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# Chemical and biological properties of conjugates and complexes of boron clusters and macromolecules

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# ABSTRACT

The doctoral thesis presents studies results in two areas: (1) interactions of boron clusters and their derivatives with serum albumin and (2) physicochemical and biological properties of conjugates of boron clusters and peptide thymosin β4.

The research undertaken in the first part of the doctoral thesis was motivated by the growing popularity of boron clusters in medical chemistry, where the unique properties of boron clusters in the design of new drugs are used. Compounds containing boron clusters can act as inhibitors of enzymes or receptor agonists or antagonists. They also show antiviral and antibacterial activity. In addition, boron clusters are used as boron carriers in the antitumor BNCT therapy. For these reasons, we aimed to determine the affinity of boron clusters and their derivatives with serum albumin, the dominant protein in the blood. The studies carried out show that the majority of boron clusters have a significant affinity for serum albumin. Metallacarboranes, especially COSAN, CoD, have the highest and dodecaborane $B_{12}H_{12}$ has the lowest affinity.

In the second part of the study, we wanted to use CoD metallacarborane to create a peptide analog with high affinity for albumin. The biological activity of peptides makes them attractive drug candidates. However, the peptides have a short half-life in the bloodstream, which reduces their effectiveness. The ability to form complexes with albumin may increase the half-life and enhance the therapeutic effect. Research in this area included synthesis, purification and separation of conjugates of thymosin β4 and metallacarborane (Tβ4-CoD) or dodecaborane (Tβ4-B12H12). Next, we determined the modification sites in the amino acid sequence of the peptide, the stability of the conjugates, their affinity for albumin and biological activity. Conjugates were obtained with the attached boron cluster to the side groups of acidic amino acids (Asp or Glu) via an ester bond. The stability of this bond depends on the amino acid that has been modified and on the pH. Tβ4-CoD conjugates have a strong affinity for albumin, whereas Tβ4-B12H12 conjugates do not interact with this protein. Studies of viability of rat H9C2 cardiomyocytes incubated in normoxia and hypoxia in the presence of conjugates showed that the conjugates are not toxic to these cells, and the Tβ4-CoD conjugates retain the activity of the unmodified peptide.