Mechanism of curcumin interaction and inclusion by two β-cyclodextrin rings: an MD study

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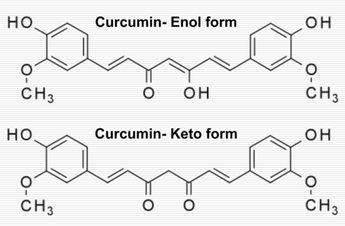
1. INTRODUCTION

Curcumin (CUR):
- hydrophobic polyphenol; turmeric-derived;
- broad pharmacological activity;

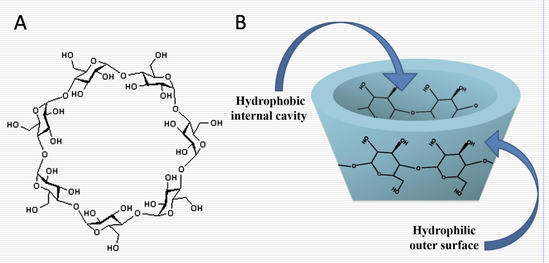
BUT poor solubility; low bioavailability



IUPAC	(1E,6E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-hepta-1,6- diene-3,5-dione)
Chemical formula	$C_{21}H_{20}O_6$
Solubility (mg/mL)	**0.0004** at pH 7.3 *[Chen et al, Int J Nanomedicine, 2020]*

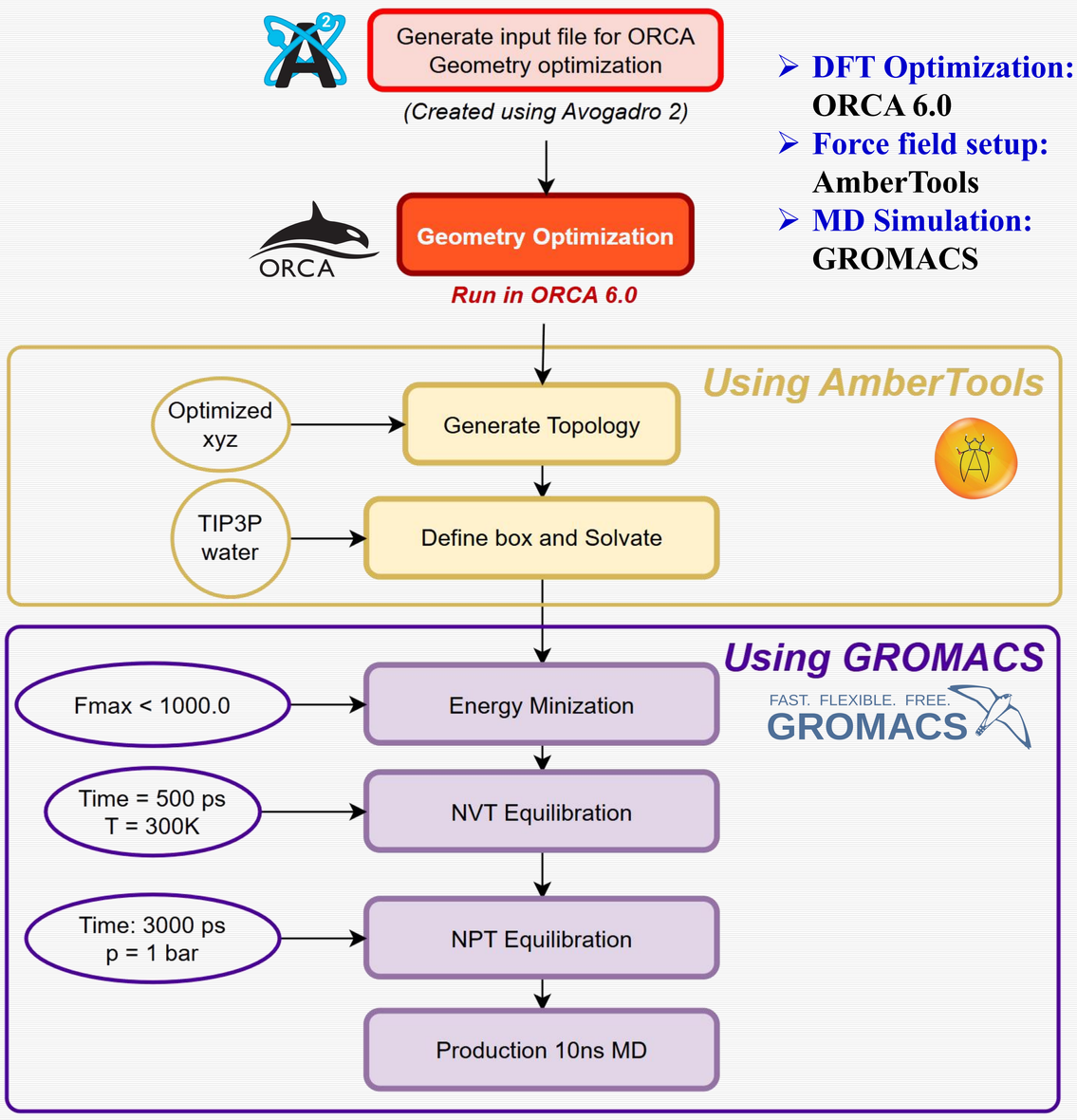
β-Cyclodextrin (β-CD):
- Hydrophobic cavity
- Hydrophilic surface

→ CUR stability ↑ via β-CD inclusion



⇨ **Aim:** Investigate the stability, interaction and inclusion behavior of CUR–(β-CD)₂ by MD simulations.

2. METHODOLOGY



- **DFT Optimization:** ORCA 6.0
- **Force field setup:** AmberTools
- **MD Simulation:** GROMACS

3. RESULTS AND DISCUSSIONS

3.1. Structure of CUR–(β-CD)₂ complex

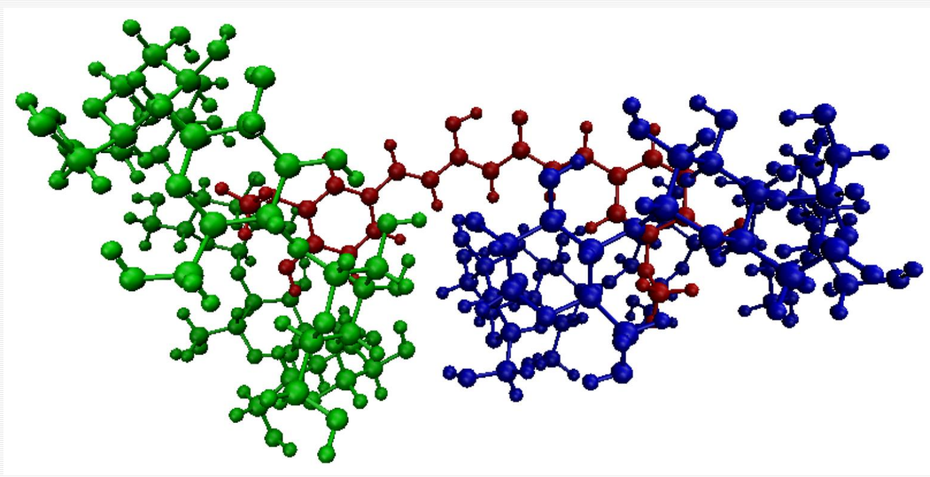


Fig. 3.1. Structure of CUR–(β-CD)₂ after geometry optimization: CUR (red) and β-CDs (green and blue).

3.2. Root-Mean-Square Deviation (RMSD)

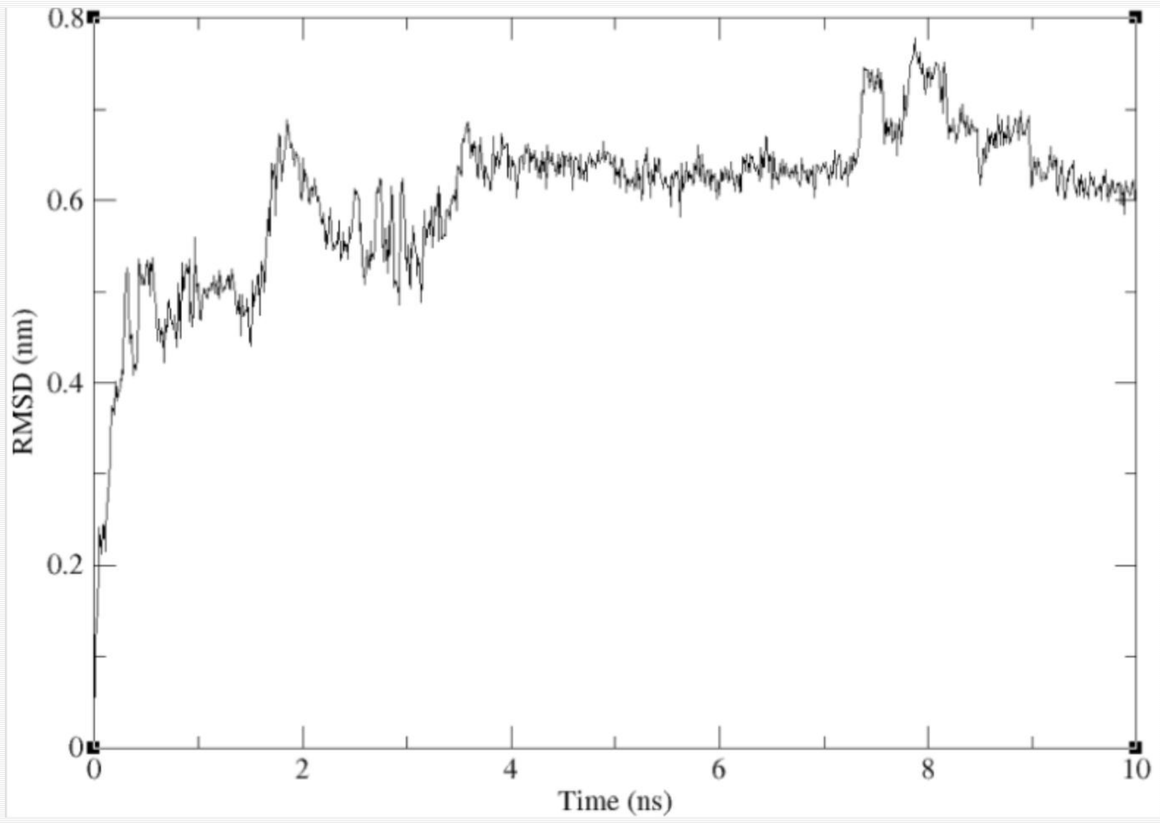


Fig. 3.2. RMSD of CUR–(β-CD)₂ over 10ns MD simulation.

3.3. Radius of Gyration

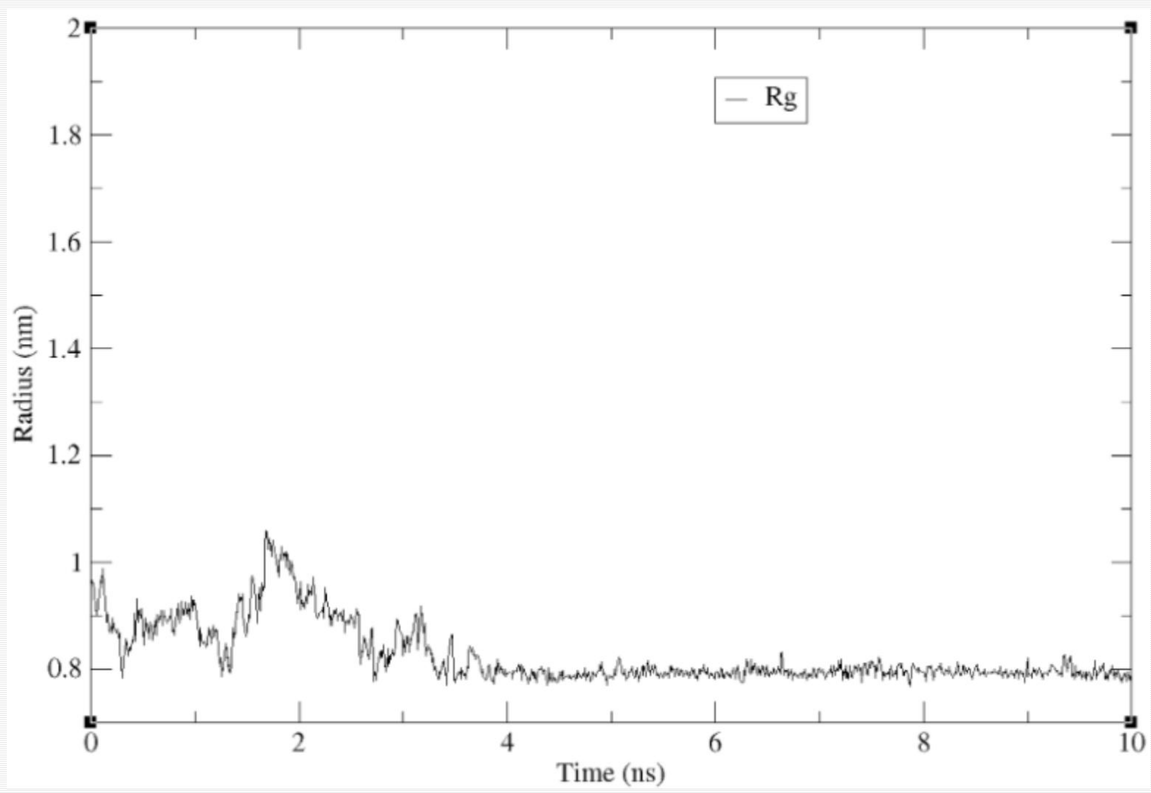


Fig. 3.3. Radius of Gyration of CUR–(β-CD)₂ over 10ns MD simulation.

➢ Equilibrium reached at ~8 ns; stable RMSD and Radius of Gyration.

3.4. Number of Hydrogen bonds

➢ Hydrogen bonds between CUR and β-CD: sparse but stable.
➢ β-CD–water H-bonds: remained abundant.
This confirmed host solvation stability.

3.5. Nonbonded Interaction Energies between CUR and β-CDs

- Short-range Lennard Jones ≫ Short-range Coulombic.

⇨ van der Waals & hydrophobic forces are the main stabilizing factors.

3.6. Solvent-accessible surface area (SASA)

➢ SASA of CUR encapsulated by β-CDs significantly decreased compared with that of free CUR.

⇨ Tight and persistent inclusion.

4. CONCLUSION

❖ *Two β-CD rings cooperatively encapsulate CUR into a compact capsule.*
❖ *Stability driven mainly by nonpolar interactions.*
❖ *Provides a molecular basis for future release-mechanism simulations and rational drug-carrier design.*