Molecular Dynamics Simulation of the Interaction Between Cholates and Cholesterol

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Abstract

Cholates are biosynthesized in the liver and play an important role in making cholesterol soluble. They were of particular interest in this research project because of their planar and amphiphilic structure. This means that one side of the molecule is hydrophilic while the other side is hydrophobic. The structure of the micelle allows the hydrophobic side to face inward and the hydrophilic side to face outward. When placed in a system of water, ions, and cholesterol, the cholate molecules aggregate together to form micelles. The motivation for this research was to find out how many cholates would make up each micelle, how much cholesterol would become encapsulated in the micelles, and what shape micelles would form. By using GROningen MAchine for Chemical Simulations (GROMACS) and Visual Molecular Dynamics (VMD), answers to the previous questions were answered.

The simulation lasted for twenty-three nanoseconds. During the simulation, cholates aggregated together to form four micelles. Three of the four micelles encapsulated cholesterol. Also, the micelles were spherically shaped. This research is useful for drug engineers because it provides a pathway to encapsulate hydrophobic medicines into these micelles for drug delivery.

Methodology

Gather structures
- Cholesterol (20), cholates (42), ions (226), water (3200)

Set up system to be simulated
- Packmol (Package used for arranging molecules)

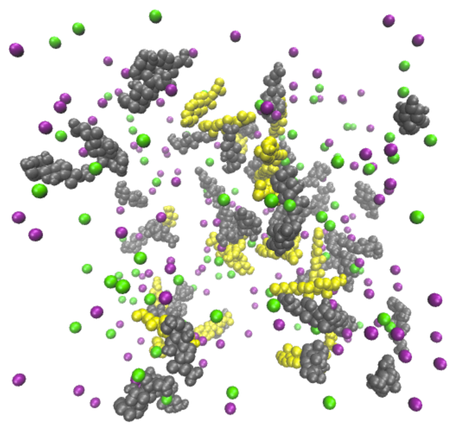
Energy minimization & Molecular dynamics
- GROMACS (Simulation Package)

Run simulation
- Super Computer (Queen Bee)

Analyze data
- VMD (Visualization software)
- Grace (2-D Graphing tool)

Gray = Cholate
Yellow = Cholesterol
Purple = Sodium Ion
Green = Chloride Ion

There are periodic boundary conditions in all directions.



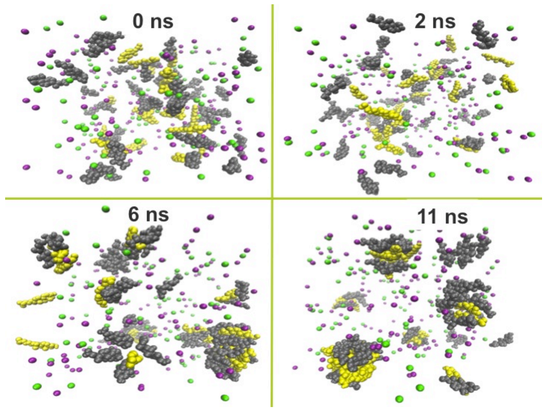
Results

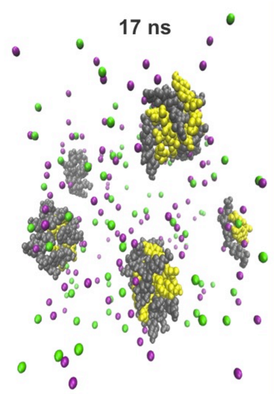
0 nanoseconds
- Initial system

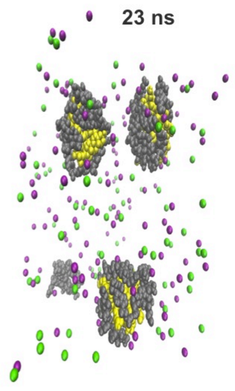
2 nanoseconds
- Molecules move closer together

6 nanoseconds
- Molecules start to aggregate together

11 nanoseconds
- Molecules begin to form micelles



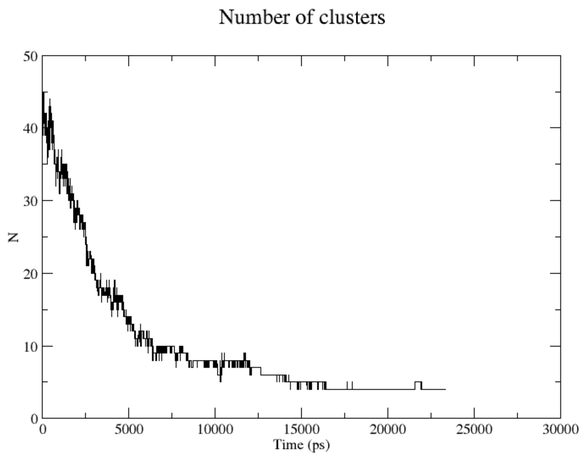




17 nanoseconds
- 5 micelles formed
- 4 contain cholesterol

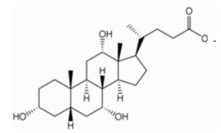
23 nanoseconds
- 2 micelles fused together leaving 4 total
- 3 contain cholesterol

Number of Clusters
- The simulation reached equilibrium when the number of clusters stopped decreasing

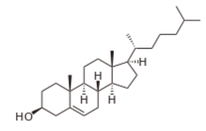


Structures

Cholate



Cholesterol



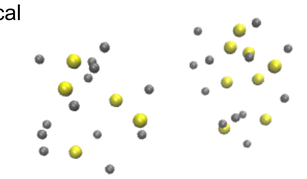
Discussion

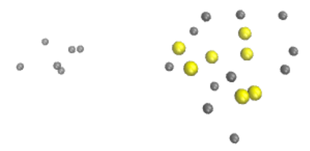
Simulation Duration
- 23 nanoseconds

Four micelles of cholates formed
- 6, 11, 12, & 13 cholates

Three micelles encapsulated cholesterol
- 5 cholesterol molecules →13 cholate micelle
- 8 cholesterol molecules →12 cholate micelle
- 7 cholesterol molecules →11 cholate micelle

Micelle Shape
- Spherical





Future Work

- Simulation of the system with a different cholate to cholesterol ratio
- Simulation of the system with cholates and a compound other than cholesterol
- Improvement of drug delivery via molecular dynamics

Acknowledgements

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