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Is proteins structural stability challenged by lipid peroxidation?

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Lipid oxidation can arise in vivo during oxidative stress and redox imbalance situations. This process involves the generation of reactive oxygen species (ROS) within the cells, which can readily attack unsaturated fatty acids in membranes through non-enzymatic mechanisms, triggering a chain reaction that generates various oxygenated small molecules. These molecules often contain reactive electrophilic carbonyl groups, including α,β-unsaturated aldehydes, which can interact with nucleophilic moieties on protein surfaces, inducing misfolding and aggregation.[1]

Lipid peroxidation significantly affects membrane organization and can modify proteins and DNA, leading to functional alterations. Consequently, it was suggested to be implicated in aging and the pathogenesis of various diseases, including atherosclerosis, neurodegenerative disorders, autoimmune diseases, and type 2 diabetes.[2]

To investigate the effects of lipid peroxidation on the conformational stability of model proteins, bovine serum albumin (BSA), hen egg white lysozyme (HEWL), ubiquitin and rabbit IgG were solubilised in phosphate buffer and studied alone or in the presence of DMPG-DOPC (at 1:1 molar ratio) small unilamellar vesicles (SUVs) at either 20° or 40°C.

Oxidative conditions were performed by collecting 30 consecutive repeated synchrotron radiation circular dichroism (SRCD) spectra at beamline B23 of the Diamond Light Source synchrotron. We have previously demonstrated that the high photon flux and brilliance of the synchrotron radiation induces water photolysis and production of ROS that can denature protein/peptide folding and is used to quantify the UV photostability of proteins/peptides with and without ligands and a as a function of environment.[3]

For HEWL in phosphate buffer (PB) and SUV at 20 °C and 40 °C, respectively, the normalised spectral changes at 192 nm reported against the number of scans revealed that the ROS damage and the effects of lipoxidation of protein was less pronounced in SUVs than in PB at higher temperature suggesting a protective property of SUVs against ROS damage on protein.

References:

[1] Á. Viedma-Poyatos et al., Antioxidants 2021, 10, 295.
[2] F. Ito et al., Antioxidants 2019, 8, 72.
[3] P. Ruzza et al, International Journal of Molecular Sciences 2021, 22(12), 6512

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