

Copper is an element necessary for the proper functioning of the human organism. It is a component of many enzymes, e.g. superoxide dismutase. This protein is responsible for the reduction of free oxygen radicals that are very reactive. As a consequence it can lead to DNA damage, which in turn can contribute to the development of cancer. There are also other copper-containing enzymes that are associated with the biosynthesis of collagen or elastin. On the other hand, copper in high concentrations is toxic. Therefore, its proper Cu (II) transport is important between the blood and the individual cells of the body. The transport of this metal from and to the cell is due to transport proteins, whose dysfunction is associated with Wilson's disease. This illness can lead to inflammation or cirrhosis of the liver, but also to neurological disorders. Unfortunately, the exact mechanism of copper transport is still not fully understood. Copper can be not only bound with such large macromolecules as proteins but also their shorter forms - peptides. Even 3-7 amino acid peptides have strong properties for binding this metal, especially if the sequence has histidine. Such molecules also play an important role in our body. An interesting example is the binding of copper to A β peptides. Such complexes are neurotoxic and are currently widely discussed in the world scientific literature, as it participates in pathogenic processes related to Alzheimer's disease.

In this project, I plan to focus not on known peptides or characteristic motifs binding copper in proteins but to analyze short model sequences. In particular, different variants of the characteristic group of peptides with histidine in the third position (His³) will be prepared. The aim of these studies is to observe the rate of formation of Cu(II) complexes with peptides. In addition, it will be checked how fast copper can be transferred between small molecules and peptides. This observation will be carried out mainly thanks to the stopped-flow technique, which allows monitoring processes in seconds and milliseconds. Thanks to cooperation with centers in Great Britain (Imperial College London) and the Netherlands (Delft University of Technology) it will be possible to study the reaction also in microsecond scale. These experiments will contribute to the understanding of the fundamental mechanism of formation of His³ peptide complexes from Cu (II).

The proposed research is an important supplement to current knowledge about the speed of these processes. In this way, factors that accelerate or inhibit the binding and exchange of copper to peptides and small biological molecules will be determined. This information will allow solving many current research problems related to, for example, the transport of copper in the body. Thanks to this, it will be possible to predict whether a peptide with a specific sequence can play an important role in biological conditions.