

**SYNTHESIS AND STUDY OF THE BIOACTIVITY OF PHTHALOCYANINES
MODIFIED WITH AXIAL DEHYDROACETIC ACID MOIETIES**Chernii S.¹, *Tretyakova I.*², Losytskyi M.¹, Gerasymchuk Yu.³, Chernii V.², Kovalska V.¹¹Institute of Molecular Biology and Genetics NASU, Kyiv, Ukraine²V. I. Vernadskii Institute of General and Inorganic Chemistry NASU, Kyiv, Ukraine³Institute of Low Temperature and Structure Research PAS, Wroclaw, Poland

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Phthalocyanines are widely studied for their biological activity; in particular, they have been shown antibacterial activity, antiprionic and antifibrillogenic properties. The spontaneous protein self-assembly into amyloid fibrils, characterizes a number of pathologies, including neurodegenerative diseases. The search for the agents that are able to suppress or redirect fibril formation could be useful for controlling protein aggregation.

Zr phthalocyanine quite easily forms axially coordinated complexes with various β -dicarbonyl compounds. In this work, we have obtained complexes with “hidden” β -diketones – dehydroacetic acid (**1**) and its condensed derivatives (**2**, **3**). For this, we have performed the Knoevenagel condensation reaction to obtain condensed dehydroacetic acid derivatives. These compounds exhibit the properties corresponding to β -diketones. They easily form complexes with metals. Their interaction with Zr phthalocyanine dichloride leads to the formation of corresponding axially coordinated complexes (Fig. 1). The resulting complexes are highly stable fine crystalline substances of dark blue color, with absorption peaks at 330 and 690 nm. For **2** and **3**, an additional absorption band is observed in the region of 400–450 nm corresponding to the absorption band of the axial ligands. The yields for this reaction are 70–80 %. Studied complexes soluble in most organic solvents.

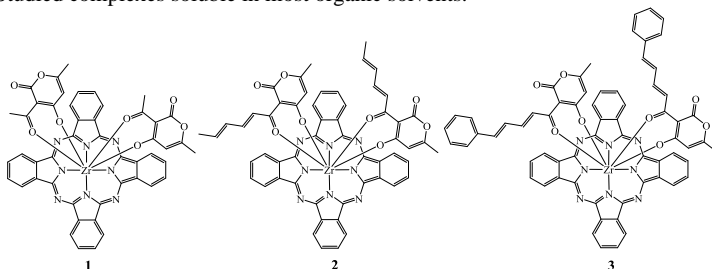


Fig. 1. Chemical structure of Zr phthalocyanines

We have also studied the effect of synthesized Zr phthalocyanines on the insulin amyloid formation. The dye-based amyloid-sensitive assay was used to examine the effect of Zr phthalocyanines on kinetics and intensity of insulin amyloid aggregation. Inhibitory activity for Zr phthalocyanines was from 45 to 68 % with the highest inhibitory activity for compound bearing dehydroacetic acid ligands. Method of scanning electron microscopy was used to determine the morphology of insulin aggregates forming in the presence of studied Zr phthalocyanines. Free insulin forms separate fibrils with length of about 2–4 μm sticking in clusters. Studied complexes induce changes in insulin aggregates morphology – noticeable elongation of insulin fibrils up to 15 μm length with formation of bigger clusters.

Thus, synthesized Zr phthalocyanines with axially coordinated ligands are considered as compounds able to modify the fibril formation reaction.

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