Simulation of pyrazinamide drug functionalized carbon nanotube and graphene with pncA protein

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ABSTRACT We have performed molecular dynamics (MD) simulations investigating the possibility of drug delivery of pyrazinamide (PZA) onto the binding site of pncA protein facilitated in presence of the nanomaterials. MD simulations provide insight into the nature of interaction of functionalized single–wall carbon nanotube (SWCNT)/PZA and graphene/PZA systems with the protein. The presence of nanotube/graphene support does not bring about any major structural deformation in the pncA nor does it form covalent bonds with the protein residues. Dynamics studies show that the presence of nanotube/graphene support facilitates in the stabilization of PZA drug making the movement of the drug less random and orienting it basically around the entering cavity of pncA following a lock and key type mechanism. The interaction of graphene with the amino acid residues is more flexible compared to SWCNT as observed from the simulation snapshots suggesting better ease in interaction using graphene based nanomaterials and the interaction between ligand and receptor is mainly hydrophobic in nature.
3.1 Introduction

Carbon nanotubes (CNTs) with its intrinsic electronic properties have paved way in almost all the forefront research areas including chemical and biological application.\(^1\)\(^-\)\(^3\) The hollow intrinsic cavity of CNT facilitates in the encapsulation of fullerenes,\(^4\) metallofullerenes,\(^5\) organic molecules,\(^6\)\(^,\)\(^7\) gases,\(^8\) peptides,\(^9\) DNA oligonucleotides\(^10\) and proteins\(^11\) along with the possibility of the outer sidewall functionalization for co-tethering functional moieties using suitable functionalization schemes. Experimental studies have shown that functionalized nanotubes are better biocompatible and nontoxic at the cellular level\(^12\)\(^-\)\(^14\) for administration providing the added capability of transporting cargos across the cell membranes via endocytosis.\(^15\)\(^-\)\(^17\)

Yeh and Hummer studied the electrophoretic transport of single-stranded Ribonucleic acid (RNA) through CNT channels using molecular dynamics (MD) simulation and showed that the transportation of RNA into the nanotube pores is controlled by the conformational dynamics and the exit of RNA strands from the tube is governed by hydrophobic attachment of RNA bases to the pores.\(^18\) In absence of electric field, RNA remains hydrophobically trapped in the membrane despite large entropic and energetic penalties and the translocation kinetics is dependent on the RNA sequence. Gao et al.\(^19\) performed the spontaneous insertion and encapsulation of DNA oligonucleotides onto CNT using MD simulation. The insertion mechanism is mainly governed by van der Waals (vdW) and hydrophobic interactions with the former playing the dominant role. Recently, studies on interaction of SWCNT with biomolecules\(^20\)\(^-\)\(^22\) have been underway to address the key issues on nanotoxicology and pharmacology.\(^23\)\(^-\)\(^25\) Research mainly focuses on the nanoparticle–protein corona formed during the adsorption of protein on the nanotubes.\(^26\) The experimental studies by Park et al.\(^27\) illustrate that CNTs of appropriate size are effective in blocking the ion channels of the cell membrane. Encapsulation of Collagen like peptides onto CNTs is facilitated by the tube dimension without drastically affecting peptide conformation. However, inherent difficulties are encountered in the course of understanding protein binding with nanomaterials especially from the point of view of interaction mechanism, aggregation property, size, shape and length of nanotubes which increases the complexity in the simulation of such systems.\(^28\)
Zuo et al.\textsuperscript{28} reported the plugging of proteins onto SWCNTs to form a stable complex finally poisoning the protein function by blocking the active sites. Size of the nanotube plays a governing role in the plugging mechanism with narrow diameter nanotubes better favoured compared to the large diameter tubes for protein interactions. Likewise, the interaction of CNTs with nano-1 amphiphilic peptides was investigated by Sansom and co-workers wherein they explored the influence of amphiphilic peptide helix termed (nano-1)/CNT ratio on CNT adsorption and the stability of $\alpha$-helix using MD simulations.\textsuperscript{29} Similar studies have been carried out by Trzaskowski \textit{et al.}\textsuperscript{30} demonstrating the encapsulation of peptides onto CNTs wherein the presence of nanotube renders stability to peptide structures. Shen \textit{et al.} performed MD simulation on the adsorption of human serum albumin onto CNTs which showed that the proteins adsorb in a stepwise manner exhibiting strong affinity to bind with the nanotube sidewall mediated by the $\pi$ stacking interactions.\textsuperscript{31}

To elucidate the means of PZA drug delivery mediated by CNTs and graphene onto active site of pncA protein, we carried out MD simulations on PZA functionalized SWCNT/graphene with wild type \textit{M. tuberculosis} pncA enzyme. The MD simulation helps in understanding the course of interaction of PZA, SWCNT/graphene, SWCNT/PZA and graphene/PZA complexes with pncA protein. In this Chapter we report a systematic study on the interaction of CNTs and graphene with pncA protein which is the target binding protein for PZA drug activation and binding. Tuberculosis (TB) chemotherapy poses major challenges with new drug resistant strains of \textit{Mycobacterium tuberculosis} resisting treatment of the disease.\textsuperscript{32} PZA (pyrazine-2-carboxamide) is one of the first-line drugs used in TB treatment recommended by the World Health Organization (WHO). PZA is metabolized into its active form (pyrazoic acid) by the amidase activity of \textit{M. tuberculosis} nicotinamidase/pyrazinamidase (MtPncA) encoded by the pncA gene.\textsuperscript{33-36} Mutation in PZAs\textit{e} coding gene (pncA) causes significant loss in PZAsc activity along with physiochemical alteration in the active metal binding (either iron or zinc).\textsuperscript{37,38} Nevertheless, administration of PZA in high dosage can cause minor to detrimental health problems and the antibiotic resistance of bacteria under prolonged exposure triggers the need for better drug delivery methods to directly bind with the TB bacteria. The role of graphene and CNTs is thus foreseen to get an insight to the nature of interaction with pncA protein.
3.2 Computational details

3.2.1 Simulation of PZA/(5,5) SWCNT with pncA protein

The MD simulation of PZA drug with pncA, (5,5) SWCNT with pncA and PZA/(5,5) CNT bound pncA protein were individually studied using GROMACS 4.0.4 simulation package with OPLSA force field.\textsuperscript{39} The starting geometries were centered in a cubic periodic box consisting of SPC216 water molecules.\textsuperscript{40} The distance between the complexes and the walls of the box was around 15 Å for all systems to minimize the inter-wall interactions. Before performing the MD simulation, energy minimization was performed using the conjugant gradient (CG) algorithm for all the three investigated systems for 1 ns at 298 K temperature and 1 bar pressure. In the modeling of the system, periodic boundary condition was assumed. The energy minimization was followed by a 20 ns MD simulation without any position restraints in the NVT ensemble at 298 K with a time step of 0.002 ps.

3.2.2 Simulation of PZA/graphene with pncA protein

Three set of systems were considered for the MD simulation: (1) protein with PZA, (2) protein with 6×6 graphene and (3) protein with PZA functionalized 6×6 graphene. Initially the graphitic nanomaterial and protein were well separated, within the distance of 20 Å (the distance between the active binding centre of protein and the graphitic nanomaterial surface). The combined systems were solvated by using TIP3P water model in a cubic periodic box, where the distance between the solute molecules and box boundary was around 15 Å. The distance criteria for long-range electrostatic interaction calculated by particle-mesh Ewald (PME) method and the vdW interaction were 1.2 and 10 Å, respectively. The energy minimization was performed for 1 ns at constant pressure (1 bar) and temperature (298 K) using the Berendsen coupling. The dynamics simulation run for 20 ns in an NVT ensemble at 298 K was then performed for all selected systems. The visualization for the simulation snapshots and analysis of the configurations was performed with the help of VMD\textsuperscript{41} and PyMOL\textsuperscript{42} packages.
3.3 Results and discussion

3.3.1 MD simulation of PZA/(5,5) SWCNT with pncA protein

Figure 3.1 depicts the snapshots at different time frames during the course of PZA drug simulation with pncA protein for 20 ns. At \( t = 0 \) ns, the PZA drug is well separated from the protein as observed in Figure 3.1a.

![Figure 3.1 Representative snapshots at various times for the interaction of PZA drug with pncA protein, (a) 0 ns, (b) 3 ns, (c) 8 ns, (d) 12 ns, (e) 15 ns and (f) 20 ns.](image)

During the course of the simulation from 3 ns onwards to 12 ns, PZA drug fluctuates within the vicinity of the protein showing no specific interactions with the amino acid residues. It is interesting to note that the drug molecule undergoes conformational changes to reach the functional site of pncA during the first 12 ns of simulation (Figure 3.1b–d). At 15 ns time frame, PZA shows affinity to bind and preferentially interact with the closely situated amino acids around the entering cavity of pncA (Figure 3.1e). It is observed that the drug molecule prefers to stays in close proximity to the functional site of protein. At 20 ns snapshot, PZA gets plugged with the pncA protein residues and undergoes interaction with the adjoining amino acid residues (Figures 3.1f and 3.2a).
Figure 3.2 (a) The representative snapshot of PZA (circled in red) with pncA protein at 20 ns simulation time, (b) the nearest interacting residues Val157, Asp158, Ala165, and Val169 in close proximity of PZA drug, (c) Root mean square deviation (RMSD) with respect to time (ps) of PZA, pncA protein and PZA–pncA protein combined. The inset picture illustrates zoom in of the RMSD up to 700 ps, (d) distance between the PZA drug and key residues of pncA as a function of time (ps), (e) the root mean square fluctuations (RMSF) of protein without the hydrogen atoms in PZA/pncA system.

The red circle in Figures 3.1f and 3.2a shows the interaction between PZA and protein residues. At 20 ns time step PZA drug exhibits interaction with Val157, Asp158, Ala165, and Val169 residues as described in Figure 3.2b. Although PZA does not enter into the binding pocket of pncA, under suitable physiological conditions, PZA molecule can bind with protein in a more effective manner. The amino acid residues along the entering pathway of pncA also play important roles during the process of drug trafficking and determine the course of interaction onto the active binding site. The root mean square deviation (RMSD) as a function of simulation time for PZA, pncA protein and PZA–pncA system is described in Figure 3.2c.
The average RMSD values of PZA and pncA are obtained around 0.015 and 0.035 nm, respectively. The RMSD for PZA remains almost uniform throughout the course of the simulation with no major fluctuations which suggests no major structural changes in PZA drug. The protein molecule also shows the similar behavior after the first 25 ps. The RMSD for PZA–pncA system is quite interesting, with significant fluctuations throughout the simulation time. At the initial time step from 0 to ~ 110 ps, the RMSD remains uniform at around 0.45 nm (Figure 3.2c inset) and then gradually increases. In the region from 2500 to ~ 4500 ps, the RMSD decreases to 0.1 nm and then increases. The RMSD plot advocate that PZA molecule keeps fluctuating till the first 15 ns simulation time and then gets stabilized towards the latter half of the simulation when it comes in closer contact with the pncA residues and makes interactions with the outer residues around the cavity.

To further elucidate the interaction of PZA with some of the functionally important amino acid residues (Val157, Asp158, Ala165, and Val169) of pncA, Figure 3.2d depicts the variation of distance between these amino acids and drug molecule, with respect to time (in ps time scale). As observed, the amino acid residues show a similar trend towards the interaction with PZA. During the first half of the simulation (0 to ~ 6000 ps), the fluctuation in the distance between selected residues and drug molecule is significant (~ 6.5 nm), and beyond 6000 ps (6 ns), the drug molecule comes closer to the residues Val157 and Asp158 residues compared to Ala165 and Val169. Further, the root mean square fluctuation (RMSF) of pncA protein in PZA/pncA system (Figure 3.2e) shows that, although fluctuations in RMSF of the protein backbone does not exhibit any deformation in the secondary structure (average value of 0.02 nm), we do observe significant variations (maximum of 0.07 nm) in atom number 200 and then around 0.065 to 0.063 for atoms around 650 and beyond 1280 which may be because of the interaction between some of the amino acid residues and PZA drug during the course of simulation.

Similar to the simulation of PZA drug with pncA, we investigated the interaction of pristine (5,5) SWCNT with pncA protein. Here, we considered only (5,5) SWCNT as the model nanotube system to understand the mode of interaction and binding as the diameter of (5,5) SWCNT is adequate enough to penetrate within the binding pocket of pncA. The
snapshots corresponding to MD simulation of (5,5) SWCNT (the dangling ends terminated by hydrogen atoms) with pncA protein is depicted in Figure 3.3.

![Representative snapshots at various times for the interaction of (5,5) SWCNT with pncA](image)

**Figure 3.3** Representative snapshots at various times for the interaction of (5,5) SWCNT with pncA, (a) 0 ns, (b) 2 ns, (c) 5 ns, (d) 10 ns, (e) 15 ns and (f) 20 ns.

It is observed that throughout the simulation time, the nanotube fluctuates around the entering cavity of pncA orienting randomly in the hollow region. We do not observe any major structural changes in the nanotube as well as in the protein. The nanotube stays close to the binding pocket of pncA and it is very much feasible to have noncovalent interactions between nanotube and the amino acid residues namely Thr167, Thr22, His137 and Ala20 lying in close proximity to the ligand binding site, as depicted in Figure 3.4a. To investigate the influence of interaction of SWCNT with pncA residues on the structural conformation of the protein as well as SWCNT, we calculated the RMSD for pncA, SWCNT and SWCNT–pncA system, shown in Figure 3.4b. The RMSD of (5,5) SWCNT shows no major change during the course of the simulation with a value of around 0.02 nm. The pncA on the other hand shows a gradual increase in the RMSD for first 25 ps, after which it attains a plateau
throughout the simulation time slightly below 0.05 nm. The RMSD for SWCNT–pncA system shows significant fluctuations during the course of the simulation.

Figure 3.4 (a) Selective amino acid residues namely Ala20, Thr22, His137, and Thr167 in close proximity to (5,5) SWCNT, (b) RMSD of (5,5) SWCNT, pncA protein and (5,5) SWCNT–pncA combined. The inset picture illustrates zoom in of the RMSD up to 500 ps, (c) distance between (5,5) SWCNT and key residues of pncA, (d) RMSF of pncA protein without the hydrogen atoms and ligand.

The interacting distance between SWCNT and the ligand binding residues Thr167, Thr22, His137 and Ala20 (Figure 3.4c) with respect to the simulation time shows that SWCNT preferentially interact with Thr167 and Ala20 residues of pncA at an average distance of 1.15 and 1.23 nm, respectively. Thr22 and His137 are in close contact with (5,5) SWCNT at an average distance of about 1.3 and 1.4 nm. Thus pristine (5,5) SWCNT exhibits strong noncovalent interactions with the selected amino acid residues. The RMSF for pncA protein remains more or less uniform around 0.021 nm with significant fluctuations in some of the protein atoms as observed from Figure 3.4d. This suggests that overall no structural
deformation in the protein conformation is observed and fluctuations in some the amino acids are accountable from the interaction with the nanotube sidewall and the edges.

We finally performed the MD simulation of pncA with PZA/(5,5) SWCNT system, the snapshots corresponding to the 20 ns simulation is described in Figure 3.5. At 0 ns simulation time, PZA drug remains stacked onto the sidewall of the nanotube (Figure 3.5a).

![Figure 3.5](image-url) Representative snapshots at various times for the interaction of PZA/(5,5) SWCNT with pncA protein, (a) 0 ns, (b) 2 ns, (c) 5 ns, (d) 9 ns, (e) 12 ns, (f) 16 ns (g) 18 ns and (h) 20 ns.

In the first 9 ns of simulation, the drug molecule remains intact with the nanotube and no significant interaction with protein was observed. At around 12 ns (Figure 3.5e), PZA drug tends to move away from the stacked conformation and interact with the adjacent residues around the binding cavity. The fluctuation in the position of PZA brings it closer to nanotube sidewall beyond 12 ns, and till the completion of the simulation at 20 ns, both the nanotube and PZA remains close to the protein. The snapshots at different time frames for PZA/SWCNT with pncA system indicates that the presence of nanotube support helps in stabilizing the haphazard movement of the drug around the protein by restricting its free
mobile motion, with PZA remaining close to the functional site of pncA rather than fluctuating randomly throughout the protein region (Figure 3.1).

Figure 3.6a shows a set of amino acids, which are close contact with drug molecule and (5,5) SWCNT during the course of MD simulation. The RMSD for perfect (5,5) SWCNT (0.02 nm) as well as for protein (~0.04 nm) remains uniform throughout the simulation as observed in Figure 3.6b.

![Image](image_url)

**Figure 3.6** (a) Selective amino acid residues namely Ala20, Thr61, Tyr64, Ser65, Trp68, Pro69, His137, Arg140, Ala165 and Asp166 in close proximity to PZA and (5,5) SWCNT, (b) RMSD of (5,5) SWCNT, pncA protein and PZA/SWCNT–pncA combined. The inset picture illustrates zoom in of the RMSD for 500 ps, (c) distance between PZA/(5,5) SWCNT and key residues of pncA, (d) RMSF of pncA protein without the hydrogen atoms and ligand.

For the combined PZA/SWCNT with pncA system, the RMSD somewhat remains uniform from 0 to 100 ps (Figure 3.6b inset) and then increases. The RMSD increases to 0.25 nm in the first 6000 ps but after that it becomes uniform (around 0.15 nm). Thus in the latter half of the simulation, the RMSD does not fluctuate much indicating no major changes or deformation in the structures. The variation of the distance between ligand binding residues
of pncA with PZA/SWCNT system is given in Figure 3.6c. It has been observed that the distance between Asp166 and drug molecule is 0.75 nm in the first 2.5 ns of simulation and after that it increases to ~1.35 nm. A similar trend is observed for all the selected amino acid residues at slightly different values of distance. The RMSF for protein (Figure 3.6d) follows a similar trend which has been observed for other simulations. It confirms that, during the simulation, the protein conformation has not been affected because of the interaction with ligand and nanotube.

3.3.2 MD simulation of PZA/graphene system with pncA protein

Figure 3.7 depicts the snapshots corresponding to the simulation of 6×6 graphene with pncA protein in absence of PZA drug.

![Representative snapshots at various times for the interaction of 6×6 graphene sheet with pncA protein](image)

**Figure 3.7** Representative snapshots at various times for the interaction of 6×6 graphene sheet with pncA protein, (a) 0 ns, (b) 2 ns, (c) 4 ns, (d) 9 ns, (e) 12 ns, (f) 15 ns, (g) 16 ns and (h) 20 ns.
Initially at 0 ns time frame, graphene sheet encloses the binding cavity of pncA (Figure 3.7a) well separated from the amino acid residues. At 2 ns time frame, graphene sheet reorients itself along the opening region with the sheet trying to move into the cavity of pncA (Figure 3.7b). From 2 ns onwards till 20 ns, graphene sheet displays strong tendency to enter the functional region within pncA and undergoes interactions with the amino acid residues in close proximity to the nanosheet. Although significant fluctuations is observed in the graphene structure with crumpling of the nanosheet at certain time frames, overall no major structural deformations both in pncA and graphene is observed. Thus graphene sheet exhibits strong tendency towards the interaction with pncA residues as observed from Figure 3.7.

The root mean square deviations (RMSD) of 6×6 graphene, pncA and pncA/6×6 graphene combined is shown in Figure 3.8a.

Figure 3.8 (a) The RMSD vs. time (ps) plot for 6×6 graphene, pncA and 6×6 graphene/pncA combined, (b) the interaction of graphene with some of the ligand binding residues of pncA.

As observed, RMSD of pncA remains uniform throughout the course of MD simulation at an average RMSD value of 0.045 nm. The RMSD for 6×6 graphene although fluctuates throughout the simulation time, the average RMSD is obtained around 0.06 nm. The changes in RMSD for graphene sheet can be accounted to the random swinging and crumpling of the nanosheet vividly observed from the snapshots in Figure 3.7. The RMSD for 6×6
graphene/pncA system combined is however interesting as observed from Figure 3.8a. At the initial simulation time from 0 to 2000 ps, RMSD deviates drastically reaching a maximum value of ~ 0.39 nm which can be accounted to the sudden flip in orientation of graphene sheet and influences the interaction with adjacent amino acid residues of pncA. From 2500 ps onwards, the RMSD remains mostly uniform at an average value of ~ 0.65 nm with fluctuations in certain time steps. Thus, overall RMSD of 6×6 graphene/pncA is more or less of similar fashion and a major contribution to the deviation in RMSD is from absorbed graphene sheet.

Figure 3.8b depicts the interaction of 6×6 graphene with some of the ligand binding residues of pncA. Here we sorted out Thr61, Asp63, Ser65, Tyr64, Trp68, Leu19, His137, Ala20 and Val163 as some of the interacting residues which may play a major role during the course of simulation and a comparison of the distances from the COM between 6×6 graphene and pncA is illustrated in Figure 3.9a.

Figure 3.9 (a) The distance between the COM of ligand binding residues of pncA with 6×6 graphene sheet, (b) RMSF of non H atoms of pncA with respect to the total number of protein atoms.

Ser65 and Asp63 demonstrate the strongest interactions with graphene at COM values of 0.045 and 0.075 nm. His137 is situated at the farthest distance from graphene sheet
suggesting weak interaction with ligand. Although the interaction is mainly noncovalent in nature, π–π stacking between the aromatic rings of graphene and amino acids along with H bonding is also quite possible as observed from the COM distance values. The RMSF of the non H atoms of pncA show fluctuations in most of the protein atoms although overall the RMSF is quite stable at around 0.020 to 0.025 nm (Figure 3.9b). The fluctuations may be accounted due to interaction of the adjoining amino acid residues of pncA in close proximity to graphene sheet.

The representative snapshot for simulation of PZA/6×6 graphene with pncA during the course of 20 ns time is given in Figure 3.10.

![Figure 3.10](image)

**Figure 3.10** Representative snapshots at various times for the interaction of PZA/6×6 graphene with pncA, (a) 0 ns, (b) 3 ns, (c) 6 ns, (d) 9 ns, (e) 12 ns, (f) 15 ns, (g) 18 ns and (h) 20 ns.

Compared to the simulation of PZA/pncA the presence of graphene somewhat stabilizes the random movement of PZA throughout the protein environment and restrains its motion mainly around the entering cavity of the protein. At 0 ns simulation time (Figure 3.10a) both
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Graphene and PZA drug remains well separated from the protein. From 3 to 6 ns, PZA drug reorients itself showing proximity towards interaction with adjoining amino acid residues (Figure 3.10b–c). We however, observe significant crumpling of graphene sheet throughout the simulation time, with both graphene and PZA exhibiting strong tendency to bind with pncA. At 15 and 18 ns time frames (Figure 3.10f–g) crumpling of graphene sheet is quite distinct although overall no major structural deformations in protein and ligand are observed.

The RMSD of ligand with pncA protein as described in Figure 3.11a predicts that pncA itself does not show any major structural changes with RMSD remaining uniform around 0.04 nm. The RMSD for graphene however fluctuates during the course of simulation and the average value is observed around 0.10 to 0.125 nm. For the combined system, RMSD although remains more or less stable at 0.125 nm, at around 4000 ps, and 18000 to 19500 ps time frames, RMSD drops down to 0.057 nm. Thus major contribution to RMSD is from the absorbed ligand rather than fluctuations from pncA protein.

**Figure 3.11** (a) The RMSD vs. time (ps) plot for 6×6 graphene/PZA, pncA and 6×6 graphene/PZA-pncA combined, (b) the interaction of PZA and graphene with some of the ligand binding residues of pncA.

Figure 3.11b illustrates the interaction of PZA/6×6 graphene with some of the ligand binding residues of pncA namely Asp63, Tyr64, Try68, Ser65, Tyr103, His137, Arg140,
Val163, and Thr167. The corresponding distance from the COM of pncA residues with the ligand is shown in Figure 3.12a. As observed from Figure 3.12a, Ser65, Tyr64 and Asp63 residues show the strongest interactions with the ligand at COM values of 0.5, 0.75 and 0.65 nm, respectively. Thus, these residues mainly influence the interactions although the other residues also play prominent role in ligand binding during the simulation time. The RMSF for non H atoms of pncA (Figure 3.12b) shows that overall, the fluctuations in the protein backbone is not very dramatic although some atoms show strong RMSF peaks which is basically accounted to the interaction with the ligand during the course of the simulation dynamics. The average RMSF value fluctuates around 0.02 to 0.025 nm for pncA throughout the simulation time.

Figure 3.12 (a) The distance between the COM of selected pncA residues with PZA drug and graphene, (b) RMSF of non H atoms of pncA with respect to the total number of protein atoms.

3.4 Conclusions

The MD simulations provide an understanding into the nature of interaction of functionalized SWCNT/PZA and graphene/PZA with pncA protein. The presence of nanotube support facilitates in the stabilization of PZA making the movement of the drug less random and orienting it basically around the entering cavity of pncA. During the course of simulation, graphene and PZA/graphene system remains close to the functional site of pncA and exhibit
significant interaction with the amino acid residues, which are close situated to the active site. The RMSD plots demonstrate the graphene sheet to be more dynamic compared to SWCNT towards interaction with the protein as observed from the dynamics snapshots at different time frames. Thus, SWCNTs along with graphene based nanomaterials can find application as suitable carrier payloads in PZA drug delivery, facilitating in controlled targeted release of PZA molecules and enhanced interaction with pncA.

References


[42] The PyMOL Molecular Graphics System, Version 1.5.0.4 Schrödinger, LLC.