Adsorption of a thione derivative on carbon, AlN, and BN nanotubes: a detailed DFT and MD investigation

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Received: 21 April 2022 / Accepted: 30 May 2022 / Published online: 6 June 2022 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

Abstract

The performance of nanotubes (NT) of carbon (CC), aluminium-nitrogen (AlN), and boron-nitrogen (BN) as a sensor and nanocarrier for mercaptopurine (MCP) was investigated by means of a theoretical approach. The calculated negative values of adsorption energy showed the interaction and adsorption of MCP. Highest-occupied molecular orbital (HOMO) and lowest-unoccupied molecular orbital (LUMO) distributions were only found on the NT counter portion of the drug-nanotube not on MCP for AlN-NT and BN-NT while HOMO is over MCP and LUMO is over NT for CC-NT. The polarizability of MCP-NTs is greater than that of MCP. Raman wavenumbers of MCP are enhanced in NTs, and hence, NTs can act as a sensor for the detection of MCP. Solvent dependency on adsorption behaviour is also presented in the manuscript, where we found that the AlN nanotube showed exceptionally high free energy of adsorption over other nanotubes in all solvent mediums. Solvation-free energies were also reported. Noncovalent interaction scattered plot also showed significant intermolecular interaction between AlN nanotubes and the mercaptopurine when compared to other nanotubes under study. To find the antiviral activity of MCP and MCP-NTs against antiviral activities, docking and molecular dynamics simulations were performed with 1HMP PDB. Recovery times show that MCP desorption occurs quickly. The MD simulations and docking results show that BN and CC-NTs with MCP show good activity as drug carriers.

Keywords DFT · MD simulations · Nanotubes · Adsorption · Mercaptopurine

Introduction

The invention of carbon nanotubes (CNT) in 1991 piqued researchers’ interest, prompting them to be the centre of attention in their efforts on organizing the novel materials [1]. Until far, the efforts have resulted in the improvement of a large quantity of data on the characterization of nanostructures [2–6]. Applications of CNT in living systems are a major priority for exploiting this unique material to improve human life quality [7]. The use of carbon nanotubes for drug delivery has been considered critical in light of the need for focused drug delivery techniques, according to the findings [8]. The covalent and noncovalent effects of the loading of different drugs on distinct nanostructures on the characteristics of each counterpart have been explored [9]. For this purpose, all in silico, in vitro, and in vivo approaches have been studied [10]. Indeed, nanostructures have been anticipated as the main system for pharmaceutical substances to convey them into biological systems, a function that must satisfy a slew of constraints [11]. As a result, getting precise and accurate information for this topic in biological systems has long been a high priority for researchers in related domains. In order to perform this, computer-based in silico research could very well yield useful information for the materials under investigation at the atomic level [12–15]. Previously noncovalent loading of pharmaceuticals at CNTs has been explored using computer-based studies, confirming the importance of nanostructures for drug delivery [16].

Nitrogen-containing heterocyclic molecules like purines and their analogs are the most frequent class that serves
critical roles in a wide range of biological processes [17]. The thiopurine derivative mercaptopurine (1,7-dihydro-6H-purine-6-thione) (MCP) is used for cancer treatment [18]. DFT studies of nanotubes with drugs are reported in the literature [19, 20]. MCP, like most anticancer medicines, has a high cytotoxicity and can cause the life-threatening side effects if not dosed properly. The situation is made worse by poorly predictable pharmacokinetic variability, which makes standardizing the administration protocol challenging. Excessive MCP consumption can also result in negative effects such as lack of appetite, vomiting, and liver damage [21, 22]. As a result, it is critical to create a sensitive, accurate, easy, and quick response technology for detecting MCP in human plasma and biological fluids. Some techniques have been used to detect the MCP drug in biological samples [23, 24]. Nanosensors are promising alternatives to these established approaches in this context [25–27]. The goal of this study is to get a basic understanding of how the MCP drug affects electronic characteristics of the nanotubes. In the present work, the interaction of mercaptopurine (MCP) with nanotubes is reported. To achieve optimum geometries for the explored model and the accompanying descriptors, quantum chemical computations were used.

The main purpose of this research was to investigate the possibility of loading MCP onto carbon nanotubes (CC-NT), aluminium-nitrogen nanotubes (AlN-NT), and boron-nitrogen nanotubes (BN-NT) and to evaluate various properties using computer modeling (Fig. 1).

Methods

Representative models of nanotubes (carbon: CC-NT, 50 atoms; aluminium-nitrogen: AlN-NT, Al 20, N 20 atom; and boron-nitrogen: BN-NT, B25, N 25 atoms) of MCP were chosen to provide a nanostructure for MCP (Fig. 1). Each geometry was first optimized, and frequency calculations were used to confirm the local minima. The model of the loaded drug at the nanotube was obtained for further exploration by doing such optimizations. Furthermore, various chemical parameters are analysed in order to better describe electrical attributes for the studied models. The CAM-B3LYP/6–311 + + G(d) basis implemented in the Gaussian 16 program with Gaussview 6.1 was used to do computations using the DFT technique [28, 29]. We estimated the drug’s solvated structures in addition to gas-phase computations. For solvent effect, PCM was utilized [30]. The solvation energies are also determined in different solvents, with low to high dielectric constants of 2.38, 8.93, 32.70, and 80.40. Multiwfn software was used to perform noncovalent interaction (NCI) and electron localized function (ELF) analysis [31].

For MD simulation, a system was formed to include protein alone (apo) and protein-MCP complex and nanotubes (AlN, BN, and CC) with solvent by system builder from Desmond 2019 [32]. MD tool of Desmond program was used for simulation (100 ns), and root-mean-square deviation (RMSD), root-mean-square fluctuation (RMSF), and H-bond data were analysed [33, 34].

![Optimized geometries of (a) mercaptopurine (MCP), (b) MCP-CC-NT, (c) MCP-AlN-NT, and (d) MCP-BN-NT](image-url)
Results and discussion

Solvation effects and adsorption studies

In order to get solvation-free energies (SFE), PCM model was used in toluene, dichloromethane, methanol, and water [35]. SFE shows us how much a molecule prefers one phase over another, but can provide insight into how solvent behaves in different environments. SFE is used to calculate the free energy changes in a molecule from an ideal gas to a solvent environment and is useful for determining features like activity coefficients and solubilities [36]. The SFEs were calculated in toluene, dichloromethane, methanol, and water for all NT systems with MCP (Table S1). In the case of all MCP-NT systems, in all solvents, the SFE is greater than that in a vacuum with a maximum value for water and a minimum value for toluene. The SFEs are maximum in MCP-AlN-NT systems and minimum for MCP-CC-NT systems. All the SFEs are increasing with an increase in the dielectric constant of the solvent. Despite the fact that all of the values obtained were negative, a comparison of the predicted SFE values suggests that water and ethanol may be preferable for MCP solubilization. The SFE in water and ethanol implies high solubility in an aqueous medium, a feature that supports MCP solubilization. The SFE shows us how much a molecule prefers one phase over another, but can provide insight into how solvent behaves in different environments. SFE is used to calculate the free energy changes in a molecule from an ideal gas to a solvent environment and is useful for determining features like activity coefficients and solubilities [36]. The SFEs were calculated in toluene, dichloromethane, methanol, and water for all NT systems with MCP (Table S1). In the case of all MCP-NT systems, in all solvents, the SFE is greater than that in a vacuum with a maximum value for water and a minimum value for toluene. The SFEs are maximum in MCP-AlN-NT systems and minimum for MCP-CC-NT systems. All the SFEs are increasing with an increase in the dielectric constant of the solvent. Despite the fact that all of the values obtained were negative, a comparison of the predicted SFE values suggests that water and ethanol may be preferable for MCP solubilization. The SFE in water and ethanol implies high solubility in an aqueous medium, a feature that supports biological activity in the sense that bioorganic activities take place in water and ethanol.

In addition, the changes in thermochemical quantities are presented in Table 1. Accordingly, for MCP-AlN-NT, in all solvents, the changes are high in comparison with MCP-CC and MCP-BN systems. The changes in the entropy during the process for all solvents are negative. Besides, the changing of the free energy ($\Delta G$) with solvents indicated the process happens in spontaneously except for all solvents in AlN-NT systems. Namely, the $\Delta G$ quantities of MCP were calculated as $-5.98$, $-39.22$, and $-7.31$ kcal mol$^{-1}$, in vacuum for MCP-CC/AlN/BN-NT systems. Also, the lowest $\Delta S$ quantities of MCP with vacuum were calculated as $-25.42$ kcal mol$^{-1}$ for MCP-CC-NT. The binding energies in the gaseous phase are $-2.89$, $-27.50$, and $-5.04$ kcal mol$^{-1}$ for MCP-CC-NT, MCP-AlN-NT, and MCP-BN-NT systems, respectively. The values of binding energy approved the development of the MCP-NT complex, which was also approved by MEP [37, 38].

Chemical and electronic properties

The primary successes of this work were evaluated based on the acquired results in relation to the goal of this work, which was to load drugs on NT for drug delivery reasons. The charge distribution on the molecular system is shown in three dimensions on the MEP plots. Charge distribution may be used to discover out how molecules interact, and MEP shows the size and shape of the molecule. The MEP is usually viewed by mapping to perceive the relative polarity of a molecule [39]. The electron density is linked to the MEP map, which is a useful predictor for electrophilic and nucleophilic reactions as well as hydrogen bonding interactions [40]. The red region was shown to have electrophilic reactivity, whereas the blue region was found to have nucleophilic reactivity. MEP/ESP plots (Figs. 2 and 3) show the most reactive sites in the systems which are evident for biological activity. In pristine nanotubes, the electrophilic cites are at both ends for CC-NT, at the N atom edge of AlN-NT and at the B atom edge of BN-NT. The nucleophilic region is at the centre part of CC-NT, Al edge of AlN-NT, and at N atoms edge of BN-NT nanotubes.

| Systems           | $\Delta E$/kcal mol$^{-1}$ | $\Delta H$/kcal mol$^{-1}$ | $\Delta G$/kcal mol$^{-1}$ | $S$/cal mol K$^{-1}$ |
|-------------------|---------------------------|----------------------------|---------------------------|---------------------|
| MCP-CC-NT (vacuum)| $-2.55$                   | $-1.60$                    | $-5.98$                   | $-25.42$            |
| MCP-CC-NT (toluene)| $-1.91$                   | $-2.09$                    | $-10.49$                  | $-42.21$            |
| MCP-CC-NT (dichloromethane)| $-1.48$ | $-2.22$                    | $-12.49$                  | $-49.343$           |
| MCP-CC-NT (methanol)| $-1.42$                  | $-2.16$                    | $-12.55$                  | $-49.331$           |
| MCP-CC-NT (water)   | $-1.42$                   | $-2.16$                    | $-12.56$                  | $-49.371$           |
| MCP-AlN-NT (vacuum) | $-27.13$                  | $-26.72$                   | $-39.22$                  | $-41.934$           |
| MCP-AlN-NT (toluene)| $-20.65$                  | $-36.84$                   | $-49.55$                  | $-40.876$           |
| MCP-AlN-NT (dichloromethane)| $-47.21$ | $-47.18$                   | $-58.14$                  | $-47.082$           |
| MCP-AlN-NT (methanol)| $-26.26$                  | $-51.10$                   | $-62.23$                  | $-46.526$           |
| MCP-AlN-NT (water)   | $-52.20$                  | $-52.15$                   | $-63.28$                  | $-46.514$           |
| MCP-BN-NT (vacuum)   | $-4.84$                   | $-4.25$                    | $-7.31$                   | $-38.788$           |
| MCP-BN-NT (toluene) | $-7.59$                   | $-7.53$                    | $-6.29$                   | $-46.273$           |
| MCP-BN-NT (dichloromethane)| $-10.16$ | $-10.06$                   | $-3.52$                   | $-45.543$           |
| MCP-BN-NT (methanol)| $-11.12$                  | $-11.01$                   | $-2.48$                   | $-45.505$           |
| MCP-BN-NT (water)     | $-11.36$                  | $-11.25$                   | $-2.21$                   | $-45.144$           |
Fig. 2  MEP and ESP plots. (a) CC-NT, (b) AlN-NT, (c) BN-NT

Fig. 3  MEP and ESP plots of (a) mercaptopurine (MCP), (b) MCP-CC-NT, (c) MCP-AlN-NT, and (d) MCP-BN-NT
In MCP, S atom and the neighbouring N atom in the pyrimidine ring are electrophilic while the H atoms are nucleophilic sites. Potential varies in all MCP-NT systems due to the adsorption of MCP on NTs (Fig. 3).

Fig. 4 HOMO–LUMO plots. (a) CC-NT, (b) AlN-NT, (c) BN-NT

Fig. 5 HOMO–LUMO plots of (a) mercaptopurine (MCP), (b) MCP-CC-NT, (c) MCP-AlN-NT, and (d) MCP-BN-NT
Highest-occupied molecular orbital (HOMO) and lowest-unoccupied molecular orbital (LUMO) distribution patterns were presented in Fig. 4 (individual NTs) and Fig. 5 (MCP and MCP@NT systems). In CC-NT, FMOs are over the entire system with interchange in polarity, while in AlN-NT, HOMO is at the Al atoms on the edge side, LUMO is over Al and N atoms near to N edge of the tube and in the BN-NT tube, and HOMO and LUMO are over the edge with interchange in polarity (Fig. 4). Surprisingly, HOMO and LUMO distributions were only found on the NT counter portion of the MCP@NT combination and not on the drug counterpart for AlN-NT and BN-NT while HOMO is over MCP and LUMO is over NT for MCP@CC-NT. This is a significant achievement that demonstrates the critical role of NT in the precise transport of MCP. It means that putting a drug at the NT causes the drug to lose its reactivity since the HOMO and LUMO distributions are only localized at the NT. The continuous representation of the MEP surface for MCP@NT was used to approve the complex formation.

In this situation, NT might serve as both a carrier and a biosensor, identifying the specific position and delivering MCP. The resulting graphical findings revealed that single drug-other chemical reactions are possible, but that its reactivity was diminished when loaded at the NT counterpart. As a result, it is possible that the delivery of such a system might be done more precisely, minimizing unwanted effects [41, 42]. The results (Table 2) showed that the values of dipole moment for MCP@NT were greater than the dipole moment for single drug and NT equivalents. In the complex systems, the dipole moment values vary in the following order: 9.4788 > 8.7138 > 5.8607 Debye for AlN-NT, BN-NT, and CC-NT systems. The polarizability of all MCP clusters is greater than that of MCP which gives NLO activity [43, 44].

Levels of HOMO and LUMO detect the impacts of such perturbation to molecular orbital systems yielding different values in complex of MCP-NT. As a result of the influences of FMOs, energy gaps are changed (Table 3). Eg of MCP-NTs are less than that of MCP (3.0163 eV) with minimum value (0.4146 eV) for CC-NT-MCP and maximum value (1.0367 eV) for AlN-NT-MCP complexes. As a result, a novel situation has emerged for MCP-NT in comparison with each individual drug and NT revealing the significance of complex formation in determining the structural functions [45]. As a result, we can conclude that MCP-NTs aid in drug

| Table 2 | NLO properties | Dipole moment (Debye) | Polarizability (x 10^-23 esu) | First-order hyperpolarizability (x 10^-30 esu) | Second-order hyperpolarizability (x 10^-37 esu) |
|---------|----------------|-----------------------|-----------------------------|----------------------------------|----------------------------------|
| MCP     | 5.8209         | 1.4075                | 1.3933                      | 3.1560                           |
| CC-NT   | 1.3908         | 7.1310                | 8.7572                      | 36.9010                          |
| AlN-NT  | 7.1287         | 8.9264                | 69.0260                     | 20.7570                          |
| BN-NT   | 4.6813         | 4.9826                | 20.3880                     | 26.2240                          |
| MCP-CC-NT| 5.8607       | 8.7565                | 95.500                      | 63.171                           |
| MCP-AlN-NT| 9.4788       | 10.735                | 74.951                      | 78.415                           |
| MCP-BN-NT| 8.7138        | 6.7557                | 14.684                      | 60.347                           |

| Table 3 | Chemical descriptors (all in eV) | HOMO | LUMO | Energy gap | Hardness | Chemical potential | Electrophilicity index |
|---------|---------------------------------|------|------|------------|----------|-------------------|-----------------------|
| MCP     | −7.3951                        | −4.3788 | 3.0163 | 1.5082     | −5.8870   | 11.4893           |
| CC-NT   | −7.5511                        | −6.9875 | 0.5636 | 0.2818     | −7.2693   | 93.7593           |
| AlN-NT  | −6.1845                        | −5.1701 | 1.0144 | 0.5072     | −5.6773   | 31.7742           |
| BN-NT   | −7.7090                        | −6.7287 | 0.9803 | 0.4902     | −7.2189   | 53.1536           |
| MCP-CC-NT| −7.4006                      | −6.986 | 0.4146 | 0.2073     | −7.1933   | 124.8036          |
| MCP-AlN-NT| −6.1774                      | −5.1407 | 1.0367 | 0.5184     | −5.6591   | 30.8882           |
| MCP-BN-NT| −6.7315                      | −5.7274 | 1.0041 | 0.5021     | −6.2295   | 38.6437           |

| Table 4 | Mulliken charges (e) | MCP | MCP-CC-NT | MCP-AlN-NT | MCP-BN-NT |
|---------|---------------------|-----|-----------|------------|-----------|
| S1      | −0.2606              | −0.2627 | −0.1051 | −0.0124 |
| N2      | −0.6382              | −0.6398 | −0.7074 | −0.6912 |
| N3      | −0.6609              | −0.6617 | −0.6481 | −0.6521 |
| N4      | −0.4862              | −0.4835 | −0.4854 | −0.4837 |
| N5      | −0.4189              | −0.4400 | −0.4207 | −0.4245 |
| C6      | 0.2808               | 0.2787 | 0.3108   | 0.2873   |
| C7      | 0.4799               | 0.4826 | 0.4889   | 0.4929   |
| C8      | 0.1445               | 0.1515 | 0.1099   | 0.1206   |
| C9      | 0.2400               | 0.2421 | 0.2426   | 0.2432   |
| C10     | 0.2389               | 0.2518 | 0.2455   | 0.2451   |
delivery. It is worth noting that molecular size research could provide information while avoiding the impacts of external interferers, allowing for the identification and characterization of pure materials. The electrophilicity indices of all MCP-NTs are higher than that of MCP (11.4893 eV), and MCP-NT was considered a stable complex preferable for research in drug delivery [46].

The charge distribution of MCP-NT is analysed using Mulliken charge values (Table 4) [47]. In MCP-CC-NT, MCP is interacted near the NT, through the C8, S1, N5, C6, and C10 atoms near to NT. Charges of atoms of pristine MCP, –0.2606 (S1), –0.4189 (N5), 0.2808 (C6), 0.1445 (C8), and 0.2389 (C10) changes to –0.2627 (S1), –0.4400 (N5), 0.2787 (C6), 0.1515 (C8), and 0.2518 (C10) in the complex due to interaction. Also, distances of the MCP to NTs are 3.6822/2.4414/2.2747 for MCP, while the corresponding values for the complexes are 0.1099 (C8) in the complex due to interaction, and these deviations are high which means a strong interaction in this case. In MCP-AlN/BN-NT, MCP is interacted near the NT, through the S1, N2, C6, and C8 atoms near to NT. Charges of atoms of MCP in the complex become –0.1051 (S1), –0.6912 (N2), 0.2873(C6), and 0.1206 (C8) in the complex due to interaction. Also, distances of the MCP to NTs are 3.6822/2.4414/2.2747 for MCP-CC/AIN/BN-NTs which are suitable for hydrogen bonding [48, 49].

The TD-DFT gives UV absorption at 296.6 nm for MCP, while the corresponding values for the complexes are 1255.61 (MCP-CC-NT), and 725.96 (MCP-AlN-NT), and 791.17 and 398.41 for MCP-BN-NT (Fig. S1). In BN-NT, the doublet for the UV absorption and in all cases, there is a shift to a higher wavenumber with a maximum for the CC-NT system. In theoretical Raman spectra (Fig. S2) of MCP and MCP-complex, functional modes are enhanced and carbon atoms in NT.

The strength of an adsorption depends on interaction, which is one of the most important aspects of designing sensors. Accordingly, to the following equation, negative Eads values result in a shorter recovery time: $\tau = \nu_0^{-1}\exp (-Eads/kT)$ where $\nu_0$ is the attempt frequency and $T$ is the temperature. At 298.15 k, recovery time for the desorbed MCP from the nanocages is determined (Table 5) and the values demonstrate that MCP desorption occurs quickly.

## NCI

The NCI assay explains both noncovalent and nonbonded interactions between two molecules via hydrogen bonding [50–53]. The hydrogen interactions are stronger with high electronegative atoms, weak hydrogen interactions also called van der Waals interactions, and hydrogen repulsions or steric hindrance of bulky groups and aromatic ring or pi-system. NCI can be supported by a reduced density gradient (RDG) of molecules.

Figure 6a–c display the NCI and NCI-RDG graphs of MCP with AlN, BN, and CC NTs. The blue colour that ranges from –0.05 to –0.03 a.u. represents strong hydrogen attractions of MCP with AlN-NT that shows sulphur, aluminium, and hydrogen atoms attached with nitrogen and carbon in MCP and nitrogen and aluminium atoms in NT and all nitrogen atom cavity in NT; likewise, BN-NT shows sulphur atoms in MCP and nitrogen and boron atoms in NT, and hydrogen atoms in MCP and nitrogen atoms in NT; similarly, CC-NT shows intra-attractions between hydrogen and sulphur in MCP. The green colour that ranges from –0.02 to 0.01 a.u. represents weak hydrogen bond or van der Waals interactions of MCP with AlN-NT that shows hydrogen atoms attached with carbon and nitrogen and carbon atoms in MCP and nitrogen atoms in the cube, sulphur, aluminium, and nitrogen atoms in NT and all intra-interaction of aluminium and nitrogen atoms (inner NT); alike, BN-NT shows hydrogen atoms attached with nitrogen and carbon atoms and boron atoms in NT and all intra-interaction of boron and nitrogen atoms (inner NT), like CC-NT that shows nitrogen and sulphur atoms in MCP and carbon atoms in NT. The red colour that ranges from 0.02 to 0.05 a.u. represents hydrogen repulsion or steric interactions and pi-system of MCP with AlN-NT that shows pi-system of MCP, sulphur in MCP and aluminium atoms in NT, and all-aluminium cavities in NT; similarly, BN-NT shows pi-system of MCP, sulphur in MCP, and boron atoms in NT and all boron cavities in NT, like CC-NT, which shows pi-system of MEP, sulphur in MCP, and carbon atoms in NT.

The graph plotted energy against RDG of MCP with AlN-NT shows a greater density of strong hydrogen bond interactions than repulsive interactions; in opposite, BN-NT and CC-NT show a greater density of repulsion interactions than strong hydrogen bond interactions.

## ELF

ELF is the evidence of the nature of electrons in molecules, explained by the probability of electrons with localization or delocalization. The localized electrons are core and...
multiple-bonded electrons, and delocalized electrons are hydrogen bonds and lone pairs of electrons in the molecules [54–58]. Figure 7a–c show the ELF of MCP with AlN/BN/CC-NT. The colour from blue to red with the range from 0.00 to 1.00 shows the probability of electrons from localization to delocalization. The blue colour represents localized electrons of MCP with AlN-NT showing at all heavy atoms like Al, N, and C atoms’ (1s², 2s² of N and C and including 2p⁶ for Al) core electrons; like BN-NT, which shows at all heavy atoms like B, N, and C atoms’ (1s², 2s² of N and C) core electrons; and alike CC-NT that shows at all heavy atoms like N and C atoms’ (1s², 2s² of N and C) core electrons. The colour red represents delocalized electrons of all H, C, N, and S atoms, which mean hydrogen atoms can be localized with more electronegative elements, like nitrogen and sulphur atoms having lone pairs of electrons and carbon atoms having pi-electrons for the resonance of MCP with AlN/BN/CC-NT complexes.

Docking and MD simulations

To find the antiviral activity of MCP and MCP-NTs against cancer, docking studies were carried out with 1HMP PDB [59] using the Patchdock server (Table 6; Fig. S3) [60, 61]. The global energies are high for all complexes with a maximum value for MCP@CC (−70.38 kcal mol⁻¹). The atomic contact energy is high for the MCP@CC complex.
Fig. 7  a ELF plots of MCP-AlN-NT.  b ELF plots of MCP-BN-NT.  c ELF plots of MCP-CC-NT
The results show that BN and CC NTs with MCP show good activity as drug carriers.

RMSD is an essential term for finding the differences between the two conformations and a high value means deviation is more. RMSD (20 to 100 ns) for apo and its complex with MCP, AlN, BN, and CC NTs are in Fig. 8(a). It is seen that apo and complexes are equilibrated after 20 ns of time. The average RMSDs (20 to 100 ns) for apo and MCP complex proteins were 3.5 Å and 2.8 Å. These RMSD results give relative stability of apo and MCP-, AlN-, BN-,

![Figure 8](https://example.com/figure8.png)

**Fig. 8**  
(a) RMSD of backbone atoms of apo and its complex with NTs.  
(b) RMSF of c-alpha atoms of apo and its complexes with NTs.  
(c) Rg of backbone atoms of apo and its complexes with MCP and NTs
and CC-NT complexes. The amino acids associated in bringing the structural deviation are given by RMSF plots [62].

RMSF analysis determines which amino acids make more movements, giving destabilization of the protein in the presence and absence of the ligands. The RMSF results (0 to 100 ns) for apo and protein with MCP, AlN, BN, and CC NTs are in Fig. 8(b) [62].

The radius of gyration gives protein’s compactness and folding and unfolding of the protein were given by Rg values (0 to 100 ns) for apo and protein with MCP, AlN, BN, and CC. The average Rg from 0 to 100 ns for apo and MCP, AlN, BN, and CC NTs complexes were 21.5 Å, 22.1 Å, 21.4 Å, 22.5 Å, and 24.2 Å (Fig. 8(c)).

Solvent accessible surface area (SASA) influences protein’s compactness to study modulation of inhibitors on the protein, and SASA value variations were very negligible for all complexes (Fig. 9(a)) [63–65]. Hydrogen bond formation stabilizes the protein–ligand complexes. In this study, the hydrogen bonds in the docking are confirmed by simulation analysis (Fig. 9(b)). Figure 9(b) shows multiple contacts between the interacting residues and the ligand, with maximum contacts with water bridges. In the active site, combination of interactions significantly promotes a stable complex. The average value and standard deviation of RMSD, RMSF, RG, and SASA were calculated for the entire 100 ns of all the systems (Table 7). The findings indicated that there

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Table 7: The calculated parameters for all the systems were obtained after 0–100 ns MD simulations

| System    | Average RMSD (nm) | RMSD (STDV) | Average RMSF (nm) | RMSF (STDV) | Average Rg (nm) | Rg (STDV) | Average SASA (nm) | SASA (STDV) |
|-----------|------------------|-------------|------------------|-------------|----------------|-----------|-------------------|-------------|
| Apo       | 3.187            | 0.253       | 0.970            | 0.624       | 21.899         | 0.079     | 19,059.341        | 263.389     |
| MCP       | 3.156            | 0.214       | 1.002            | 0.684       | 21.847         | 0.063     | 18,534.489        | 252.392     |
| MCP-AlN   | 3.231            | 0.228       | 1.038            | 0.836       | 21.956         | 0.080     | 19,264.543        | 309.755     |
| MCP-BN    | 2.999            | 0.182       | 1.018            | 0.629       | 21.757         | 0.079     | 18,414.160        | 281.427     |
| MCP-CC    | 3.223            | 0.306       | 0.970            | 0.624       | 21.899         | 0.079     | 19,059.341        | 263.389     |
is not much difference in the system. Further experimental studies will be required to validate our findings.

Conclusions

In this manuscript, we presented the adsorption behaviour of MCP over AlN, BN, and CC nanotubes. It is found that the compound adsorbs well with all the three tubes under consideration. The binding energies in the gaseous phase are $-2.89 \text{ kcal mol}^{-1}$ for MCP-CC-NT, $-27.50 \text{ kcal mol}^{-1}$ for MCP-AlN-NT, and $-5.04 \text{ kcal mol}^{-1}$ MCP-BN-NT. Free energy values indicated that the free energy of adsorption is high when AlN nanotube is used, which may be attributed to the high polarity of the tube over CC and BN tubes. NCI-RDG scattered plot supports this with evidence of very high noncovalent interaction between the compound and AlN. The dipole moment of that cluster is high over the other two. Also, it is found that in all three cases, the presence of solvents positively enhances the free energy of solvation compared to that of vacuum. Thus, it can be concluded that AlN clusters can effectively be found with mercaptopurine and hence can be used as better carriers of similar drugs to the target positions. To find the antiviral activity of MCP and MCP-NTs against cancer, docking and MD simulations were carried out with 1HMP PDB and the average RMSDs for apo and MCP complex proteins were 3.5 Å and 2.8 Å.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s00894-022-05179-8.

Acknowledgements

The authors express their gratitude to Princess Nourah Bint Abdulrahman University Researchers Supporting Project number (PNURSP2022R13), Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia.

Author contribution

Jamelah S. Al-Otaibi: software, supervision, manuscript preparation, and data analysis.

Muhammad Shabeer: manuscript preparation, conceiving the problem, and data analysis and correction.

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Funding

Funding was received from Princess Nourah Bint Abdulrahman University Researchers Supporting Project number (PNURSP2022R13), Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia.

Data availability

The supplementary information files include additional materials.

Code availability

No new codes have been created. Existing codes were utilized and quoted correctly.

Declarations

Conflict of interest

The authors declare no competing interests.

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