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| **Modulating protein-surfactant interactions for enhanced protein thermal stability and bioactivity** |
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| **Background:** Surfactant-mediated stabilization of proteins is a commonly used strategy in the food, chemical and pharmaceutical industries. Through non-covalent association, surfactants can enhance protein stability and bioactivity in non-native environments. These favorable local conformational changes have enabled valuable biocatalytic transformations in organic solvents, helped with the formulation of therapeutic monoclonal antibodies and facilitated protein encapsulation in polymeric and lipid-based drug delivery systems. Protein-surfactant binding is however complex and dynamic, with concurrent interactions leading to stabilization and destabilization processes. Deconstructing this assortment of interactions is key to rationalizing surfactant-mediated stabilization and advancing protein applications. In this study, we report the impact that sodium dodecyl sulphate (SDS) has on the thermal stability and biocatalytic activity of the antimicrobial enzyme lysozyme. |
| **Methods:** Lysozyme-SDS interactions were assessed at increasing SDS concentrations. Complexation efficiency was determined by protein quantification assays and the dependence of surfactant dissociation determined as a function of ionic strength. Differential scanning calorimetry measurements were used to measure the impact that SDS has on lysozyme thermal stabilisation.  |
| **Results:** Differential scanning calorimetry measurements showed that the melting temperature of lysozyme increased with surfactant association, highlighting the role of SDS in thermal stabilisation. Maximum binding efficiency was achieved at pH 4.5 in the presence of SDS concentration that corresponding to the 1:1 charge ratio to lysozyme which led to lysozyme precipitation and loss of aqueous solubility. Increasing ionic strength led to surfactant dissociation and protein re-solubilisation, emphasising the role that SDS has on modulating protein aqueous solubility. Protein structural and bioactivity assays are currently on-going to deconvolute the impact of surfactant association. LogP study will further be performed to validate the increasing lipophilicity of protein via hydrophobic ion pairing process |
| **Conclusions:** Within this study, key role of surfactants could be confirmed i.e. enhancing thermostability and lipophilicity of protein without irreversibly affecting the structure and activity of the therapeutic protein based on the non-covalent lipidation process, thereby highly effectively incorporating into the lipid-based nanocarriers, which provide a potential strategy for the oral protein drug delivery. |