Analyzing Beta-Cyclodextrin as an effective carrier for the synergy of Curcumin and Piperine in anticancer bioactivity

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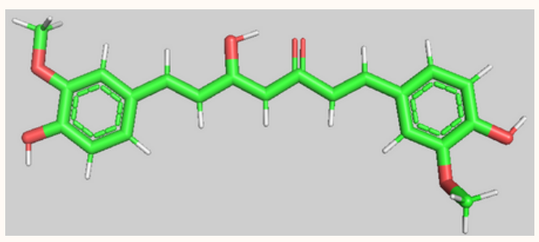
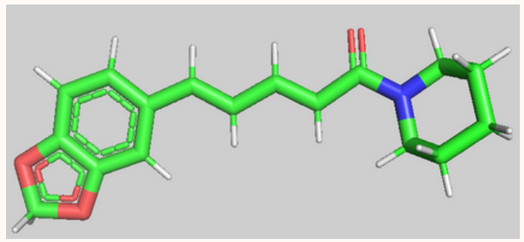
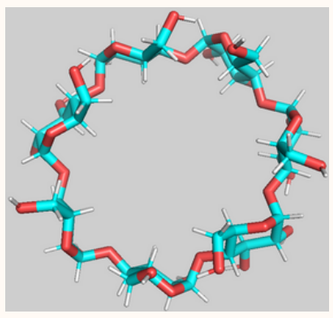
INTRODUCTION

Curcumin (CUR) and piperine (PIP) show anticancer activity but suffer low bioavailability.

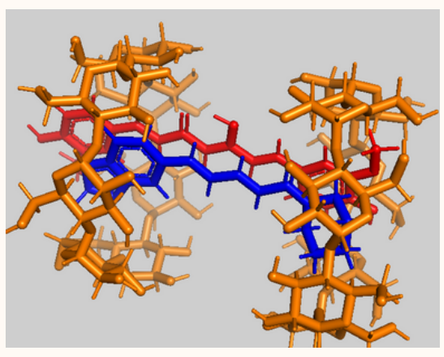






β-Cyclodextrin (β-CD) can encapsulate hydrophobic drugs to improve solubility/stability.

Aim: assess co-encapsulation of CUR+PIP in a β-CD dimer (1:1:2) and its synergy-relevant stability in water.



PROCESS

Using ORCA to find the Optimized Geometry of the Complex

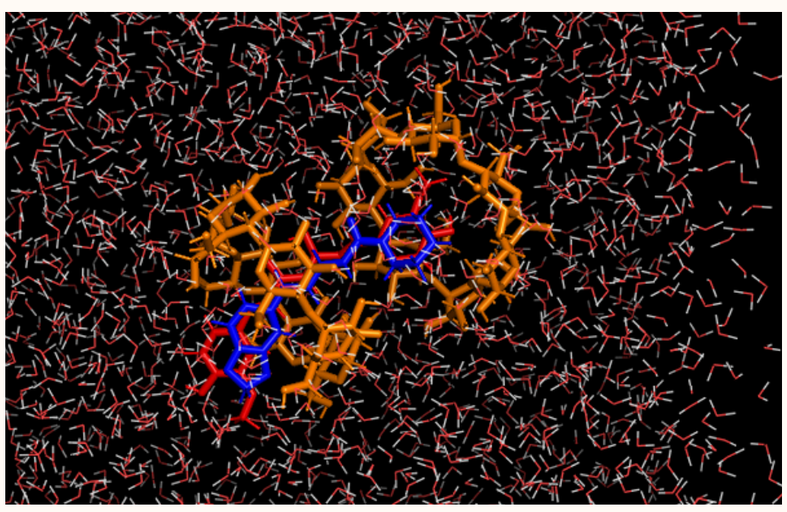
ORCA 6.0 – DFT Simulation Program

Using GROMACS sets up the suitable stimulating enviroment for Molecular Dynamics (MD)

$$E_{bondedterms} = \sum_{bonds} K_b(b - b_0)^2 + \sum_{angles} K_\theta(\theta - \theta_0)^2 + \sum_{diherals} K_\phi(1 + \cos(n\phi - \delta)) + \sum_{angles} K_\psi(\psi - \psi_0)^2 + \sum_{Urey-Bradley} K_{UB}(r_{1,3} - r_{1,3;0})^2$$

$$E_{nonbondedterms} = \sum_{nonbonded} \frac{q_i q_j}{4\pi D r_{ij}} + \varepsilon_{ij} \cdot \left[\left(\frac{R_{min,ij}}{r_{ij}}\right)^{12} - 2\left(\frac{R_{min,ij}}{r_{ij}}\right)^{6}\right]$$

Forcefield CHARMM36FF applied from CGenff



RESULTS AND DISCUSSIONS

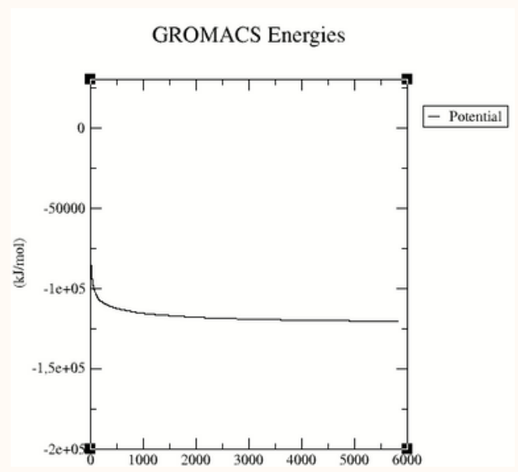


Fig. 1 .Potential Energy Equilibration Profile.

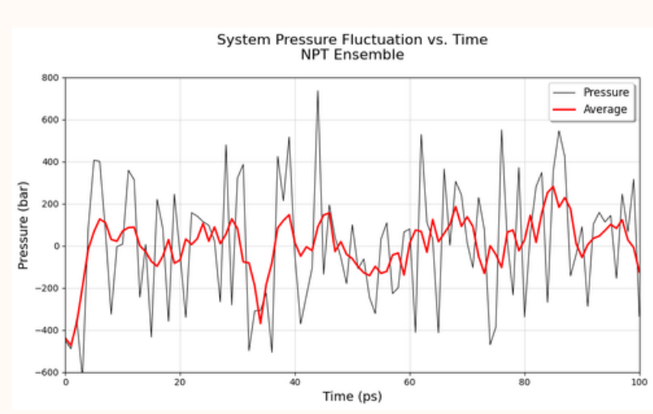


Fig. 2 . System Pressure Fluctuation vs. Time

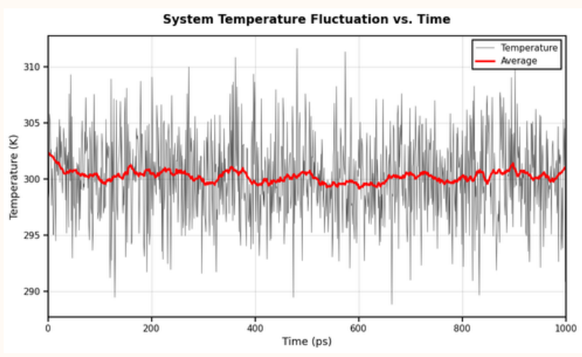


Fig. 3.System Temperature Fluctuation vs. Time

1. The system's potential energy is minimized successfully.
2. The system temperature fluctuates tightly around 300 K, indicating proper thermal equilibration.
3. Average pressure is around 0 bar; pre-MD preparation is as expected.

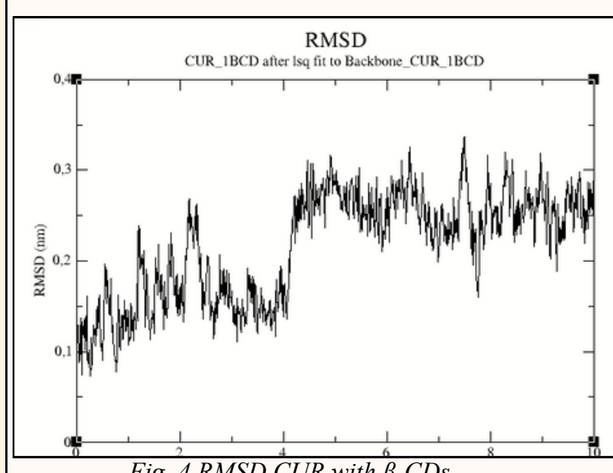


Fig. 4.RMSD CUR with β-CDs

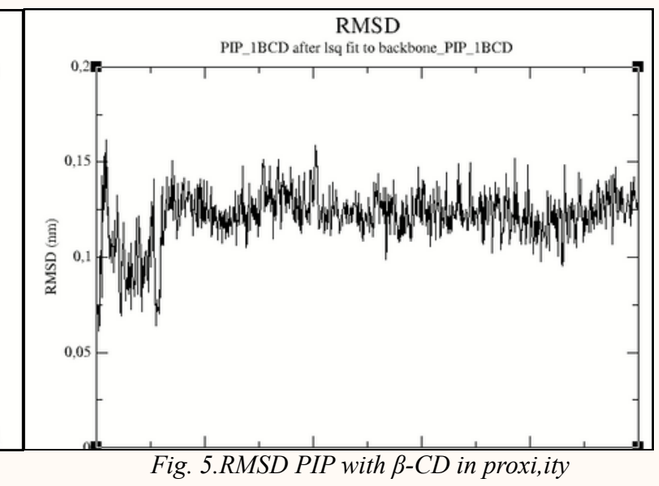


Fig. 5.RMSD PIP with β-CD in proxi,ity

- Though the complex showed a low RMSD value, CUR's RMSD had not converged yet, while PIP's value had converged quite early
- While CUR was centered between 2 β-CD, PIP had moved toward β-CD which is near its methylenedioxyphenyl ring, which is noteworthy

CONCLUSION

- The complex shows somewhat stability, though need some changes to make CUR more stable
- More related infomation (Radius of Gyration, distance between compounds, etc) need to be taken into consideration
- PIP's behavior during MD process is unexpected and need to be tested in more experiments.

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https://sci-hub.st/10.1021/acs.jcim.5b00152