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Sections:

1. Biomaterials
2. Bioactive Compounds
3. Cancerogenesis
4. Gene Expression
5. Metabolites and Correction of Metabolic Processes
6. Proteomics and Protein Functions
7. Molecular Basis of Physiological Functions

OXIDIZED LIPIDS SUPPRESS AMYLOID FIBRIL FORMATION: SEARCHING FOR A MECHANISM

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Preventing of amyloid fibril formation *in vivo* has long been a focus of extensive studies, since this process plays a key role in a molecular etiology of Alzheimer's disease, type II diabetes, systemic amyloidosis, etc. However, effective strategy of treating these diseases is still not developed.

This study was aimed at assessing the inhibiting effects of oxidatively modified phospholipids, viz. 1-palmitoyl-2-azelaoyl-sn-glycero-3-phosphocholine (PazePC), and 1-palmitoyl-2-(9′-oxononanoyl)-sn-glycero-3-phosphocholine (PoxnoPC) on the protein fibrillization.

Lipid dispersions of PazePC and PoxnoPC in sonicator. Alternatively, the extrusion technique was employed to obtain liposomes composed of 80 mol% phosphatidylcholine (PC) and its mixtures with PazePC (20 mol%) or PoxnoPC (20 mol%), referred to here as PazePC20 and PoxnoPC20, respectively. The lysozyme (insulin) fibrillization was initiated at pH 2 (7.4), 60 °C, at lipid concentration 16 μM. The kinetic parameters for amyloid fibril formation, viz. lag time, apparent rate constant for the fibril growth (k) and maximal fluorescence of the dye (Fmax), were obtained by approximation of the time dependence of the Thioflavin T (ThT) fluorescence intensity at 480 nm with the sigmoidal curve.

It appeared that Fmax values of lysozyme- (insulin-) bound ThT were about 20% (86%) lower in the presence of PazePC20/PoxnoPC20, as compared to those in control samples. The revealed effects were attributed to the decrease in the extent of amyloid fibril formation. The inhibition of lysozyme aggregation was accompanied by the reduction of the lag time and increase of the k values, while the opposite effect was observed for insulin. Furthermore, lipid vesicles, containing PazePC and PoxnoPC, inhibited protein aggregation into mature fibrils, unlike lipid dispersions, highlighting the important role of the polar surfaces of the lipids in the reduction of the protein fibrillization extent. The obtained results point to significant impact of PazePC-lysozyme hydrophobic interactions on the inhibition of the protein fibrillogenesis. In turn, Shiff bases could be formed between insulin monomers and PoxnoPC domains of the lipid vesicle, thereby stabilizing an aggregation-resistant protein conformation.

comprehensive testing of oxidized lipids as potential anti-amyloid agents.