Secondary Structure Stabilization of three differents peptides by glycerol/water mixtures using molecular dynamics.

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INTRODUCTION

Several experimental evidences have been collected regarding the effects of solutes that may act either as a stabilizing agent or as a denaturing agent. For instance, trifluorethanol[1], some salts[2], sugars and polyols[3] are known to stabilize proteins in aqueous solutions, whereas guanidine hydrochloride[4] and urea[5] act as denaturing agents. Polyhydric alcohols and sugars are among the best stabilizing agents for proteins in aqueous solution.

Molecular dynamics have been performed to investigate the secondary structure stabilization of three different peptides sequence, having 16 glycines, serines and alanines in zwitterionic α-helix conformation at glycerol/water binary mixtures (0:100, 50:50 and 80:20 v/v composition).

METHODS

All simulations were conducted in the NpT (constant number of particles, pressure and temperature) ensemble with Berendsen and V-rescale couple to pressure and temperature bath, respectively. Standard periodic boundary conditions were considered, a 1.2 nm cut-off for the non-bonded interactions and long-range correction was used. The motion equations were integrated using the leap-frog algorithm with a time step of 0.8 fs. The potential energy surface was described using the OPLS-AA force field for the peptide and glycerol, and the TIP4P model for water. The box was built with packmol filling it in a triclinic box. The initial structures of the peptide solutions were optimized by energy minimization runs using steepest descent and then conjugate gradient algorithm to obtain an energy gradient below 100 $kJ.mol^{-1}.nm^{-1}$. Thenceforth 2 ns NpT calculation was performed with peptide been fixed with a force constant of 1000.0 $kJ.mol^{-1}.nm^{-2}$ over all atoms. Finally, a 15 ns trajectory was obtained and in the analyses was performed excluding the first 10 nm. All calculations were performed using Gromacs 4.5.5.

RESULTS AND DISCUSSION

The peptides are more stabilized by glycerol relative to water due to the hydrogen bonding interaction of glycerol three hydroxyl group with amine and carbonyl groups from backbone peptide and hydroxyl groups from side-chain (for serine). This stabilization mechanism can be associated to the simultaneous hydrogen bonding of a glycerol molecule with different amino acids of a given peptide.

It is observed that the peptide secondary structure is more stabilized with the increase of glycerol molecules in the mixture. Therefore, an augment in the glycerol concentration increase the probability of hydrogen bonding between peptides and glycerol molecules leading to stabilization of the α-helix structure.

CONCLUSIONS

Compared to pure water, the increase of glycerol molar fraction in mixture raises the stabilization of the three peptides studied here. The stabilization process is related to the higher number of hydrogen bonding between glycerol molecule and different aminoacids of the same peptide, therefore preserving the α-helix structure.

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