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Title: Detergent-induced aggregation of an amyloidogenic intrinsically disordered protein

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Intrinsically disordered proteins (IDPs) Keywords:

Sodium dodecyl sulfate (SDS)

Reduced and carboxymethylated (RCM)

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Intrinsically disordered proteins (IDPs) belong to an important class of proteins that do not fold up spontaneously. The conformational flexibility of IDPs allows them to adopt a wide range of conformations depending upon their biochemical environment. Many IDPs undergo profound conformational conversion that is often coupled to amyloid aggregation in the presence of negatively charged lipid membranes. Here, we show the effect of a well-known anionic lipid mimetic, sodium dodecyl sulfate (SDS), on the aggregation mechanism of a model amyloidogenic IDP, namely, bovine \(\upkappa \)-casein. In the absence of SDS, the aggregation kinetics of reduced and carboxymethylated (RCM) \(\upkappa \)-casein followed a nucleation dependent polymerization model that comprises both lag- and assembly phases. On the contrary, in the presence of sub-micellar concentration of SDS, the aggregation kinetics did not exhibit a lag phase and appears to follow a non-nucleation pathway. Additionally, the morphologies of the aggregates formed in the absence and presence of SDS were found to be different. In the absence of SDS, \(\upkappa \)-casein aggregation proceeded to typical amyloid fibrils, whereas, in the presence of SDS, the aggregation yielded large oligomers. Our results provide important molecular insights into the aggregation mechanism that can be utilized for the designing of novel protein/amyloid based nanomaterials with desired properties.

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