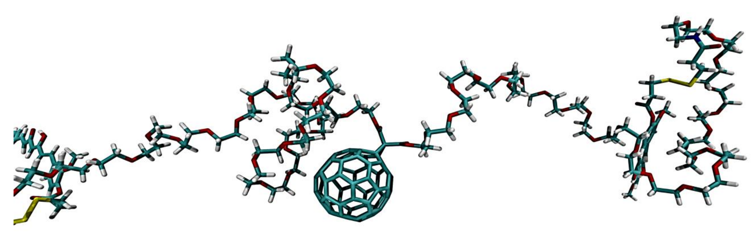
Fullerene–poly(ethylene glycol) corona stabilizes curcumin in water: Quantitative insights from atomistic molecular dynamics

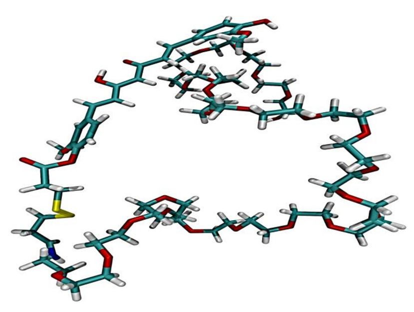
Ngoc Khoa Huynh, Vu Phuc Le, Thu Hanh Tran Thi
Ho Chi Minh City University of Technology (HCMUT), VNU-HCM, Ho Chi Minh City, Vietnam

1. Introduction

- Curcumin shows strong bioactivity but suffers from extremely low water solubility and conformational instability, causing aggregation and loss of function.
- Polymer coronas are employed to shield hydrophobic molecules, minimizing water exposure and enhancing stability.
- A C_{60}–PEG–curcumin covalent conjugate was designed and compared with PEG–curcumin controls to assess whether a fullerene-centered PEG corona can microencapsulate and stabilize curcumin in aqueous environments.



Model A. FU–PEG25–CUR conjugate (starting conformation)



Model B. PEG25–CUR control (starting conformation)

2. Methods

2.1. Systems:

Conjugate: C60–(poly(ethylene glycol)$_{25}$–curcumin)$_2$ in water (two curcumin; each PEG25 chain carries one curcumin).

Control: poly(ethylene glycol)$_{25}$–curcumin in water (one curcumin; no fullerene).

2.2 Engine and force field:

GROMACS; General Amber Force Field 2 and TIP3P water.

2.3. Conditions:

Constant pressure and temperature (NPT) at 310 K and 1 bar.

Production length 100 nanoseconds per system.

Long-range electrostatics computed with particle mesh Ewald.

2.4. Preprocessing for analysis:

Periodic boundary unwrapping and least-squares alignment.

3. RESULTS AND CONCLUSIONS

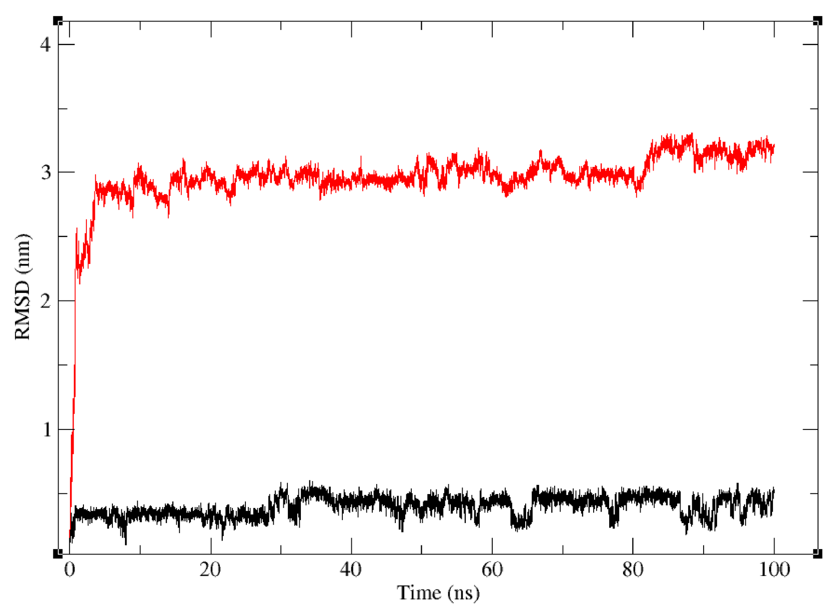


Figure 1. RMSD of curcumin
CUR in FU–PEG–CUR (Red) and CUR in PEG–CUR control (Black).

- Red (both CURs) rise 2–5 ns, plateau ~3.0 nm; small uptick at 80–90 ns is reversible.
- Black control ~0.5 nm; tighter conformational space.

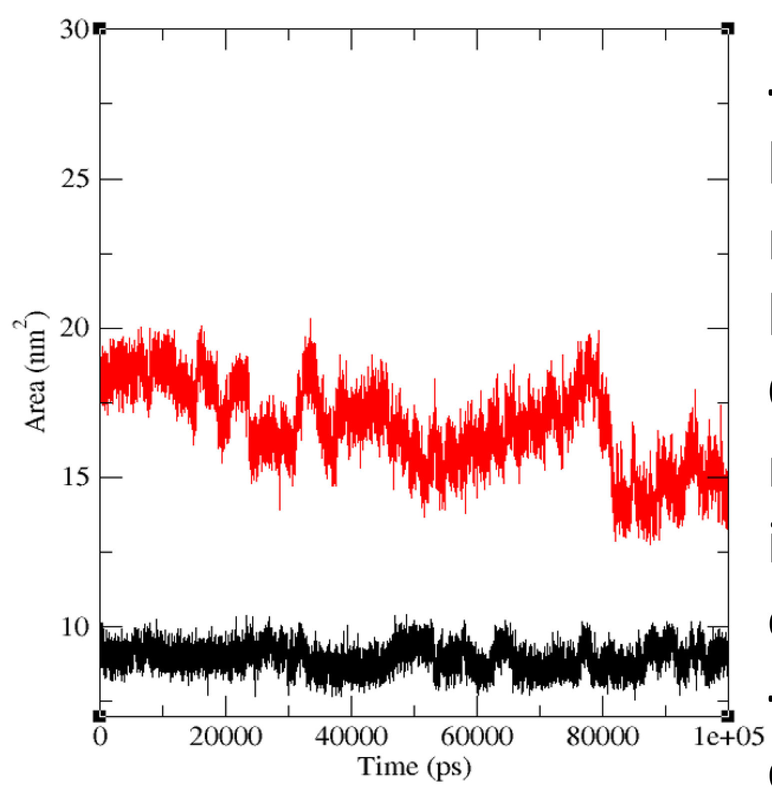


Figure 4. Solvent-accessible surface area (SASA) of curcumin
Curcumin in FU–PEG–CUR (Red), curcumin in PEG–CUR control (Black).

- **Red (FU–PEG–CUR):** total SASA for both CURs stays ~17–19 nm² until ~80 ns, then drops to ~15 nm² and remains low. This suggests a late hydrophobic CUR–CUR association inside the PEG-rich corona, burying the CUR–CUR interface and reducing per-molecule exposure.
- **Black control:** flat at ~8–10 nm², consistent with a single, non-dimerizing CUR.

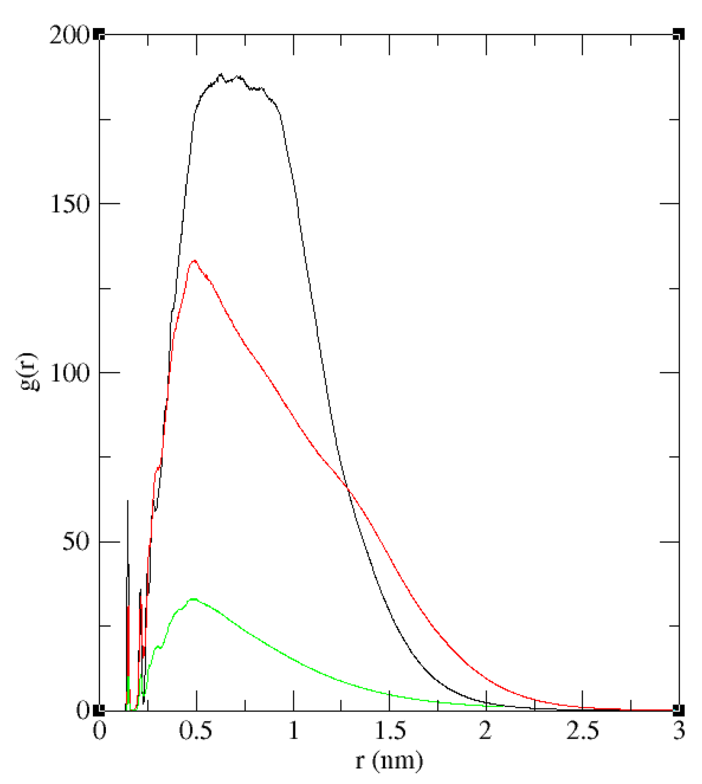


Figure 2. Corona RDFs: polymer packing
Fullerene–poly(ethylene glycol) (Black), curcumin–poly(ethylene glycol) in FU–PEG–CUR (Red), curcumin–poly(ethylene glycol) in PEG–CUR control (Green).

- **Black (C60–PEG):** first peak r ≈ 0.63 nm with a broad shoulder to ~1.5 nm; indicates a dense corona on C60.
- **Red (CUR–PEG, conjugate):** peak ~0.49 nm; elevated 0.25–1.5 nm; tighter, more persistent PEG contacts around CUR.
- **Green (control, no fullerene):** lower, narrower peak ~0.47 nm; rapid decay; weaker local packing.

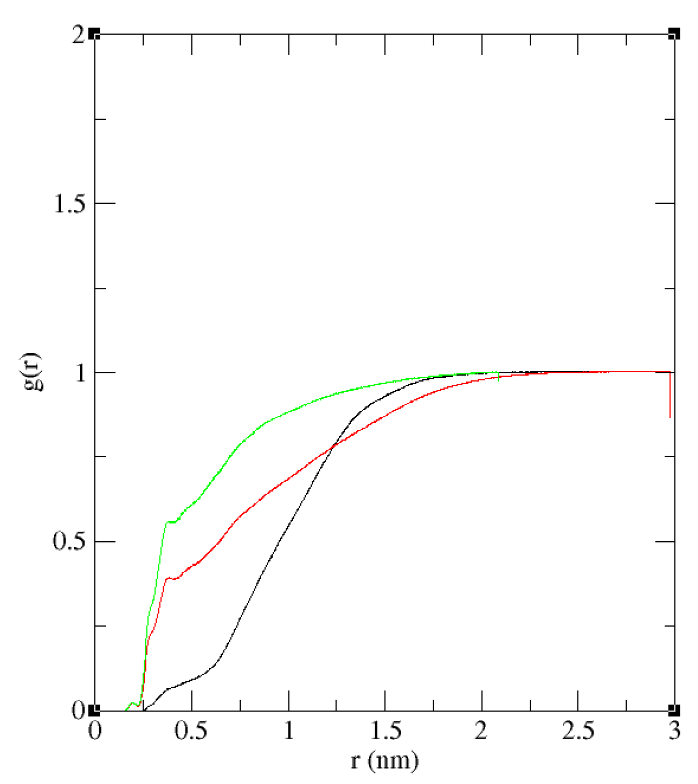


Figure 3. Water RDFs: solvent shielding
Fullerene–water (Black), curcumin–water in FU–PEG–CUR (Red), curcumin–water in PEG–CUR (Green).

- **Black (C60–water):** onset at r_{on} ≈ 0.35 nm; bulk reached only at r_{95} ≈ 1.57 nm and r_{99} ≈ 1.83 nm → hydrophobic depletion around C60.
- **CUR–water:** FU–PEG–CUR (red) returns to bulk more slowly than PEG–CUR (green): r_{95} 1.79 vs 1.33 nm; r_{99} 2.13 vs 1.76 nm.

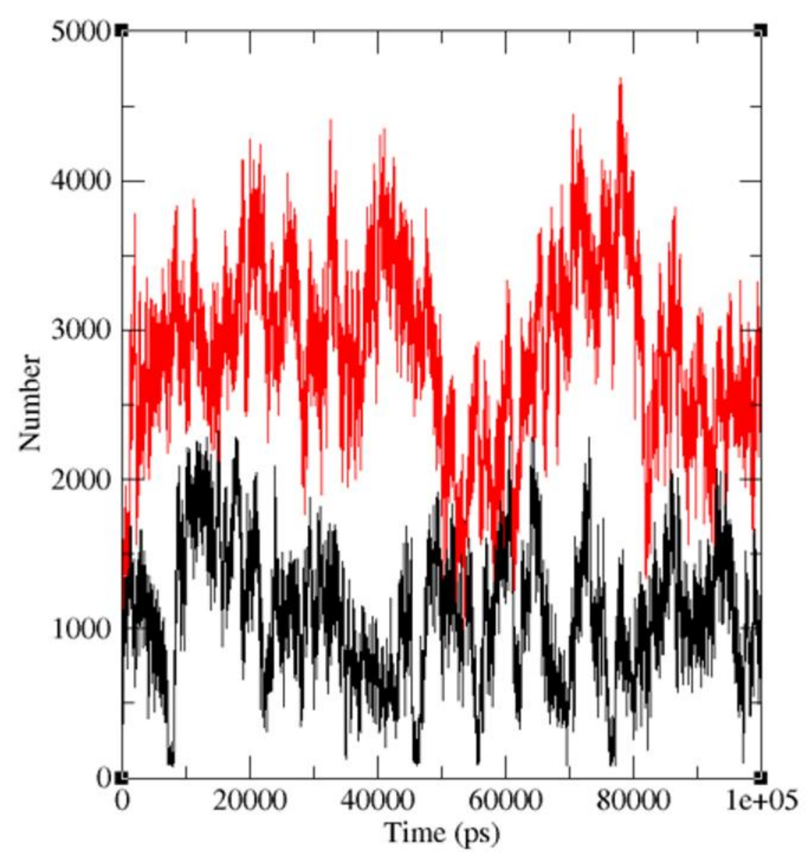


Figure 5. Curcumin–PEG contacts (< 0.6 nm)
Curcumin in FU–PEG–CUR (Red), curcumin in PEG–CUR control (Black).

Red (FU–PEG–CUR; sum of both CURs) stays above black. Sustained CUR–PEG contacts in the fullerene-centered corona. Broad oscillations reflect corona breathing on an elevated baseline.

CONCLUSION

- **A dense PEG corona forms on C60 and engages curcumin strongly (corona RDF peak position/width).**
- **CUR–water RDFs show stronger shielding in FU–PEG–CUR (r_{95} ≈ 1.79 nm, r_{99} ≈ 2.13 nm) versus control (1.33, 1.76 nm).**
- **With two CURs, shielding persists; a late hydrophobic CUR–CUR association (80–100 ns) lowers SASA and slightly reduces CUR–PEG contacts.**

Overall, the C60-centered PEG corona stabilizes CUR in water and limits direct solvent access.

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