

**THE INHIBITION OF HEAT-INDUCED BETA-LACTOGLOBULIN  
AGGREGATION BY AXIALLY COORDINATED Zr PHTHALOCYANINES**

*Chernii S. V.*<sup>1</sup>, *Tretyakova I. M.*<sup>2</sup>, *Selin R. O.*<sup>2</sup>, *Losytskyy M. Yu.*<sup>1</sup>, *Chernii V. Ya.*<sup>2</sup>,  
*Kovalska V. B.*<sup>1</sup>

<sup>1</sup>Institute of Molecular Biology and Genetics NASU, Kyiv, Ukraine

<sup>2</sup>V. I. Vernadskii Institute of General and Inorganic Chemistry NASU, Kyiv, Ukraine  
chernii.sv@gmail.com

Formation of the beta-pleated protein aggregates – amyloid fibrils – involve into a group of amyloid-associated disorders as well as into physiological processes. Moreover, specific proteins found in food sources, particularly beta-lactoglobulin (BLG), are able to aggregate into fibrils under heat treatment. The development of agents that would effectively control aggregation is an active area of research to prevent fibril formation. Phthalocyanine complexes were selected for this aim as they are known as compounds with high anti-prionic and anti-amyloidogenic activity.

Zr phthalocyanines with thiopropionic and lysine axially coordinated ligands were obtained by the reaction of ligand exchange (Fig. 1). The use of Zr phthalocyanine dihydroxide, unlike dichloride, in this reaction is not accompanied by the release of hydrogen chloride. Thereby, the reaction proceeds under mild conditions, which is essential in the case of sulfur- or nitrogen-containing ligands.

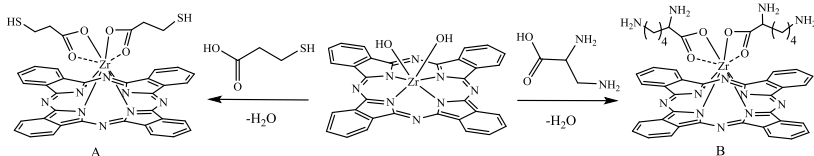


Fig. 1. Scheme of the synthesis of Zr phthalocyanines with thiopropionic (A) and lysine (B) ligands

The aggregation reactions of beta-lactoglobulin (BLG) using different protocols both in acidic and neutral pH conditions were performed. The aim was to evaluate the anti-fibrillogenic activity of two Zr phthalocyanines with axially coordinated thiopropionic and lysine ligands on BLG heat-induced aggregation.

The inhibitory effect of both Zr phthalocyanines on the kinetics of BLG amyloid aggregation under acidic conditions (pH 2) was about 90 %. The morphology of BLG aggregates formed in acidic and neutral pH was studied by scanning electron microscopy (SEM). Studied compounds bearing thiopropionic and lysine ligands residue demonstrated a similar high inhibitory effect on aggregation in acid conditions, while led to the formation of aggregates of different morphology. Free BLG fibrils are characterized by length up to 1  $\mu\text{m}$  with sticking into clusters. The presence of Zr phthalocyanine with lysine ligands residues led to the formation of a small amount of width fibrils with length up to 1.5  $\mu\text{m}$ . Moreover, Zr phthalocyanine with thiopropionic ligands alters the morphology of fibrils even more strongly, leading to the formation of thin fibrils up to 4  $\mu\text{m}$  in length is observed. The formation of branchy linear aggregates was shown for free BLG under neutral conditions (pH 7). The presence of Zr phthalocyanine with the thiopropionic ligands slightly affect the morphology of the BLG aggregates and reduces their tendency to cluster formation. In contrast, the presence of Zr phthalocyanine with lysine ligands residues changed the morphology of BLG aggregates and significantly reduced their number and clusters size.

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