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Original Research Article

Desipramine Interaction with Fullerene (C_{20}): DFT Studies

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ABSTRACT

In this investigation, the function of the smallest fullerene (C_{20}) as a sensor and nano-carrier for the tricyclic antidepressant drug desipramine was scrutinized through density functional theory simulations. The achieved adsorption energies showed the interaction of desipramine with C_{20} is experimentally possible. The calculated ΔG_{ad}, ΔH_{ad} and K_{th} showed the adsorption process is spontaneous, exothermic and reversible. The influences of solvent and temperature on the interactions were also studied and the results showed the adsorption process is more favorable in lower temperatures and the presence of solvent does not have any effect on the nature of interactions. The NBO analysis showed no chemical bond has been created between desipramine and nanostructure and the existing interaction is a physisorption. The frontier molecular orbital analysis results showed the bandgap of fullerene decline -35.30% from 7.678 (eV) to 2.484 (eV) indicating this nanomaterial can be an ideal sensor for the detection of desipramine. The values of dipole moment and chemical hardness showed C_{20} can be employed as an appropriate nano-carrier for the drug delivery of desipramine.

Keywords: Desipramine, Density functional theory, Adsorption, sensor, Nanocarrier, Tricyclic antidepressants

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Introduction

Desipramine (DPM, Fig. 1) is a widely prescribed tricyclic antidepressant used for the treatment of major depressive disorder, attention-deficit hyperactivity disorder (ADHD), neuropathic pain, and cocaine dependence [1-3]. It primarily functions as a selective norepinephrine reuptake inhibitor, although it also exhibits other effects such as weak serotonin reuptake inhibition, α1-blocking, antihistamine, and anticholinergic properties [4-6]. Unfortunately, common side effects of DPM include dry mouth, constipation, urinary retention, blurred vision, and cognitive or memory impairments [7-9]. Consequently, it is of great importance to discover a suitable nanocarrier for delivering DPM in order to mitigate these side effects and enhance its therapeutic effects. Furthermore, the rapid determination of antidepressants is crucial due to their potential impact on individuals younger than 25 years old, particularly within the first month of prescription [10-12]. 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]. Fullerene (C_{20}, Fig. 1), the smallest nanomaterial with a dodecahedral cage structure, possesses unique characteristics that make it an excellent candidate as both a sensing material and nanocarrier [15-17]. Its highly curved structure consists of pentagonal rings and offers high conductance, a large surface area-to-volume ratio, and exceptional reactivity [18-20]. Therefore, this study aims to evaluate the performance of C_{20} as a nanocarrier and sensor for the delivery and detection of DPM through density functional theory simulations. By exploring the potential of C_{20} in drug delivery and sensing applications, we hope to contribute to the development of more effective and efficient therapies while minimizing unwanted side effects. In conclusion, the utilization of nanocarriers and electrochemical sensors holds great promise in improving drug delivery systems and facilitating the rapid detection of antidepressants like DPM. Through the evaluation of C_{20} as a potential nanocarrier and sensing material modifier, this study aims to advance our understanding of these applications and pave the way for future advancements in pharmaceutical research.

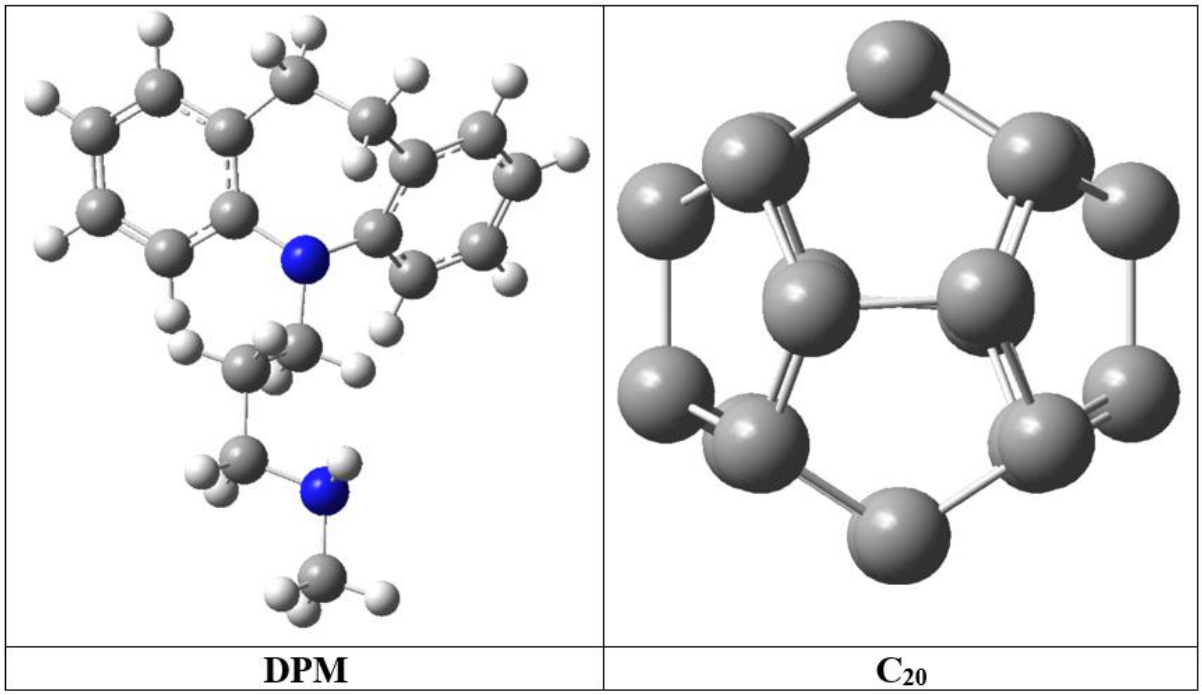

Figure 1. The optimized structures of DPM and C_{20}

Computational Methods

The structures of C_{20}, DPM, 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 DPM and C_{20} was conducted to determine the most stable conformer. Two different configurations, A-Conformer and B-Conformer, were studied. In A-Conformer, the drug approached C_{20} through its three fused rings, while in B-Conformer, the nanostructure was located near the aliphatic chain of the drug molecule. 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 total electronic energies and adsorption energies. The total electronic energies 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 DPM and C_{20} 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 DPM increased significantly after its adsorption on the surface of C_{20}, suggesting that DPM-C_{20} complexes are more soluble in polar solvents compared to the pure drug without the nanostructure [18]. Furthermore, the reactivity and bioavailability of DPM improved noticeably after its interaction with fullerene, indicating that C_{20} 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].

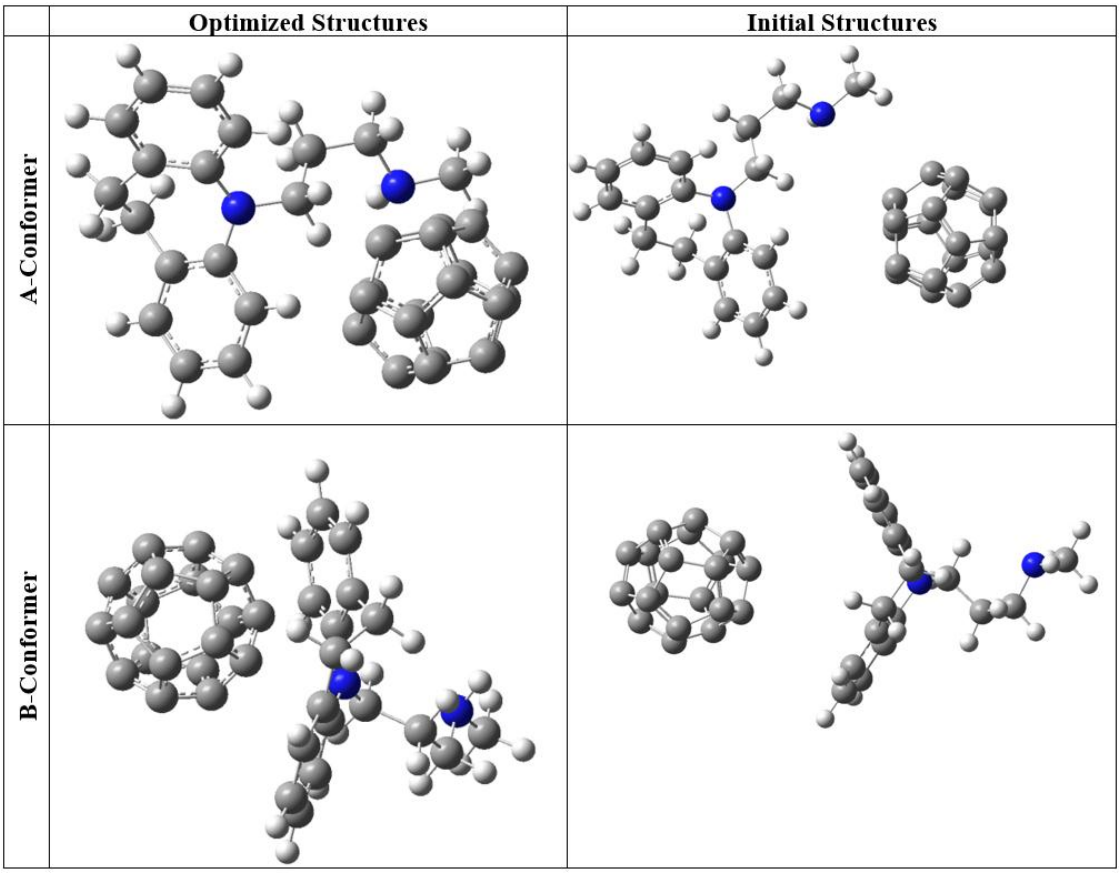

Figure 2. Initial and optimized structures of DPM-C_{20} complexes

Table 1. The calculated structural properties of DPM, C_{20} and their complexes in both vacuum and aquoeuss phases

NO	Total electronic energy (a.u)	Adsorption energy (kcal/mol)	ZPE (kcal/mol)	ν_{min} (cm^{-1})	ν_{max} (cm^{-1})	Dipole Moment (Debye)
DPM-Vacuum	-793.173	---	86.792	90.149	3734.135	1.289
C_{20}-Vacuum	-747.072	---	132.332	312.028	1436.408	0.002
A-Conformer-Vacuum	-1540.278	-87.056	167.975	100.659	2064.909	2.828
B-Conformer-Vacuum	-1540.288	-114.096	168.746	191.279	2055.939	3.146
DPM-Water	-793.181	---	169.108	202.729	2052.349	1.345
C_{20}-Water	-747.069	---	129.568	229.779	1436.391	0.003
A-Conformer-Water	-1540.269	-49.400	165.105	120.469	2049.019	3.185
B-Conformer-Water	-1540.275	-65.000	165.766	192.489	2046.959	3.009

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. The relatively low values of K_{th} suggest that these interactions are reversible [20]. Furthermore, the negative values of ΔSad indicate that aggregation occurs in the complexes following the interaction of DPM with fullerene [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 aquoes phases in the temperature range of 298-318 K

NO	ΔH_{ad} (kcal/mol)	ΔG_{ad} (kcal/mol)	ΔS_{ad} (cal/mol)	K_{th}
A-Conformer-Vacuum-298	-87.061	-55.843	-106.147	$6.148\times10^{+09}$
A-Conformer-Vacuum-308	-83.649	-50.602	-108.503	$3.820\times10^{+08}$
A-Conformer-Vacuum-318	-80.237	-45.361	-110.859	$2.826\times10^{+07}$
A-Conformer-Water-298	-49.405	-18.187	-99.012	$1.542\times10^{+03}$
A-Conformer-Water-308	-47.271	-17.206	-100.911	$8.282\times10^{+02}$
A-Conformer-Water-318	-45.137	-15.225	-102.810	$3.169\times10^{+02}$
B-Conformer-Vacuum-298	-114.101	-82.883	-105.139	$3.377\times10^{+14}$
B-Conformer-Vacuum-308	-110.689	-77.642	-107.495	$1.472\times10^{+13}$
B-Conformer-Vacuum-318	-107.277	-72.401	-109.851	$7.816\times10^{+11}$
B-Conformer-Water-298	-65.005	-33.787	-115.123	$8.366\times10^{+05}$
B-Conformer-Water-308	-62.871	-32.806	-117.022	$3.663\times10^{+05}$
B-Conformer-Water-318	-60.737	-30.825	-118.921	$1.157\times10^{+05}$

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, the researchers aimed to investigate the potential of fullerene as an electroactive sensing material for detecting DPM. They evaluated the variations in bandgap during the adsorption process to assess the material's suitability for this purpose. The data presented in Table 3 clearly

demonstrate that the bandgap of C_{20} is initially 7.678 eV. However, when DPM adsorbs onto the surface of C_{20}, this parameter decreases by 28.599% and 35.306% for the A and B conformers, respectively. Consequently, the bandgap values for the A and B conformers become 5.482 eV and 4.967 eV, respectively. This significant decrease in bandgap indicates a substantial enhancement in the electrochemical conductivity of C_{20} during the adsorption process of DPM [19]. Therefore, C_{20} can be considered an excellent sensing material for detecting DPM. The chemical hardness of DPM was found to be 6.021 eV. However, when DPM interacts with the nanostructure (A and B conformers), its chemical hardness decreases to 2.741 eV and 2.484 eV, respectively. This decrease suggests an improvement in the chemical reactivity of DPM 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 DPM were found to be 0 and 0.01 eV, respectively. However, when DPM is adsorbed onto the fullerene surface, both indices experience a significant increase [23]. This suggests that DPM-C_{20} complexes are more electrophilic and have a higher tendency to absorb electrons compared to pure DPM without the nanostructure. In conclusion, the findings of this study indicate that fullerene (C_{20}) can serve as an excellent electroactive sensing material for detecting DPM. The adsorption of DPM onto C_{20} leads to a decrease in bandgap and an enhancement in electrochemical conductivity. Additionally, the chemical reactivity of DPM 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)
DPM	-6.079	5.962	12.041	---	6.021	-0.058	0.000	0.010
C_{20}	-4.463	3.215	7.678	---	3.839	-0.624	0.051	0.162
A-Conformer	-3.186	2.296	5.482	-28.599	2.741	-0.445	0.036	0.162
B-Conformer	-2.984	1.983	4.967	-35.306	2.484	-0.501	0.050	0.202

Conclusion

The detection and drug delivery of DPM are of great importance. Therefore, In this investigation, we have conducted density functional theory simulations to examine the function of the smallest fullerene (C_{20}) as a sensor and nano-carrier for the DPM. Our findings demonstrate that the interaction between DPM and C_{20} is indeed feasible, as evidenced by the achieved adsorption energies. The calculated values of ΔG_{ad}, ΔH_{ad}, and K_{th} indicate that the adsorption process is spontaneous, exothermic, and reversible. Furthermore, we have explored the influence of solvent and temperature on these interactions. Our results reveal that the adsorption process is more favorable at lower temperatures and that the presence of solvent does not affect the nature of the interactions. Through NBO analysis, we have determined that no chemical bond is formed between DPM and the nanostructure. Instead, the existing interaction is classified as physisorption. Additionally, our frontier molecular orbital analysis indicates a significant decline in the bandgap of fullerene by 35.30%, from 7.678 eV to 2.484 eV. This suggests that C_{20} can serve as an ideal sensor for the detection of DPM. Moreover, we have evaluated the values of dipole moment and chemical hardness, which demonstrate that C_{20} can be effectively utilized as a nano-carrier for the delivery of DPM. Overall, our study provides valuable insights into the potential applications of C_{20} as both a sensor and a nano-carrier for DPM. The experimental feasibility, spontaneous and reversible adsorption process, and the favorable influence of lower temperatures make C_{20} a promising candidate for further exploration in drug delivery systems and sensing technologies.

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