In vitro studies of antidiabetic potential of nitrosyl iron complex with thiosulfate ligands

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The widespread prevalence of type 2 diabetes mellitus (T2DM) and the lack of effective therapy determine the relevance of this study, making the task of finding effective antidiabetic agents one of the most important for medicinal chemistry. Modern clinical drugs for the treatment of T2DM have a symptomatic effect, exhibit serious side effects, long term use of them leads to resistance, so combination therapy and individual selection of drugs are required. Many biological systems are involved in the pathogenesis and progression of T2DM. Therefore the most promising approach to the development of effective drugs for the treatment of T2DM is the search for pharmacologically active compounds that are selective for a complex of therapeutic targets of T2DM: oxidative stress, non-enzymatic glycosylation of proteins, and the polyol pathway of glucose metabolism. This approach is one of the most topical for modern medicinal chemistry.

In this work, we studied the iron nitrosyl complex with thiosulfate ligands $Na_2[Fe_2(S_2O_3)_2(NO)_4]\cdot 4H_2O$ (complex 1) synthesized in the Laboratory of Structural Chemistry, IPCP RAS. Binuclear dinitrosyl iron complexes with functional sulfur-containing ligands are structural synthetic analogs of the active center of non-heme iron-sulfur proteins; they are considered to be natural reservoirs of nitric oxide (NO). Due to their ability to donate NO without additional activation under physiological conditions, these compounds are of considerable interest for the development of potential antidiabetic drugs. Antidiabetic effect of complex 1 was carried out *in vitro* study. It was found that complex 1 acts on the therapeutic targets of T2DM: it inhibits the processes of lipid peroxidation (IC_{50} = 0.4 мМ) and non-enzymatic glycosylation of albumin protein (IC_{50} = 47.4 ± 7.6 мкМ), also reduces the catalytic activity of the aldose reductase: enzyme of the polyol pathway of glucose metabolism ($K_i = 5.25\cdot 10^{-4}$ M). We present for the first time that one of the mechanisms of the antioxidant action of complex 1 is its ability to scavenge free radicals due to NO donation. The data obtained indicate the prospects for further study of iron nitrosyl complexes in order to create a new class of effective drugs for the treatment of T2DM and its complications.

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