

**Influence of Salt and Temperature on the Self-assembly of Cyclic Peptides in Water: A Molecular Dynamics Study**

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**Abstract**

It is found in the literature that the cyclic peptides (CPs) possess the property to self-assemble in water to form cyclic peptide nanotubes (CPNTs) and are used extensively in the field of nanotechnology. Several factors influence the formation and stability of these nanotubes in water. However, an extensive study of the contribution of several important factors is still lacking. The purpose of this study is to explore the importance of temperature and salt (NaCl) on the association tendency of CPs. Furthermore, the self-association behaviour of CPs in aqueous solutions at various temperatures are also thoroughly discussed. Cyclo-[(Asp-D-Leu-Lys-D-Leu)2] is considered for this study and a series of classical molecular dynamics (MD) simulations at three different temperatures, viz. 280 K, 300 K, and 320 K, both in pure water and in various concentrations of NaCl salt are carried out. The calculations of radial distribution functions, preferential interaction parameters, cluster formation and hydrogen bonding properties suggest a strong dependence of NaCl concentration in the association propensity of CPs. Low NaCl concentration hinders CP association while high NaCl concentration facilitates the association of CPs. Besides this, the association of CPs is found to be enhanced at low temperature. Furthermore, the thermodynamics of CP association is predominantly found to be enthalpy driven in both presence and absence of salt. No crossover between enthalpy and entropy in CP association is observed. In addition, the MM-GBSA method is used to investigate the binding free energies of the CP rings that self-assembled to form nanotube like structures at all three temperatures.



**Figure**: Schematic representation of the self-assembly of CP units to form nanotube like structures in presence of salt and at different temperatures.

**References:**

1. R. Moral, S. Paul, *Phys. Chem. Chem. Phys.* **2023**, *25*, 5406-5422.