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# HSA Oxidation Improves Thermal Stability and Inhibits Amyloid Fibril Formation.

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Oxidative stress and amyloid fibrils formation have been suggested to underlie the loss of cellular function in the developing of aging associated neurodegenerative pathologies like Parkinson's and Alzheimer's disease. The comprehension of the complex and temperate relationship between protein oxidation and aggregation processes can be of fundamental importance in understanding molecular basis of degeneration. A number of evidences shows that even small changes due to the interaction of protein with reactive oxygen species (ROS) may have a large effect on the conformation and stability of proteins and it was found that oxidatively modified protein deposits accumulate during aging processes disrupting cellular functions, but a clear link among protein aggregation, oxidative stress, and neurodegeneration is not established yet.

Here we show that oxidation of Human Serum Albuimin (HSA) inhibits amyloid fibrils formation. Structural properties and aggregation pathways of non-oxidised and oxidised HSA were studied by means UV-Vis absorption and fluorescence spectroscopy, Circular Dichroism, FTIR spectroscopy and light scattering. The oxidation of amino acids and in particular of methionines, was found to cause variations in protein tertiary structure leading to the compaction of HSA molecule while substantial secondary structure changes are not observed. HSA oxidation results in an increased thermal stability and in a reduced association propensity of HSA molecules. Subtle changes in protein structure induced by oxidation, cause an alteration in the aggregation process and in the intermediate states changing in this way the mutual interactions of molecular mechanisms that contributes to HSA fibril formation As confirmed by TEM measurements in the selected experimental conditions HSA forms thin and straight amyloid fibrils while the fibrillar nature of oxidized HSA aggregates is strongly reduced and curly and amorphous aggregates are found in the sample.

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