Modeling the Solvated Structure of two Forms of Melittin

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The helical polypeptide Melittin is a major component of honeybee (*Apis Mellifera)* venom, and occurs naturally in both N-formylated and unformylated forms. The molecular modeling program, NAMD, and its graphical interface, VMD, were employed to study the differences in secondary structure of the two forms melittin in various solvents and temperatures. As the lytic action of melittin is directly related to helicity at the protein's N-terminus, the effect of the formylated N-terminal glycine on the stability of the helix may have implications for the lytic capability of formylated melittin.

After optimizing the proteins' amino acid side chains, simulations were completed for both melittin forms in the CHARMM forcefield at 300, 400, and 600 K in water solvent and at 600 K in methanol. The stability of the helix was analyzed by comparing the number of hydrogen bonds, averaged every 20 ps, along the protein backbone for the duration of the simulations. The results of the simulations revealed that the melittin helices are more stable in methanol than in water solvent and that melittin is more stable when formylated at the N-terminus. The limited unwinding of the proteins in water prompted an investigation of how the forcefield influences the stability of secondary protein structure in molecular dynamics simulations. We repeated the 300 and 400 K aqueous simulations using the AMBER forcefield, and found a decrease in helical stability of melittin. The results of these trajectories have encouraged further exploration of the stability of secondary protein structure in relation to solvent hydrogen bonding character, temperature variation, and the forcefield utilized in molecular dynamics simulations.