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Effect of the precursor conformation on the structure of polypeptide single chain nanoparticles (SCNPs)

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Single chain nanoparticles are soft nano-objects made from individual polymer chains crosslinked intramolecularly. Due to the internal random crosslinking between functional groups of the same chain, a sparse conformation is usually achieved which displays many common structural features with intrinsically disordered proteins (IDPs). Lately, there has been great interest in expanding SCNPs to biodegradable and biocompatible polymers, such as proteins.
We synthesized two types of SCNPs: poly- L- lysine- and bovine serum albumin (BSA) using disuccinimide ester linkers that mainly react with lysine moieties. To understand the role of the chain conformation of the precursor on the resulting SCNP morphology, we have systematically varied the solvent conditions: pH, salt and for the case of BSA-SCNPs, the denaturant concentrations, as well as the cross-linker concentration. By studying the resulting SCNPs with dynamic and static light scattering as well as small angle neutron scattering, we found that indeed the precursor conformation has a strong effect on the SCNP morphology. For BSA-SCNPs, more extended precursor conformations are able to collapse more by intramolecular crosslinking. Also, the longer cross-linker is more effective in chain compaction due to its ability to form larger intramolecular loops. Similarly, for the cationic PLL, pH and salt variation affect the chain conformation. However, the crosslinking results in aggregation due to the stiffness of the precursor.

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