



Research article

Tuning the nanocarrier potential of fullerene C₆₀ through endohedral encapsulation of B, N, Si, and P: A density functional theory study

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Abstract: The fullerene C₆₀ is widely studied as a potential nanoscale drug carrier for hydrophobic anticancer compounds; however, its practical application in biomedicine has been limited due to low polarity and water solubility. Herein, we utilized Density Functional Theory (DFT) calculations to study the impact of endohedral encapsulation of several heteroatoms (boron, nitrogen, silicon, and phosphorus) on the structure and electronic properties of C₆₀. Each atom was placed within the confines of the fullerene cage adjacent to the same pentagonal carbon group to compare interactions and stability. Optimization results showed minimal impact on C-C bond length due to encapsulation, maintaining a stable fullerene cage structure. Calculated interaction energies showed that encapsulation of B, N, and Si within the fullerene cage is energetically favourable, whereas P encapsulation is less favourable. C₆₀N exhibited the highest interaction as a result of large charge transfer between the cage and nitrogen atom, while C₆₀Si was found to have the greatest dipole moment, suggesting increased polarity. HOMO-LUMO analysis showed a decreased gap upon encapsulation of all molecules, which suggests higher chemical softness. Density of states (DOS) analysis revealed noticeable changes in the electronic structure following encapsulation. The suitability of the investigated systems as drug carriers was evaluated using temozolomide (TMZ) as a model anticancer drug. Among the studied complexes, SiC₆₀-TMZ exhibited favourable interaction characteristics and enhanced solvation stability. Overall, C₆₀Si presents an optimal balance of stability, polarity, and electronic softness, highlighting its potential as an efficient nanocarrier for hydrophobic drug delivery applications.

Keywords: Fullerene C₆₀; adsorption energy; density of states; charge transfer; electronic properties

1. Introduction

Nanotechnology has transformed modern biomedical research by offering new approaches to address longstanding challenges in diagnosis, therapy, biosensing, and regenerative medicine [1]. The integration of nanotechnology with computational modelling has accelerated the development of nanoscale systems capable of interacting with biological environments in a controlled manner [2]. Among biomedical applications, targeted drug delivery has received considerable attention because it enables the preferential accumulation of therapeutic agents in diseased tissues while reducing systemic exposure [3]. However, many clinically used anticancer drugs suffer from poor aqueous solubility, rapid clearance, and non-specific biodistribution, which limit their therapeutic efficacy and increase adverse side effects. These limitations have driven the search for nanocarriers with improved solubility, prolonged circulation time, and enhanced tumor-targeting capability [4].

Zero-dimensional nanostructures have emerged as promising candidates for drug-delivery applications because of their compact geometry and tunable physicochemical properties. Among these materials, fullerene C₆₀, consisting of sixty carbon atoms arranged in a truncated icosahedral cage, has attracted considerable attention due to its remarkable structural stability, high electron affinity, and versatile surface characteristics [5]. These features have enabled its exploration in photodynamic therapy, antioxidant systems, biosensing, and molecular encapsulation. Despite these advantages, pristine C₆₀ is inherently hydrophobic and exhibits poor dispersibility in physiological media, which restricts its direct use as a drug-delivery nanocarrier [6]. Consequently, modification of the physicochemical properties of C₆₀ is necessary to improve its polarity, hydrophilicity, and compatibility with biological environments [7].

One of the most effective approaches for modifying the physicochemical properties of C₆₀ is endohedral encapsulation, in which foreign atoms are confined within the fullerene cage [8]. Unlike surface functionalization, this strategy places atoms inside the inner cavity of C₆₀, allowing significant electronic interactions while preserving the structural integrity of the carbon framework [9]. Encapsulation of elements such as boron, nitrogen, silicon, and phosphorus can alter the internal charge distribution of the fullerene cage, leading to changes in polarization and electronic properties. These modifications can influence charge-transfer processes, enhance chemical reactivity, and improve the polarity of the system, thereby strengthening its interaction with therapeutic molecules [10].

Besides endohedral encapsulation, heteroatom doping has been widely explored as an effective strategy for tailoring the properties of zero-dimensional nanostructures such as fullerenes [11]. The incorporation of foreign atoms within or onto the carbon framework of C₆₀ can significantly modify its electronic structure. Such modifications may introduce localized electronic states within the energy gap, alter the HOMO-LUMO separation, and enhance charge polarization throughout the nanostructure. These effects can influence chemical reactivity, interaction strength, and the affinity of the nanostructure toward external molecules. Furthermore, dopants with different electronegativities and atomic radii can induce structural distortion and charge redistribution, leading to enhanced polarity and improved solubility of otherwise hydrophobic fullerene systems [12]. Previous studies have demonstrated that doped fullerene nanostructures exhibit improved stability, tunable electronic behaviour, and enhanced interaction characteristics compared with pristine C₆₀, highlighting their

potential as efficient nanocarriers for biomedical applications.

Recent advances in computational materials science, particularly Density Functional Theory (DFT), have enabled detailed investigations of encapsulated fullerene systems at the atomic level. DFT provides valuable insight into structural stability, charge redistribution, and the electronic modifications induced by heteroatom encapsulation within the C₆₀ cage [13]. The method allows quantitative evaluation of interaction energies, structural relaxation, frontier molecular orbitals, and electronic reactivity descriptors. In addition, DFT calculations can be used to predict properties such as dipole moment and polarity, which are closely related to solubility and dispersion in biological environments. Owing to its ability to provide detailed electronic and structural information prior to experimental synthesis, DFT has become a powerful tool for screening potential nanocarriers and identifying systems with desirable characteristics for drug-delivery applications [14].

Although several studies have investigated individual encapsulated atoms in C₆₀, systematic comparisons performed under identical computational conditions remain limited. The encapsulated species considered in such studies differ significantly in electronegativity, atomic size, and bonding characteristics, leading to distinct structural and electronic responses within the fullerene cage. These variations can influence interaction strength, charge-transfer behaviour, stability, and the ability of the nanocarrier to load and release therapeutic molecules effectively [15]. In addition, changes in polarity and dipole moment resulting from encapsulation can affect the dispersion of nanocarriers in aqueous environments, which is an important factor for biocompatibility. Therefore, a consistent comparative investigation of different encapsulated systems is necessary to identify fullerene-based nanostructures with favourable properties for biomedical applications [16]. Computational studies on modified fullerene systems have increased considerably, significant gaps remain in understanding how different encapsulated atoms influence the behaviour of C₆₀ as a nanocarrier. Each encapsulated species can induce distinct structural distortions, affect stability, and modify the electronic characteristics of the fullerene cage, thereby influencing its interaction with therapeutic molecules [17]. Such changes can alter the reactivity, polarity, and dispersibility of the nanostructure, ultimately affecting its performance under physiological conditions [18]. Therefore, a systematic comparative investigation of different encapsulated systems is required to identify the most promising nanocarriers for the delivery of anticancer drugs, many of which suffer from poor aqueous solubility and dose-dependent toxicity [19].

Motivated by these considerations, the present study employs DFT calculations to investigate pristine C₆₀ and fullerene systems containing encapsulated boron (B), nitrogen (N), silicon (Si), and phosphorus (P) atoms [20]. These elements were selected because they possess distinct electronic characteristics that can influence the fullerene cage in different ways. Boron and phosphorus are relatively electron-deficient species, whereas nitrogen is electron-rich. Silicon exhibits unique behaviour because of its larger atomic radius and carbon-like valence configuration [21]. The differences in electronegativity, atomic size, and electronic structure among these elements provide an opportunity to examine how heteroatom encapsulation affects charge distribution, interaction strength, structural stability, and electronic properties of the fullerene cage. Boron, nitrogen, silicon, and phosphorus have been widely employed to modify carbon-based nanomaterials because of their ability to tailor electronic and physicochemical properties for applications in sensing, catalysis, and drug delivery [22]. Therefore, their incorporation within the C₆₀ cage provides a suitable platform for investigating the influence of endohedral encapsulation on nanocarrier performance [23]. To ensure a consistent comparison, each atom was positioned near the same pentagonal region of the fullerene

structure prior to optimization. This approach allows the observed differences to be attributed primarily to the intrinsic properties of the encapsulated atoms rather than their initial placement within the cage [24].

To evaluate the influence of encapsulation, a range of structural and electronic properties were analyzed. Changes in bond lengths and geometric parameters provide insight into the structural stability of the resulting nanohybrid and the extent of distortion induced by the encapsulated atom [25]. Interaction energies were calculated to assess the strength and stability of the interaction between the encapsulated species and the fullerene cage. Frontier molecular orbital analysis was performed to examine changes in electronic reactivity following encapsulation [26]. In addition, electronic descriptors including chemical potential, hardness, softness, and electrophilicity were evaluated to understand the charge-transfer characteristics of the investigated systems. Charge distribution and dipole moment analyses were used to assess polarity and the potential dispersibility of the nanocarriers in aqueous environments. Furthermore, density of states (DOS) calculations were carried out to examine modifications in the electronic structure resulting from encapsulation and to determine how these changes may influence the interaction of the nanocarrier with therapeutic molecules [27].

These analyses enable a detailed comparison of the investigated fullerene systems. The main objective is to identify the encapsulated C₆₀ structure that exhibits favourable polarity, strong interaction characteristics, and good electronic stability. Such features are important for designing nanocarriers capable of transporting hydrophobic anticancer drugs efficiently while reducing unwanted side effects. This study also provides insight into the influence of endohedral encapsulation on the structural and electronic properties of fullerene-based nanomaterials. By examining the relationship between interaction energies, electronic behaviour, and polarity, the suitability of C₆₀ nanostructures for drug-delivery applications can be assessed. The results may assist future experimental studies and contribute to the development of fullerene-based nanocarriers for biomedical applications.

2. Materials and methods

The optimization of C₆₀ and C₆₀X structures were carried out using on the Synopsis QuantumATK Software Package within the framework of density functional theory. The LCAO basis set calculator was used with generalized gradient approximation (GGA) formulated by Perdue, Burke and Ernzerhof [28–32]. A tolerance of 10^{−5} and density mesh cutoff of 150 Rydberg were used as suitable parameters for optimization. In order to obtain the minimum potential energy, the C₆₀ and C₆₀X structures were perturbed, reoptimized and verified for the changes in overall total energy to an accuracy of 0.005 eV [33]. All calculations were performed under neutral charge conditions (total charge = 0) and spin-unpolarized (closed-shell) configurations, as all systems considered (pristine C₆₀ and adsorbed C₆₀X structures) do not possess unpaired electrons in their ground state.

The adsorption energy (E_{ads}) which indicates the stability of the modified structures were calculated using [34]:

$$E_{\text{ads}} = E_{\text{complex}} - E_{\text{fullerene}} - E_{\text{dopant}}$$

where E_{complex}, E_{fullerene} and E_{dopant} are the total energy of the doped structure, pristine fullerene and the added adsorbent respectively.

In order to understand the structure reactivity with the adsorbent, the quantum descriptors such as ELUMO and EHOMO, chemical potential (μ), hardness (η), electrophilicity index(ω) and dipole

moment were calculated.

The chemical potential (μ) is defined as:

$$\mu = \frac{E_{Lumo} + E_{Homo}}{2}.$$

The hardness (η) [35] which is a measure of a structure resistance to deformation can be calculated using:

$$\eta = \frac{E_{Lumo} - E_{Homo}}{2}.$$

where ELUMO and EHOMO are the energies of the lowest unoccupied molecular orbital (LUMO) and highest occupied molecular orbital (HOMO) respectively.

The softness (S), which is the inverse of hardness and represents the ease of charge transfer, is expressed as:

$$S = \frac{1}{2\eta}.$$

The electrophilicity index (ω) [36] which is a measure of the tendency to attract an electron is defined as

$$\omega = \frac{\mu^2}{2\eta},$$

where μ is the chemical potential of the complex.

The dipole moment (p) [37] which is a measure of the degree of polarization is calculated as:

$$p = \delta \cdot d$$

where δ is the partial charges on the adsorbent and d is distance between the adsorbent and the nearest neighboring Carbon atom of the fullerene structure.

3. Results and discussion

3.1. Equilibrium geometry of C_{60} and $C_{60}X$

Pristine C_{60} fullerene was taken and energy minimization was achieved with the bond length of 1.45 Å and bond angle of 108° which is accordance with the studies carried out by Kvyatkovskii et al [38]. Then, the adsorbents X were added to the void space of one of the pentagon lattices, at a constant distance for all the structures. The average value of bond lengths (bond angles) of adsorbent added C_{60} structures are obtained in the range of 1.46 Å–1.502 Å (107.62–108.002°). The bond lengths of $C_{60}X$ are found to vary to an extent of 0.7%–3.5%. It is found that the inclusion of adsorbents does not significantly alter the bond angles of C_{60} and retains the sp^3 character. The B, N, Si, P were adsorbed with respect to the nearest C at a distance of 1.96 Å, 2.26 Å, 1.58 Å, 2.10 Å respectively. All of the adsorbents (B, P, Si) except N, were adsorbed inside the cage via physisorption whereas, N was adsorbed inside the cage through chemisorption. (Figure 1).

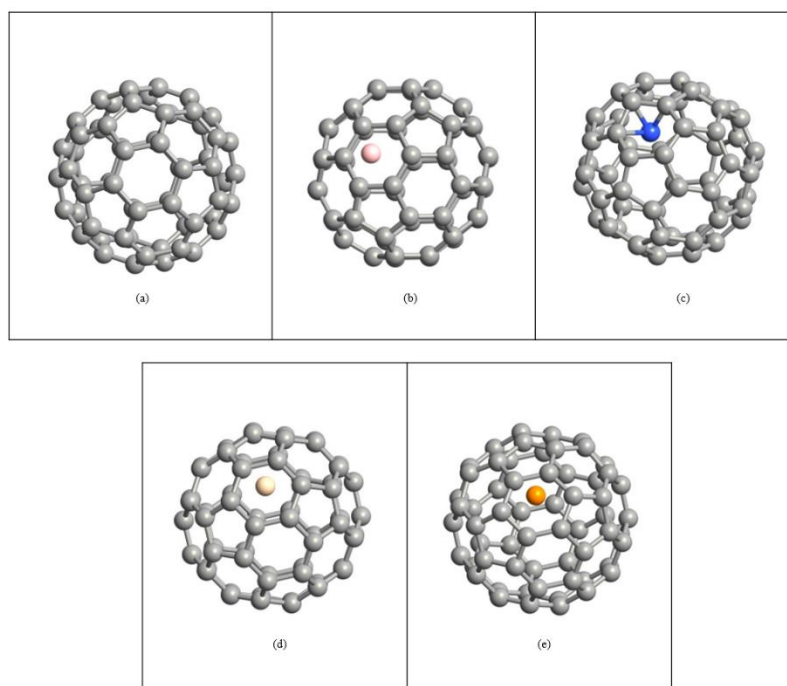


Figure 1. Geometrically optimized structures of (a) C_{60} , (b) $C_{60}B$, (c) $C_{60}N$, (d) $C_{60}Si$, and (e) $C_{60}P$.

3.2. Adsorption energy and stability of C_{60} and $C_{60}x$

The interaction energy reflects the strength of interaction between the encapsulated atom and the fullerene cage and provides useful information about the relative stability of the investigated systems. As shown in Table 1, the stability trend follows the order $C_{60}N > C_{60}Si > C_{60}B > C_{60}P$. Negative interaction energies correspond to favourable and exothermic interactions, whereas positive values indicate energetically unfavourable behaviour under the present DFT conditions [39]. After encapsulation of B, N, Si, and P within the C_{60} cage, all systems exhibited exothermic interactions except $C_{60}P$, which showed an endothermic character and lower stability. Although $C_{60}P$ was retained for comparison under identical computational conditions, its positive interaction energy indicates that this configuration is less favourable for nanocarrier applications. Among the studied systems, $C_{60}N$ displayed the most negative interaction energy, indicating the strongest interaction with the fullerene cage. This observation agrees with its chemisorption-like character. $C_{60}Si$ exhibited the second strongest interaction and maintained a physisorption-like interaction with the cage. Interaction energy alone does not completely describe the suitability of a nanocarrier. While $C_{60}N$ exhibits the strongest interaction and the highest energetic stability, factors such as polarity, charge distribution, and electronic properties must also be considered. In this regard, $C_{60}Si$ shows a favourable balance between interaction strength, polarity, and electronic behaviour, supporting its potential use in drug-delivery applications.

Table 1. Adsorption energy (E_{ads} , eV), hardness (η), Electrophilicity Index (ω), partial charges on the adsorbent (δ , e), distance to nearest C neighbor of C₆₀ (Å), dipole moment (D), and chemical potential (μ) (eV) of C₆₀ and C₆₀X structures.

System	C ₆₀	C ₆₀ B	C ₆₀ N	C ₆₀ Si	C ₆₀ P
E_{ads} (eV)	-	-1.245	-1.807	-1.517	0.552
Hardness (η)	0.850	0.514	0.367	0.509	0.398
Electrophilicity Index (ω)	21.05	21.89	42.03	22.72	27.70
Partial charges on the adsorbent (δ , e)	-	-0.156	1.96	0.917	-4.742
Distance to nearest C neighbor of C ₆₀ (Å)	-	-0.186	2.26	0.881	-5.551
Dipole moment (D)	-	0.392	1.58	2.468	-4.807
Chemical potential (μ , eV)	-5.981	0.018	2.10	0.122	-4.693

3.3. Qualitative reactivity descriptors

3.3.1. HOMO-LUMO gap (H-L gap), ΔE_{g}

The HOMO-LUMO gap describes the difference in energy between the highest occupied and lowest unoccupied molecular orbitals. Lowering of the H-L gap increases biological activity and is more suitable for drug delivery applications. Figure 2 shows that, in comparison to pristine fullerene, the H-L gap of all C₆₀x structures decreased. The H-L gap of C₆₀P and C₆₀N was lower than 1 eV with higher % ΔE_{g} values (greater than 50%), indicating increased reactivity [40]. On the other hand, the H-L gap of C₆₀Si and C₆₀B was higher than 1 eV with lower % ΔE_{g} values (lower than 50%); such systems are more suitable as nanocarriers for drug delivery applications [41], as shown in Table 2.

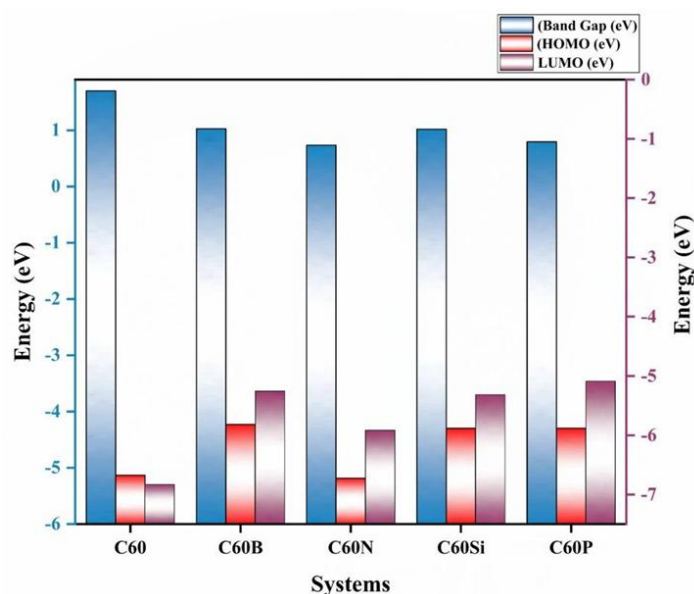


Figure 2. H-L gap of the C₆₀x structures in comparison with pristine C₆₀.

Table 2. HOMO and LUMO levels (eV), H-L gap ΔE_g (eV), ΔE_g difference (eV), softness, and $\% \Delta E_g$.

System	C ₆₀	C ₆₀ B	C ₆₀ N	C ₆₀ Si	C ₆₀ P
HOMO (eV)	−6.83	−5.255	−5.917	−5.315	−5.09
LUMO (eV)	−5.131	−4.228	−5.184	−4.298	−4.295
H-L gap ΔE_g (eV)	1.699	1.027	0.733	1.017	0.795
ΔE_g difference (eV)	-	−0.672	−0.966	−0.682	−0.904
Softness	0.589	0.974	1.364	0.983	1.258
$\% \Delta E_g$	-	−39.55	−56.86	−40.14	−53.21

3.3.2. Partial density of states (PDOS)

The partial density of states (PDOS) provides insight into the contribution of the encapsulated atoms to the overall electronic structure of the system. The PDOS was calculated in the energy range from −7 to −2 eV, as shown in Figure 3.

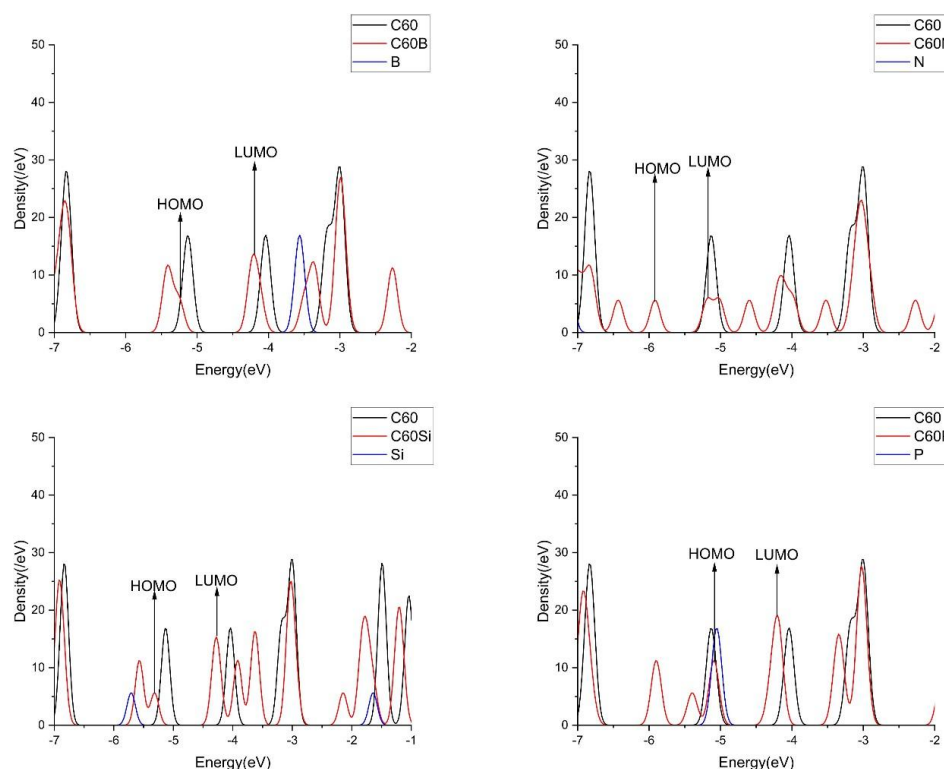


Figure 3. PDOS of C₆₀, X (B/N/Si/P), and C₆₀X structures.

The PDOS profiles reveal that the interaction between the encapsulated atom and the C₆₀ cage depends strongly on the nature of the heteroatom. For C₆₀B, C₆₀Si, and C₆₀P, the states associated with the encapsulated atoms show little overlap with the electronic states of the fullerene near the HOMO-LUMO region. The limited overlap suggests weak electronic coupling and minimal orbital hybridization, which is consistent with a physisorption-like interaction. A different behaviour is observed for C₆₀N. In this system, a noticeable overlap exists between the nitrogen-derived states and

the electronic states of the fullerene cage, particularly in the vicinity of the frontier orbitals. This overlap indicates stronger electronic coupling between the nitrogen atom and the surrounding carbon framework. In addition, redistribution of electronic density is observed in the frontier region, accompanied by modifications in the energy levels. These changes suggest that nitrogen has a greater influence on the electronic structure of C_{60} than the other encapsulated atoms. The stronger interaction observed for $C_{60}N$ is consistent with its shorter interaction distance and larger interaction energy. The overlap of electronic states, redistribution of density, and modification of energy levels collectively indicate a strong interaction between nitrogen and the fullerene cage, supporting the chemisorption-like character of this system.

3.3.3. Frontier molecular orbitals

The distribution of HOMO and LUMO orbitals for pristine C_{60} and the encapsulated systems ($C_{60}B$, $C_{60}P$, $C_{60}N$, and $C_{60}Si$) is presented in Figure 4. Owing to its highly symmetric fullerene framework, pristine C_{60} exhibits a relatively uniform distribution of electron density, consistent with previous reports by Alipour [42]. Encapsulation leads to noticeable changes in the frontier molecular orbitals, and the extent of these changes depends on the nature of the heteroatom. For $C_{60}B$ and $C_{60}P$, the HOMO and LUMO densities remain largely delocalized across the fullerene cage, indicating relatively weak interaction between the encapsulated atom and the carbon framework. This behaviour is consistent with the physisorption-like character observed for these systems. In contrast, $C_{60}N$ exhibits pronounced localization of the frontier orbitals around the nitrogen atom. The localized electron density suggests stronger orbital coupling and partial charge localization, supporting the stronger interaction observed for this system. This behaviour is consistent with its chemisorption-like character [43]. The most significant redistribution of frontier orbital density is observed for $C_{60}Si$. The HOMO becomes largely delocalized across the central region of the fullerene framework while remaining partially localized at the opposite ends of the cage. The LUMO shows reduced density around the silicon atom and increased delocalization elsewhere in the structure. These changes indicate substantial modification of the electronic structure and enhanced charge polarization following encapsulation. Overall, the frontier molecular orbital analysis demonstrates that heteroatom encapsulation produces distinct electronic responses depending on the nature of the encapsulated atom, resulting in system-dependent modifications of the electronic properties of C_{60} .

3.3.4. Electronic reactivity descriptors

The electronic behaviour of the investigated systems was analysed using chemical hardness (η), chemical potential (μ), electrophilicity index (ω), charge distribution, and dipole moment.

Compared with pristine C_{60} , all encapsulated systems exhibit lower chemical hardness values, indicating an increased tendency to respond to electronic perturbations. Among the investigated structures, $C_{60}N$ shows the lowest hardness value and therefore the highest reactivity, whereas $C_{60}B$ and $C_{60}Si$ retain comparatively higher hardness values, suggesting greater stability. This trend is consistent with the HOMO-LUMO gap analysis discussed previously [44].

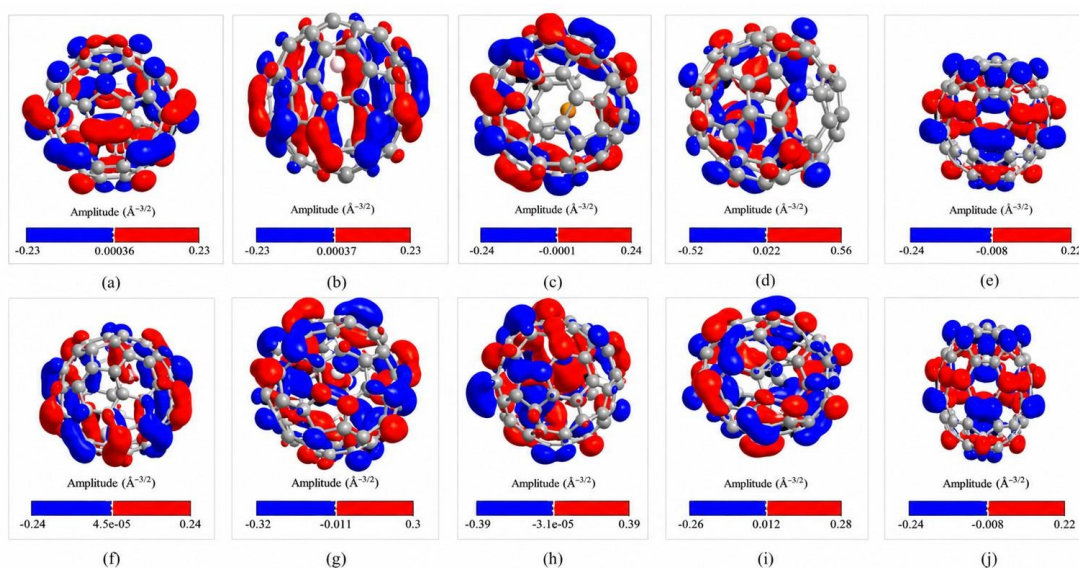


Figure 4. Homo orbitals for (a) C₆₀, (b) BC₆₀, (c) PC₆₀, (d) NC₆₀, and (e) SiC₆₀ and LUMO orbitals for (f) C₆₀, (g) BC₆₀, (h) PC₆₀, (i) NC₆₀, and (j) SiC₆₀.

The introduction of encapsulated atoms also affects the chemical potential of the fullerene cage [45]. The calculated values indicate a decrease in chemical potential relative to pristine C₆₀, reflecting modifications in the electronic environment of the system. Based on the calculated values, the reactivity trend follows:

$$C_{60} < C_{60}N < C_{60}Si < C_{60}B < C_{60}P.$$

The electrophilicity index further highlights the influence of encapsulation on the electron-accepting ability of the fullerene systems. Among the investigated structures, C₆₀N exhibits the highest electrophilicity value, indicating the strongest tendency to accept electrons, whereas C₆₀B shows the lowest value [46]. The behaviour of C₆₀P differs from the remaining systems because its energetically less favourable configuration affects the relationship between chemical potential and hardness.

Charge-transfer characteristics were evaluated using Mulliken population analysis. The calculated partial charges indicate donor-acceptor interactions between the encapsulated atoms and the fullerene cage. Although Mulliken charges are sensitive to the population scheme employed, they provide useful qualitative information regarding charge redistribution within the investigated systems.

Dipole moment analysis provides additional insight into the polarity of the encapsulated fullerene structures. Higher dipole moments generally correspond to greater polarization and improved interaction with polar environments. Among the studied systems, C₆₀Si exhibits the highest dipole moment value, indicating enhanced polarity and potentially improved compatibility with aqueous media. In contrast, C₆₀P shows the lowest dipole moment value. The higher polarity observed for C₆₀Si is consistent with its favourable solvation behaviour and supports its suitability as a potential nanocarrier [47].

A general correlation is observed between dipole moment and chemical potential. Small deviations from this trend, particularly for C₆₀N and C₆₀P, can be attributed to differences in their electronic structures and density-of-states distributions. These variations influence the relative contributions of frontier orbitals and ultimately affect the polarization behaviour of the systems.

3.4. Solvation energy

To evaluate the influence of the solvent environment, implicit solvation calculations were performed using the COSMO model. The calculated solvation energies (kcal/mol) are -4.15 for C_{60} , -4.53 for $C_{60}B$, -4.60 for $C_{60}N$, -4.80 for $C_{60}P$, and -4.97 for $C_{60}Si$. The negative solvation energies obtained for all systems indicate favourable stabilization in aqueous media. The encapsulated fullerene systems exhibit more negative solvation energies than pristine C_{60} , suggesting stronger interactions with the solvent. Among the investigated structures, $C_{60}Si$ shows the most favourable solvation energy, indicating the highest degree of stabilization in the aqueous environment. This behaviour can be attributed to the increased polarization and charge redistribution induced by the encapsulated silicon atom. The improved solvation characteristics observed after encapsulation are particularly relevant for drug-delivery applications, where dispersion and stability in aqueous environments are important considerations. The results indicate that encapsulation enhances the solvent compatibility of C_{60} , with $C_{60}Si$ displaying the most favourable solvation behaviour among the investigated systems.

3.5. Phonon band structure

The vibrational properties of the optimized structures were examined through phonon dispersion calculations to evaluate their dynamic stability. Among the investigated systems, $C_{60}Si$ was selected for further analysis because it exhibited the most favourable combination of interaction strength, polarity, and solvation behaviour. Phonon calculations were performed using the TorchX_MACE_MP_0_L0_2023 machine-learned potential, which provides an accurate description of atomic forces and vibrational properties in complex systems. The calculated phonon dispersion spectrum for $C_{60}Si$ is presented in Figure 5. No imaginary frequency modes were observed throughout the sampled Brillouin zone, indicating that the optimized $C_{60}Si$ structure is dynamically stable. In addition, the vibrational modes remain well defined after encapsulation, with no evidence of structural instability or lattice distortion. These results confirm that the Si-encapsulated fullerene retains its mechanical stability following optimization and supports the feasibility of the proposed nanocarrier configuration.



Figure 5. Phonon band structure for $C_{60}Si$.

3.6. Drug interaction study

To evaluate the practical applicability of the proposed nanocarrier, an explicit drug–carrier interaction study was performed using temozolomide (TMZ) as a model anticancer drug. Based on the structural, electronic, and solvation analyses, C₆₀Si was identified as the most promising nanocarrier candidate because of its favourable balance of stability, polarity, and solvent compatibility. Therefore, the interaction between C₆₀Si and TMZ was investigated to assess its suitability for drug-delivery applications.

The TMZ molecule was initially positioned at a distance of 3.0 Å from the surface of the nanocarrier. Following structural optimization, the separation decreased to 2.7 Å, indicating the formation of a stable interaction between the drug and the nanocarrier. The calculated binding energy of −0.5438 eV further confirms a favourable association between C₆₀Si and TMZ without causing significant structural distortion to either component. The moderate binding strength is advantageous for drug-delivery systems because it enables efficient drug loading while still allowing controlled release at the target site.

Mulliken population analysis revealed only a small degree of charge redistribution between C₆₀Si (−0.056 e) and TMZ (−0.059 e). The small charge difference suggests weak electronic coupling and the absence of covalent bond formation, which is beneficial for reversible drug adsorption and release.

To evaluate the behaviour of the complex in a biological environment, COSMO solvation calculations were performed. The calculated solvation energy of the C₆₀Si-TMZ complex is −13.50 kcal/mol, which is considerably more negative than that of the isolated C₆₀Si nanocarrier (−3.90 kcal/mol) (As shown in Figure 6). This enhanced stabilization suggests improved compatibility with aqueous physiological environments and favourable dispersion characteristics.

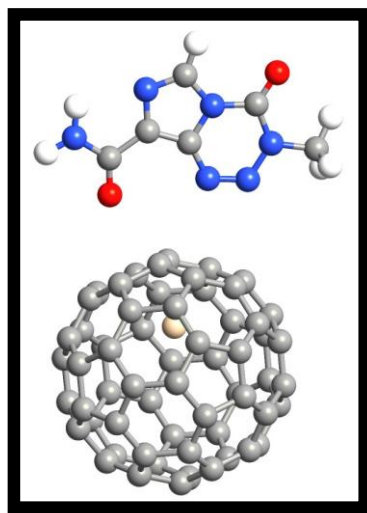


Figure 6. Optimized structure of C₆₀Si–TMZ.

Overall, the combination of moderate binding energy, favorable charge redistribution, and enhanced solvation behavior indicates that the C₆₀Si nanostructure exhibits strong potential as an

efficient nanocarrier for temozolomide. These findings support the suitability of the encapsulated C₆₀Si system for targeted drug delivery applications and provide a more realistic validation of its biomedical relevance.

The formula for recovery time (τ) is given by

$$\tau = (v_0)^{-1} \exp \left(- \frac{E_{B,E}}{k_B T} \right),$$

where v_0 represents the attempt frequency, taken as 10^{12} s^{-1} , $E_{B,E}$ is the binding energy, k_B is the Boltzmann constant, and T is the temperature (300 K). Using this relation, the recovery time of the C₆₀Si-TMZ complex was calculated to be 1.34 ms. This millisecond-scale recovery time indicates that the interaction between temozolomide and the C₆₀Si nanocarrier is sufficiently strong to ensure effective drug loading while still allowing rapid desorption under physiological conditions. Excessively long recovery times may hinder drug release, whereas extremely short recovery times may reduce drug retention. Therefore, the calculated recovery time suggests that C₆₀Si provides a favourable balance between interaction stability and drug-release capability, supporting its suitability as a nanocarrier for temozolomide delivery.

Density Functional Theory (DFT) calculations were employed to investigate fullerene C₆₀ as a potential nanocarrier through endohedral encapsulation of boron (B), silicon (Si), nitrogen (N), and phosphorus (P) atoms. Encapsulation significantly modified the structural and electronic properties of C₆₀ while preserving the integrity of the fullerene cage. Interaction energy calculations revealed favourable exothermic interactions for C₆₀B, C₆₀Si, and C₆₀N, whereas C₆₀P exhibited an energetically less favourable endothermic interaction. Analysis of the interaction characteristics indicated physisorption-like behaviour for C₆₀B, C₆₀Si, and C₆₀P, while C₆₀N displayed a stronger chemisorption-like interaction. Frontier molecular orbital analysis showed a reduction in the HOMO-LUMO energy gap for all encapsulated systems relative to pristine C₆₀, indicating enhanced electronic responsiveness and chemical reactivity. Among the investigated structures, C₆₀Si exhibited the most favourable combination of polarity, hardness, and hydrophilicity, as reflected by its dipole moment and charge-distribution characteristics. Drug-carrier interaction studies with temozolomide further supported the suitability of C₆₀Si as a nanocarrier, demonstrating favourable interaction energy, limited charge transfer, and enhanced solvation behaviour.

4. Conclusions

The present study provides computational insight into the influence of endohedral encapsulation on the structural and electronic properties of fullerene C₆₀ and explores its potential application as a nanocarrier for drug-delivery systems. Structural, electronic, and reactivity analyses were performed to evaluate the effect of different encapsulated atoms on the properties of the fullerene cage. The results demonstrate that endohedral encapsulation can effectively modify the electronic softness, charge distribution, and polarity of C₆₀ while preserving its structural integrity. Among the investigated systems, encapsulation of nitrogen, silicon, and boron produced favourable electronic modifications, whereas phosphorus resulted in an energetically less favourable configuration. C₆₀Si exhibited the most balanced combination of stability, polarity, charge redistribution, and solvation behaviour, indicating improved compatibility with biological environments and enhanced interaction capability with

therapeutic molecules. Further investigation using temozolomide as a model anticancer drug showed that the C₆₀Si-TMZ complex possesses favourable interaction energy, limited charge transfer, and enhanced solvation stability. These characteristics suggest that C₆₀Si is a promising candidate for efficient drug loading and controlled release applications. Overall, the structure–property relationships identified in this work provide useful guidance for the design of fullerene-based nanocarriers and establish a theoretical foundation for future studies involving drug loading, transport, release behaviour, and solvent interactions.

Author contributions

Samuel D: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **V.Abinaya:** Writing – review & editing, Validation, Formal analysis. **J.Sneha:** Visualization, Software, Methodology. **C.Poornimadevi:** Software, Formal analysis. **Bharath Shirpi Thasan. K.S:** Investigation, Data curation. **D. John Thiruvadigal:** Resources, Project administration. **R.M. Hariharan:** Validation, Supervision, Software, Project administration, Methodology. **K. Janani Sivasankar:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

Use of Generative-AI tools declaration

The authors declare they have used “Grammarly, Quilbot” to improve the language and grammar of the manuscript.

Data availability

The data that support the research findings of this study are not publicly available due to confidentiality of the information, data protection, and privacy, and they can be provided upon reasonable request through the proper channel.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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