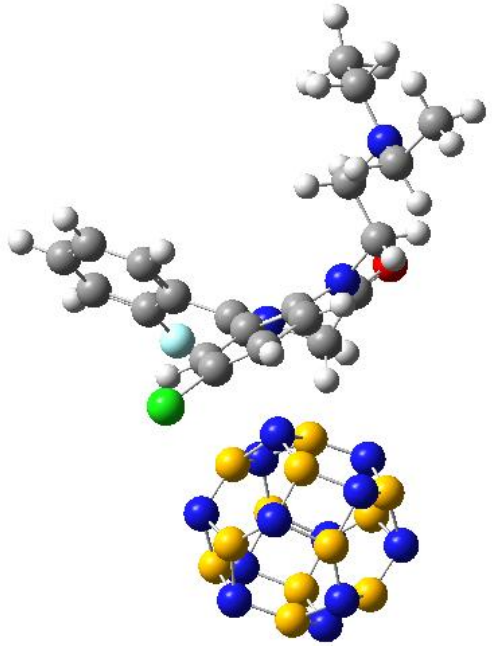
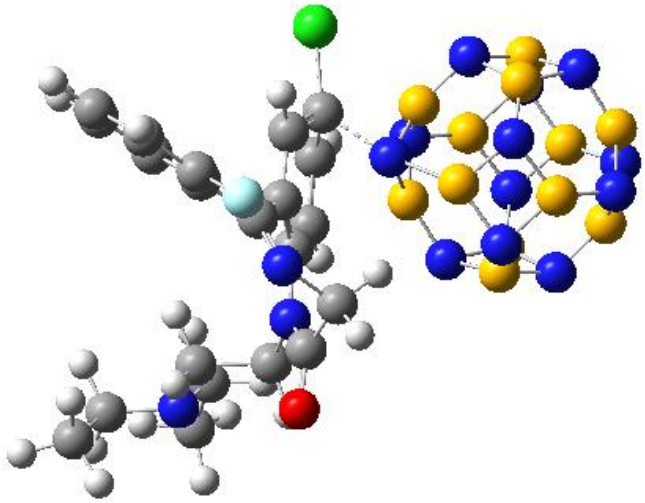
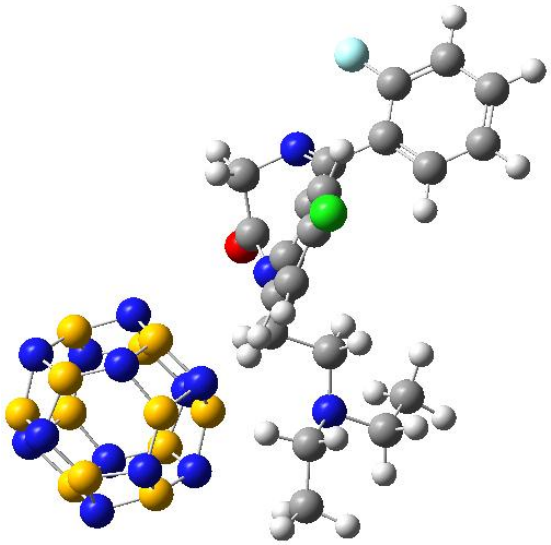
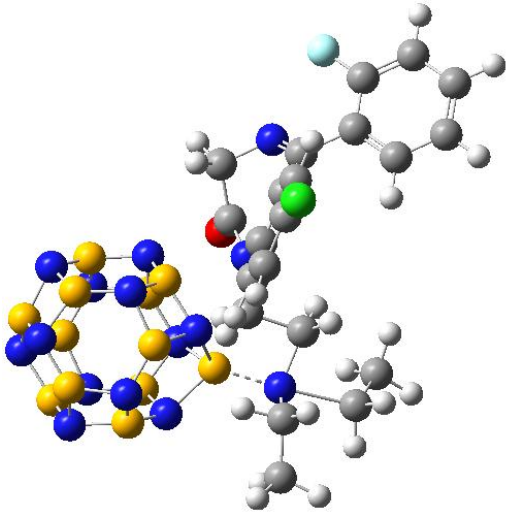
	Initial Structures	Optimized Structures
A-Conformer		
B-Conformer		

Figure 2. Initial and optimized structures of flurazepam-$B_{12}N_{12}$ complexes

Table 1. The calculated structural properties of flurazepam, $B_{12}N_{12}$ and their complexes in both vacuum and aquoeuss phases

NO	Adsorption energy (kcal/mol)	ZPE (kcal/mol)	ν_{min} (cm^{-1})	ν_{max} (cm^{-1})	Dipole Moment (Debye)
Flurazepam-Vacuum	---	77.143	91.388	3735.374	2.30
$B_{12}N_{12}$-Vacuum	---	133.607	313.267	1437.647	0.00
A-Conformer-Vacuum	-75.127	164.526	101.898	2066.148	2.14
B-Conformer-Vacuum	-98.544	163.133	192.518	2057.178	4.58
Flurazepam-Water	---	170.197	203.968	2053.588	2.88
$B_{12}N_{12}$-Water	---	131.068	231.018	1437.630	0.00
A-Conformer-Water	-38.187	171.025	121.708	2050.258	3.09
B-Conformer-Water	-54.729	175.076	193.728	2048.198	4.973

Thermodynamic Parameters

In order to gain further insight into the thermochemistry of the adsorption process, various adsorption thermodynamic parameters were calculated and are presented in Table 2. It is evident that both conformers, in both vacuum and aqueous phases, exhibit negative values for ΔH_{ad} and ΔG_{ad}, indicating the exothermic and spontaneous nature of the interactions. Furthermore, the negative values of ΔSad indicate that aggregation occurs in the complexes following the interaction of flurazepam with nanocage [20]. The influence of solvent and temperature on all of the calculated parameters was investigated, and the results obtained demonstrate that the adsorption process is more favorable at lower temperatures [16]. Additionally, it was observed that the presence of solvent does not have a significant impact on the interactions [16, 17].

Table 2. The calculated thermodynamic parameters in vacuum and aqueous phases in the temperature range of 298-318 K

NO	ΔH_{ad} (kcal/mol)	ΔG_{ad} (kcal/mol)	ΔS_{ad} (cal/mol)
A-Conformer-Vacuum-298	-76.185	-44.967	-95.271
A-Conformer-Vacuum-308	-72.773	-39.726	-97.627
A-Conformer-Vacuum-318	-69.361	-34.485	-99.983
A-Conformer-Water-298	-38.529	-7.311	-88.136
A-Conformer-Water-308	-36.395	-6.330	-90.035
A-Conformer-Water-318	-34.261	-4.349	-91.934
B-Conformer-Vacuum-298	-103.225	-72.007	-94.263
B-Conformer-Vacuum-308	-99.813	-66.766	-96.619
B-Conformer-Vacuum-318	-96.401	-61.525	-98.975
B-Conformer-Water-298	-54.129	-22.911	-104.247
B-Conformer-Water-308	-51.995	-21.930	-106.146
B-Conformer-Water-318	-49.861	-19.949	-108.045

FMO Analysis

The bandgap, which refers to the energy difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), plays a crucial role in determining the electrochemical conductivity of a compound [18]. A narrower bandgap indicates higher conductivity, while a wider bandgap implies lower conductivity. In the context of this study, it was aimed to investigate the potential of BN nanocluster as an electroactive sensing material for detecting flurazepam. For this purpose, variations in bandgap during the adsorption process to assess the material's suitability was evaluated. The data presented in Table 3 clearly

demonstrate that the bandgap of $B_{12}N_{12}$ is initially 6.72 eV. However, when flurazepam adsorbs onto the surface of $B_{12}N_{12}$, this parameter decreases by 31.95% and 44.60% for the A and B conformers, respectively. Consequently, the bandgap values for the A and B conformers become 4.57 eV and 3.72 eV, respectively. This significant decrease in bandgap indicates a substantial enhancement in the electrochemical conductivity of $B_{12}N_{12}$ during the adsorption process of flurazepam [19]. Therefore, $B_{12}N_{12}$ can be considered an excellent sensing material for detecting flurazepam. The chemical hardness of flurazepam was found to be 4.65 eV. However, when flurazepam interacts with the nanostructure (A and B conformers), its chemical hardness decreases to 2.29 eV and 1.86 eV, respectively. This decrease suggests an improvement in the chemical reactivity of flurazepam upon interaction with the nanostructure [20]. Furthermore, the negative values of the chemical potential for all studied structures indicate that these structures are thermodynamically stable [22]. Additionally, the electrophilicity and maximum transferred charge capacity of flurazepam were found to be 0.17 and 0.27 eV, respectively. However, when flurazepam is adsorbed onto the $B_{12}N_{12}$ surface, both indices experience a significant increase [23]. This suggests that flurazepam -$B_{12}N_{12}$ complexes are more electrophilic and have a higher tendency to absorb electrons compared to pure flurazepam without the nanostructure. In conclusion, the findings of this study indicate that $B_{12}N_{12}$ can serve as an excellent electroactive sensing material for detecting flurazepam. The adsorption of flurazepam onto $B_{12}N_{12}$ leads to a decrease in bandgap and an enhancement in electrochemical conductivity. Additionally, the chemical reactivity of flurazepam improves upon interaction with the nanostructure. The thermodynamic stability of the studied structures further supports their potential applications in sensing and detection processes.

Table 3. The calculated FMO parameters

NO	E_{HOMO} (eV)	E_{LUMO} (eV)	E_g (eV)	$\%\Delta E_g$	η (eV)	μ (eV)	ω (eV)	ΔN_{max} (eV)
Flurazepam	-5.90	3.41	9.31	---	4.65	-1.24	0.17	0.27
$B_{12}N_{12}$	-7.95	-1.24	6.72	---	3.36	-4.60	3.15	1.37
A-Conformer	-4.07	0.50	4.57	-31.95	2.29	-1.79	0.70	0.78

B-Conformer	-3.50	0.22	3.72	-44.60	1.86	-1.64	0.73	0.88

Conclusion

The research undertaken investigated the potential utilization of boron nitride nanocluster as a sensor for the electrochemical detection of flurazepam. Through the use of IR, FMO, and NBO computations, the feasibility of flurazepam interacting with the nanostructure was comprehensively examined. The obtained negative values of adsorption energy and thermodynamic parameters indicate that not only is the interaction experimentally viable, but also exothermic and two-sided in nature. Furthermore, the study on the influence of solvent and temperature revealed that flurazepam adsorption is possible in an aqueous phase and more favorable at lower temperatures. The NBO results provided valuable insights by indicating that the interactions between flurazepam and the boron nitride nanoclusters have a non-covalent nature. Additionally, the FMO calculations yielded substantial findings, demonstrating that the bandgap of the BN nanocluster experiences a significant decrease of 44.6% when flurazepam adsorbs on its surface, indicating its potential for sensitive detection of flurazepam. Overall, the findings emphasize the promising suitability of boron nitride nanoclusters as a sensor for the electrochemical detection of flurazepam.

References

[1] J. R. Swanson, et al., *J Forensic Sci*., 42, 335 (1994).

[2] J. C. Nelson, *J Clin Psychiatry*., 45, 10 (1984).

[3] A. Ghanizadeh, *Curr Drug Saf.*, 8, 169 (2013).

[4] D. S. Janowsky B. Byerley *J Clin Psychiatry*. 45, 3 (1984).

[5] R. O. Friedel, *J Clin Psychiatry.*, 45, 46 (1984).

[6] J. F. Rosenbaum, *J Clin Psychiatry*. 45, 17 (1984).

[7] F. R. Sallee, *Clin Pharmacokinet*., 18(5), 346 (1990).

[8] L. Hearn, et al., *Cochrane Database Syst Rev*., 2, 10 (2014).

[9] D. Healy, C. Whitaker, *J Psychiatry Neurosci*., 28, 5 (2003).

[10] N. Perroud, *CNS Drugs*., 25, 459 (2011).

[11] Y. Wang, H. Xu, J. Zhang, G. Li, Sensors., 8, 2043 (2008).

[12] F. M. Alipour, etal., *Int J New Chem*., 10, 197 (2023).

[13] B. J. Privett, et al., *Anal Chem*., 82, 4723 (2010).

[14] R. Farahani, T. Madrakian, A. Afkhami, *Int J New Chem*., 9, 383 (2023).

[15] J. Paier, M. Marsman, G. Kresse, *J Chem Phys*., 127, 2 (2007).

[16] M. R. Sameti, M. B. Naghibi. *Int J New Chem*., 11, 15 (2023).

[17] R. Mousavi, et al., *Int J New Chem*., 10, 268 (2023).

[18] A. E. Frisch, R. E. Plata, D. A. Singleton. Gaussian 09W Reference. J Am Chem Soc. 137, 3811 (2009).

[19]. Frisch M.J., Trucks G.W., Schlegel H.B., Scuseria G.E., Robb M. a., Cheeseman J.R., [1]. Scalmani G., Barone V., Petersson G. a., Nakatsuji H., Li X., Caricato M., Marenich a. V., Bloino J., Janesko B.G., Gomperts R., Mennucci B., Hratchian H.P., Ortiz J. V., Izmaylov a. F, Sonnenberg J.L., Williams, Ding F., Lipparini F., Egidi F., Goings J., Peng B., Petrone A., Henderson T., Ranasinghe D., Zakrzewski V.G., Gao J., Rega N., Zheng G., Liang W., Hada M., Ehara M., Toyota K., Fukuda R., Hasegawa J., Ishida M., Nakajima T., Honda Y., Kitao O., Nakai H., Vreven T., Throssell K., Montgomery J.r. J. a., Peralta J.E, Ogliaro F., Bearpark M.J., Heyd J.J., Brothers E.N., Kudin K.N., Staroverov V.N., Keith T. a., Kobayashi R., Normand J., Raghavachari K., Rendell a. P, Burant JC, Iyengar S.S., Tomasi J., Cossi M., Millam J.M., Klene M., Adamo C., Cammi R., Ochterski J.W., Martin R.L., Morokuma K., Farkas O., Foresman J.B., Fox D.J. G16_C01. 2016. p. Gaussian 16, Revision C.01, Gaussian, Inc., Wallin.

[20]. Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., ... & Fox, D. J. (2009). Gaussian 2009. *Revision A*, *2*.

[21] M. R. Jalali Sarvestani, R. Ahmadi, *Asian J Nanosci Mater*., 3, 103 (2020).

[22] GaussView, Version 6.1, Roy Dennington, Todd A. Keith, and John M. Millam, Semichem Inc., Shawnee Mission, KS, (2016).

[23] S. Melchor, J. A. Dobado, *J. Chem. Inf. Comput. Sci*, 44, 1639 (2004).

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