Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Molecular dynamics simulation study of Boron-Nitride Nanotubes as a drug carrier: from encapsulation to releasing

1. Computational Details

1.1. MD simulation (Orientation of gemcitabine into BNNT)

In order to indicate the positions of drug atoms related to the BNNT, the distances between some selected atoms of drug (which were shown in Fig. S2) from the BNNT were calculated and listed in Table S1. The distances of the hexagonal ring atoms indicate that the ring positioned horizontally on the BNNT, almost in a parallel orientation related to the BNNT which is obvious in Fig. S3. Although the different distances between the atoms of the pentagonal ring and Fig. S3 illustrate that the ring is placed in nearly vertical configuration relative to the BNNT.

1.2. MD simulation (Interaction Energies of C60-C60, C48B12-C48B12, GMC-C60, GMC- C48B12)

The molecular dynamics simulation was performed in order to calculate the interaction of drug with C_{60} and $C_{48}B_{12}$ and the interaction of C_{60}-C_{60} and $C_{48}B_{12}$ - $C_{48}B_{12}$. We performed geometrical optimizations to obtain the energy minimization of initial configurations via conjugate gradient method. A NVT dynamics simulation in the periodic boundary conditions was performed for 5 ns at T = 298 K. The intra and intermolecular interactions within the systems were determined using Universal forcefield. The Andersen thermostat was used to maintain the simulation temperature. The cutoff distance for the nonbonded interactions, the van der Waals and electrostatic forces, was 12 Å. The obtained results from Table S3 showed that the

interaction of C_{60}- C_{60} and $C_{48}B_{12}$ - $C_{48}B_{12}$ was stronger than the interaction between drug and C_{60} and $C_{48}B_{12}$ and due to the strong interaction between $C_{48}B_{12}$- $C_{48}B_{12}$, the drug could only be expelled from BNNT.

2.1. DFT calculations

To present validation of the employed MD simulation, Density functional theory (DFT) was applied in Quantum ESPERESSO ["J.Phys.Condens.Matter, 2009, 21, 395502", "www.quantum-espresso.org"] to optimize the atomic structures. The generalized gradient approximation (GGA) within the Perdew Burke Ernzerhof (PBE) ["Phys. Rev. Lett. 1996, 77, 3865–3868"] was used to describe the exchange correlation energy. The $2 \times 2 \times 1$ Monkhorst-Pack grid was used for k-points sampling of the Brillouin zone with an energy cutoff of 310 eV. The periodic boundary condition was employed and height of the super cell (c) was tested and find to include enough vacuum buffer between the BNNT and the encapsulated molecules in the adjacent periodic box.

We investigated the effect of encapsulation of GMC, $C_{48}B_{12}$ and C_{60} on the work function (WF) of BNNT. The work functions were determined from the difference between the Fermi level and the vacuum level. The obtained results of the work function indicated that the WF value of BNNT+ GMC was very close to the work function of BNNT 5.30 (eV). In the presence of C_{60}, the (WF) of BNNT was increased but the changing of electronic properties of BNNT due to the presence of $C_{48}B_{12}$, caused to decrease the WF. Fig. S7. It can be suggested that the electrons can be transmitted more easily in the BNNT/$C_{48}B_{12}$ than the two others which can be caused to stronger interactions. The stronger interaction between BNNT and $C_{48}B_{12}$ than the others

(BNNT/GMC and BNNR/C_{60}) which was also observed in MD simulation results, plays as effective driving force for drug releasing.

The band structure for the encapsulated molecules into BNNT and pristine BNNT is shown in Fig. S8. In comparison with the pristine BNNT, the encapsulation of $C_{48}B_{12}$, C_{60} and GMC into the BNNT decreased the energy gap of the pristine BNNT, however the encapsulation of $C_{48}B_{12}$ had a strongest effect on the energy gap of the BNNT. According to the band structure, the band gap of BNNT considerably was changed in complex BNNT + $C_{48}B_{12}$ with the decrement of 4.19 Ev which can be indicated the more electron transmission and strong interaction in BNNT+$C_{48}B_{12}$ which is consistent with WF results. Consequently the results of WF and band structure which could validate our MD simulations confirm that the stronger interaction in BNNT/$C_{48}B_{12}$ can be an efficient role on releasing the drug from the BNNT.

In the following section, we considered the charge transfer for BNNT+ $C_{48}B_{12}$, BNNT+ C_{60} and BNNT+GMC (Table S2). Negative values of charge transfer revealed that the direction of charge transfer was from BNNT to $C_{48}B_{12}$ and C_{60} but in the case of BNNT+ GMC the direction of charge transfer was from GMC to BNNT. In addition, in order to understand the effect of the encapsulated molecules on the electronic properties of BNNT, the density of states (DOS) of BNNT, BNNT+ GMC, BNNT+ C_{60} and BNNT+ $C_{48}B_{12}$ were plotted near the Fermi energy level in Fig. S9.

Furthermore, based on the Quantum mechanical calculations, the dipole moment of GMC was shown as a green arrow Fig. S4. The direction of dipole moment arrow indicated that the negative pole of the drug molecule was located on the hexagonal ring side. Therefore, based on charge transfer (Table S2), which illustrated electron donating role of the drug in BNNT cavity, the electron transmission could implemented from this side of the molecule. On the other hand

the MD results showed that the drug came near the BNNT and wall from the Nitrogen atom and hexagonal ring (Fig. S3), which now the drug orientation in the cavity can be confirmed by the obtained Quantum results**.**

2. Supplementary Tables

Table S1. The distance between drug atoms from the BNNT in equilibrated system

Atoms	Distance (Å)
Atom 1	2.73
Atom 2	3.55
Atom 3	3.57
Atom 4	3.58
Atom 5	4.45
Atom 6	3.61
Atom 7	3.01
Atom 8	3.62
Atom 9	4.55
Atom 10	4.41

Table S2. The calculated charge transfer ΔQ (e), and the work function W (eV) of BNNT+ GMC, BNNT+ C_{60}, BNNT+ $C_{48}B_{12}$

Structure	ΔQ (e)	W (eV)
BNNT+GMC	+0.300	5.29
BNNT+ C_{60}	-0.237	5.33
BNNT+ $C_{48}B_{12}$	-0.442	5.08

Table S3. The interaction energy of GMC- C_{60}, GMC- $C_{48}B_{12}$ and C_{60}- C_{60} and $C_{48}B_{12}$ - $C_{48}B_{12}$

System	Interaction energy (kcal mol^{-1})
GMC-C_{60}	-10.3
GMC-$C_{48}B_{12}$	-8.9
C_{60}-C_{60}	-10.8
$C_{48}B_{12}$-$C_{48}B_{12}$	-13.6

3. Supplementary Figures

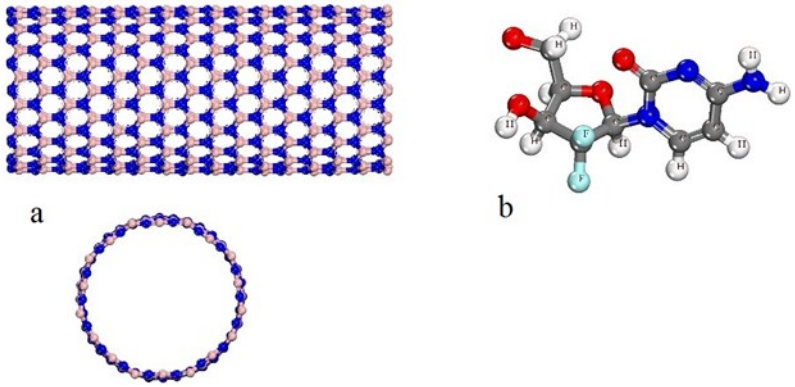

Fig. S1. (a) Initial structure of BNNT (18, 0). (b) The structure of gemcitabine (GMC)

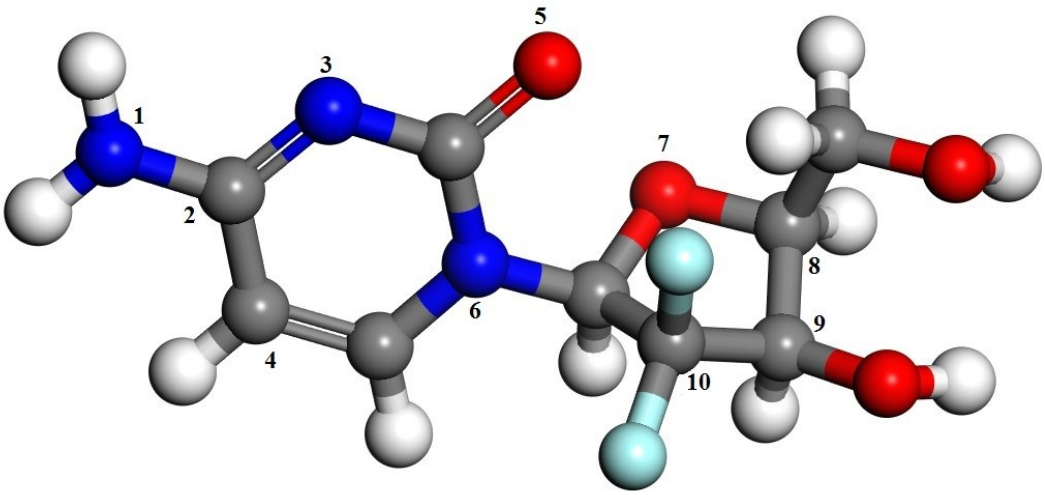

Fig. S2. The numbering of some selected atoms of the drug

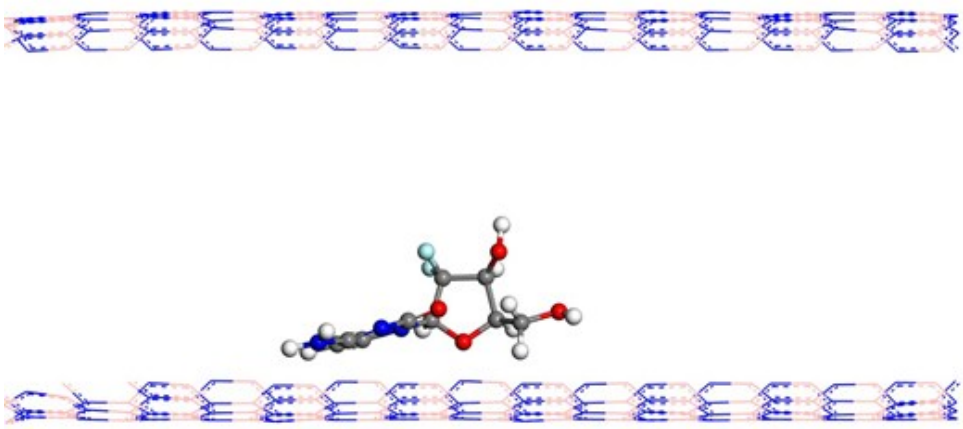

Fig. S3. The orientation of the drug in BNNT (for more clarification the water molecules and some front and back parts of BNNT wall were deleted).

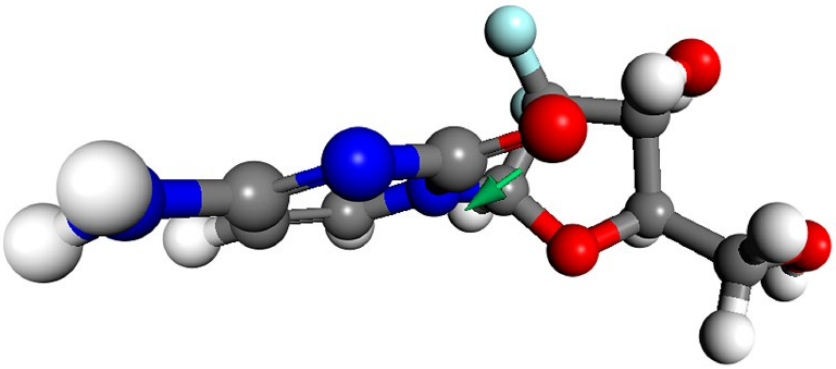

Fig. S4. The dipole moment of GMC was shown as a green arrow

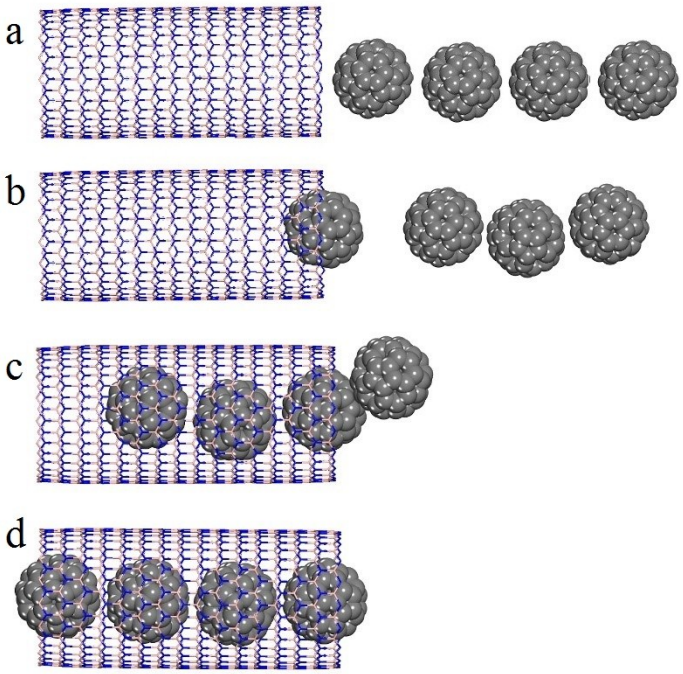

Fig. S5. (a) 0 ps, the initial structure of (BNNT+ C_{60}), (b) 45 ps C_{60} molecules approach the BNNT, (c) 4000 ps three C_{60} are inserted, and (d) 4030 ps fullerene molecules are fully inserted

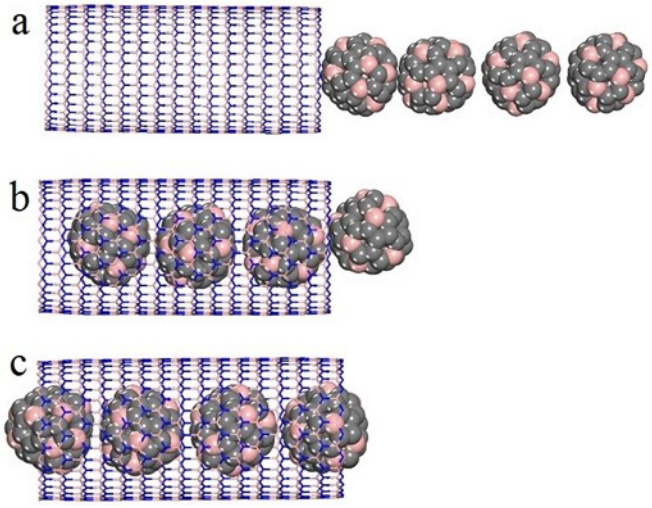

Fig. S6. (a) 0 ps, the initial structure of (BNNT+ $C_{48}B_{12}$), (b) 3500 ps three $C_{48}B_{12}$ molecules are inserted, and (d) 3800 ps fullerene molecules are fully inserted

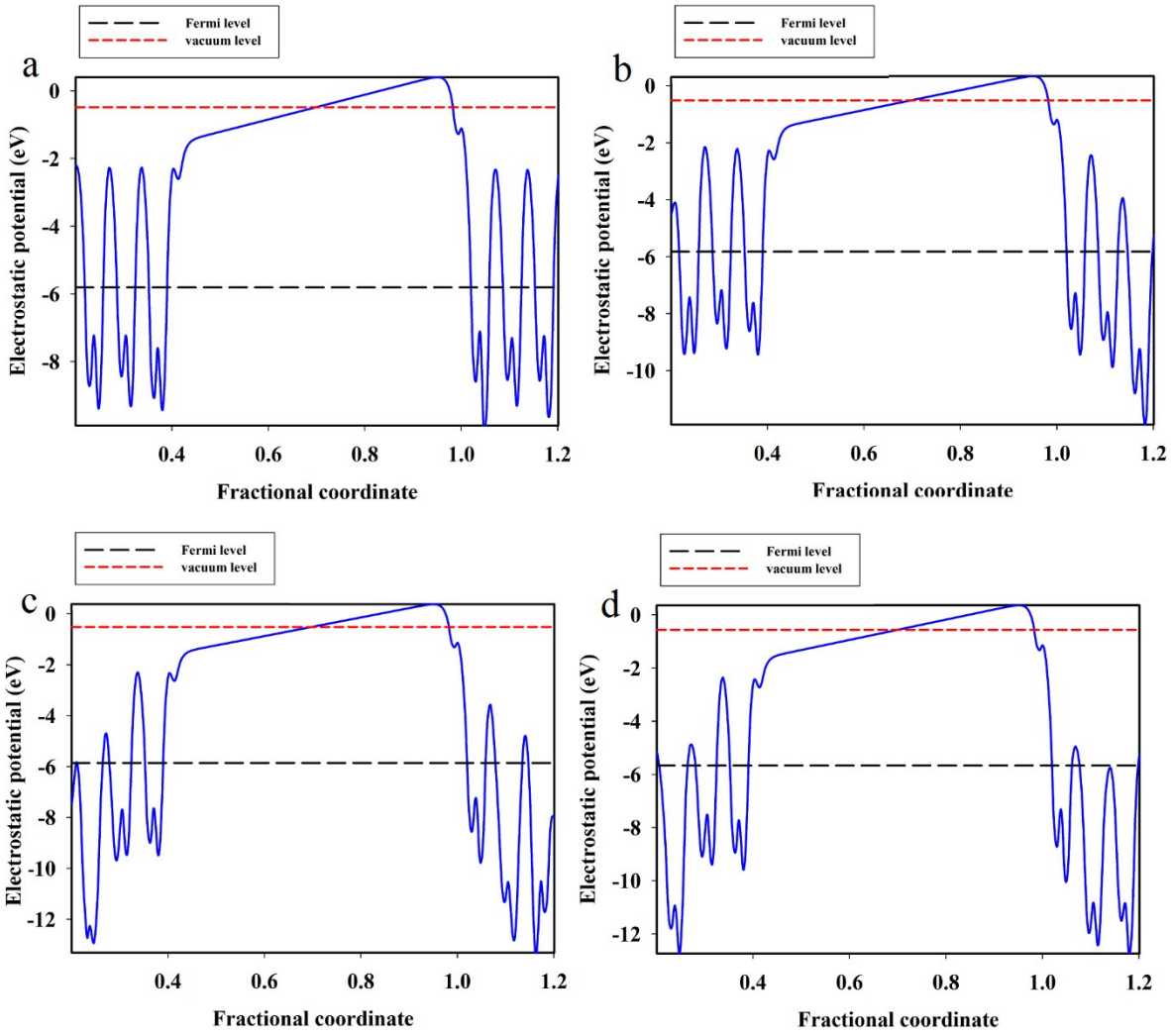

Fig. S7 Work function of (a) BNNT, (b) BNNT+GMC, (c) BNNT+C_{60}, (d) BNNT+$C_{48}B_{12}$

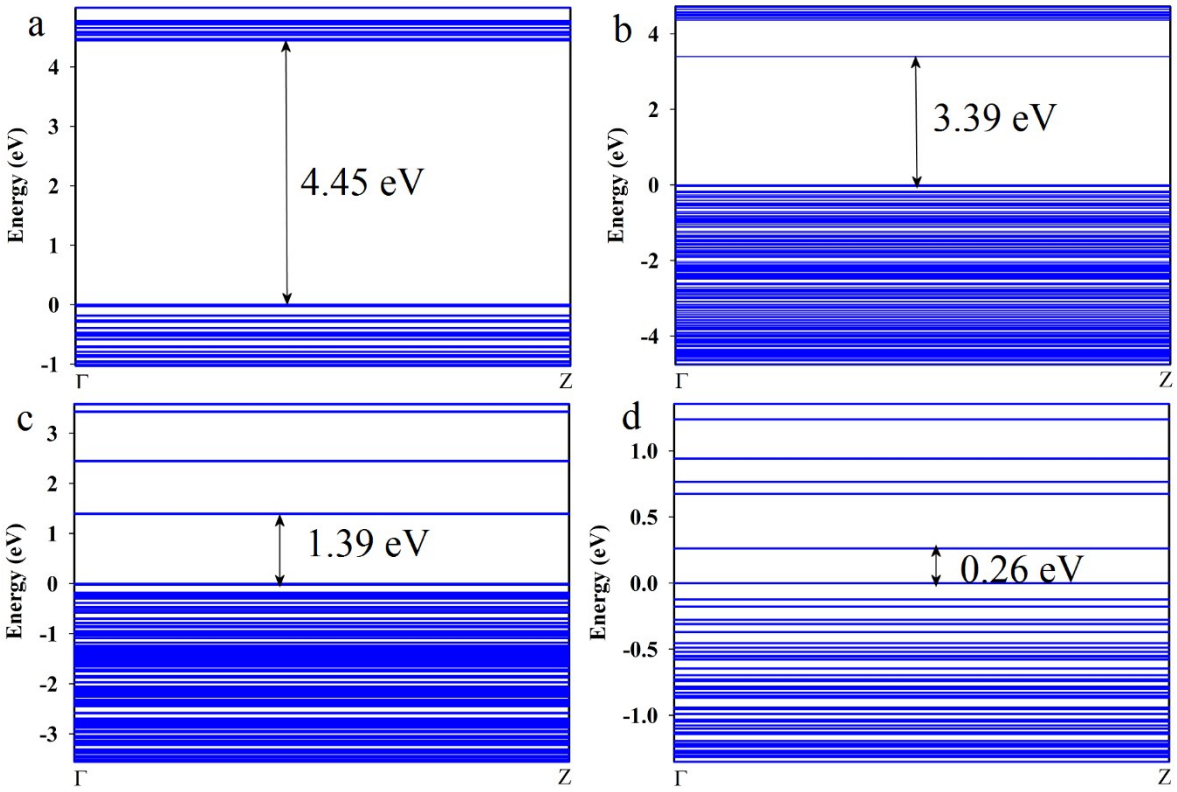

Fig. S8. Electronic band structures of (a)BNNT, (b) BNNT+GMC, (c) BNNT+C_{60}, (d) BNNT+C48B12

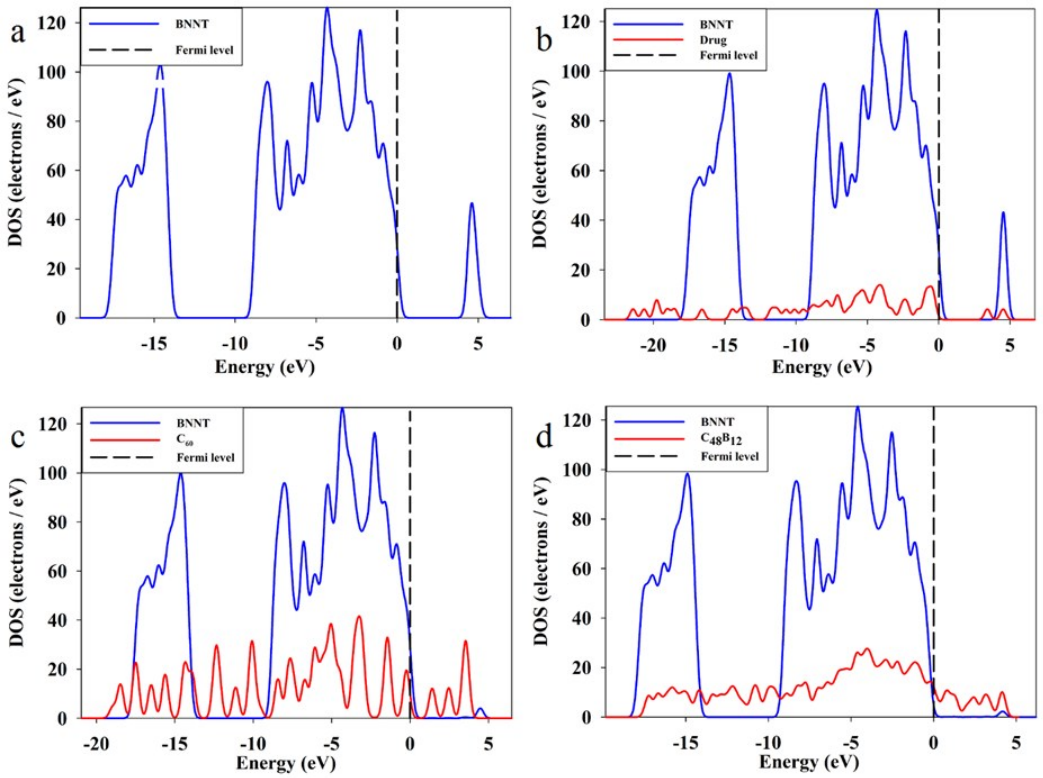

Fig. S9 Electronic density of states (DOS) (a) BNNT, (b) BNNT+GMC, (c) BNNT+C_{60}, (d) BNNT+ $C_{48}B_{12}$