

“Interactions of new supramolecular systems with biomolecules”

Martyna Szymańska

STRESZCZENIE W JĘZYKU ANGIELSKIM

Supramolecular chemistry is an amazing discipline that combines the different fields of science: chemistry, physics and biology. Thanks to that, it was possible to synthesize very complex systems due to the phenomenon of self-assembly. An example of self-organization in living organisms is the DNA helix. Intermolecular interactions are a very important element for creating complex systems from smaller elements. Such structures have completely different properties than their precursors. They can have a wide variety of properties such as: optical, magnetic, catalytic and biological.

The PhD thesis consists of four scientific publications. The synthesis and properties of complex compounds with Schiff base ligands are described therein. *d*-Electron metal ions were selected for their synthesis due to their diverse properties and various coordination motifs. The work mainly focused on understanding the mechanism of binding of the obtained compounds with model biomolecules such as: CT-DNA and BSA protein.

In the first paper (*Molecules*, 2019, 24(17), 3173), various Fe(II/III) complexes with six different Schiff ligands were studied. The influence of the structure of ligands and complexes related to their ability to form hydrogen bonds on their interaction with CT-DNA was determined. Studies have shown that the absence of free hydrogen bonding donors and acceptors in the ligand molecule facilitates the sliding of compounds between base pairs.

The aim of the second paper (*J. Mol. Liq.*, 2020, 319, 11418) was to introduce a thiophene group to the thiophene benzothiazole ligand **TBT C₁₃H₁₁N₃S₂** and to determine its effect on the type of interaction of compounds with DNA and BSA. The **TBT C₁₃H₁₁N₃S₂** and the complex compound **[Ag(TBT)₂]⁺** were re-synthesized. The study showed that the ligand molecule **TBT C₁₃H₁₁N₃S₂** with a thiophene subunit plays a key role in binding to DNA. Fluorescence quenching and UV thermal melting studies have shown that the type of binding of the **[Ag(TBT)₂]⁺** complex to DNA is intercalation. Both compounds bind to BSA, but the complex compound **[Ag(TBT)₂]⁺** has a higher affinity to the protein.

In the third paper in the series (*Biomolecules*, 2021, 11(10), 1449), a two-pocket ligand **L** $C_{14}H_{16}N_4S_2$ with thiazole molecules and its bimetallic complex $[Ag_2L_2]^{2+}$ were synthesized. Then, using UV titration, fluorescence titration, UV thermal melting studies, CD measurements and synchronous fluorescence, their types of binding to model biomolecules CT-DNA and BSA were investigated. The influence of the introduction of two metal ions into the complex $[Ag_2L_2]^{2+}$ on the type of interaction was tested. The ligand **L** $C_{14}H_{16}N_4S_2$ and the complex $[Ag_2L_2]^{2+}$ interact similarly with DNA. However, the difference can be seen in the case of the binding of the $[Ag_2L_2]^{2+}$ complex compound to BSA compared to the ligand **L** $C_{14}H_{16}N_4S_2$. CD studies indicate that the $[Ag_2L_2]^{2+}$ complex causes changes in the secondary structure of the protein, while the ligand **L** $C_{14}H_{16}N_4S_2$ does not. Comparing the last two papers, which concerned Ag(I) complexes and their ligands having a thiophene moiety or a thiazole molecule in their structures, it can be concluded from the binding constants that the addition of the second Ag(I) ion results in a stronger binding of the $[Ag_2L_2]^{2+}$ complex to DNA compared to the $[Ag(TBT)_2]^+$ complex.

In the last work (*Dalton Trans.*, 2022, 51, 15648 – 15658), the ligand **L** $C_{26}H_{24}N_4$ based on the *trans*-1,4-diaminocyclohexane subunit was synthesized. Then complexes of a "grid" type with Cu(I) ions and a "triangle" type with Ni(II) ions were obtained. Two multivalent metalosupramolecular complexes of different topologies were obtained due to the selection of metal ions with different coordination numbers. All compounds were structurally and spectroscopically characterized. What is important, the NMR and UV-Vis titration studies show that the reaction with the Cu(I) salt is selective and leads only to the formation of a "grid" compound $[2 \times 2]$. The aim of the research was to check how larger complexes interact with DNA and BSA, and whether they affect the formation of G-quadruplexes. Based on spectroscopic studies, the type of intercalation binding mode of the $[Cu_4L_4]^{4+}$ complex was determined. On the other hand, ligand **L** $C_{26}H_{24}N_4$ and complex compound $[Ni_3L_3]^{6+}$ weakly interacted with DNA. However, it should be mentioned that the $[Ni_3L_3]^{6+}$ complex compound can induce the formation of folded Tel22. It was also checked how the multicationic complexes will bind to the BSA protein. CD studies have shown that the complex compound $[Ni_3L_3]^{6+}$ alters the secondary structure of the protein to some extent, and in turn the complex compound $[Cu_4L_4]^{4+}$ alters the structure of BSA to a great extent. The ligand **L** $C_{26}H_{24}N_4$ does not show significant interactions with BSA. From this study and the fluorescence titration study of BSA, it appears that the $[Ni_3L_3]^{6+}$ complex can be efficiently transported by serum albumin.