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Kinetics of amyloid fibril formation in the presence of metal ions and low-molecular-weight compounds

Jelica Milošević[*1], Nemanja Mijin[1], Luka Matić[1], Aleksandra Milovanović[2], Branko Jovčić[3,4], Natalija Polović[1]

[1]*Department of Biochemistry, Faculty of Chemistry, University of Belgrade, Belgrade, Serbia*
[2]*Institute of Chemistry, Technology and Metallurgy - Center of Chemistry, University of Belgrade*
[3]*Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Belgrade*
[4]*Institute of Molecular Genetics and Genetic Engineering, University of Belgrade*

**e-mail: jelica@chem.bg.ac.rs*

Proteins are prone to structural changes due to their marginal stability. There are multiple pathways of structural rearrangements leading to misfolding and aggregation among which amyloids stand out as highly ordered and remarkably stable forms which appear to be a global minimum of protein free energy landscape of all proteins. *In vitro* studies on different proteins show that destabilizing conditions that favor the state of molten globule are likely to lead to ordered fibril formation. The presence of various organic and inorganic molecules was reported to affect amyloid fibril formation, eighter as stimulators or inhibitors. We investigated the formation of amyloid fibrils of human serum albumin, ovalbumin and papain in the presence of metal ions, as well as low-molecular-weight compounds. Proteins were incubated in destabilizing conditions optimized to prolong the solubility of molten globule state and induce amyloid-like structural changes. The effects of inorganic and organic additives on fibrillation process were monitored using Thioflavin T fluorescence, 8-Anilinonaphthalene-1-sulfonic acid fluorescence, Attenuated total reflection Fourier-transform infrared spectroscopy, electrophoretic and microscopy techniques. Our results show that the kinetics of amyloid formation is dependent on the presence of iron, copper, zinc and aluminum salts, as well as different lipophilic low-molecular-weight compounds. While some compounds act as complete inhibitors of fibrillation, others increase the rate of fibrillation process and promote the formation of mature fibrils.

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