ABSTRACT

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Oxidative stress plays an important role in many disorders including cardiovascular diseases. Fenton reaction catalysed by intracellular redox-active iron is an important source of highly reactive and toxic hydroxyl radicals. Hence, shielding of free iron ions seems to be an advantageous strategy for prevention of further propagation of oxidative stress and myocardial damage. Results from our laboratory as well as other groups have shown promising cardioprotective effect in *vitro* as well as *in vivo* experiments. On the other hand, excessive depletion of iron may result in toxicity to the cells.

The aim of this project was therefore to examine new iron prochelators, which chelating activity develops only after activation by reactive oxygen species. Boronyl ester of salicylaldehyde isonicotinoyl hydrazone (BSIH) and its derivate BSIH-PD were examined *in vitro* for their potential protective properties against toxic reactive oxygen species (ROS). Furthermore, own toxicities of studied compounds were examined.

Cytotoxicities were assayed on H9c2 cardiomyoblast cell line by MTT and neutral red uptake assays on 96 well plates. Epifluorescence microscopy was used for photo documentation of cellular morphology and damage, together with fluorescent stainings for mitochondrial inner membrane potential (JC-1 probe) and apoptosis/necrosis (propidium iodide and Hoechst 33342).

Results of these experiments have shown very low own toxicity of BSIH, which was also able to significantly protect the H9c2 cells from the oxidative injury induced

by exposure of cells to 200 μM H_2O_2. The lowest effective concentration of BSIH was 100 μM, and its protective effects further increased with concentration. Second prochelator BSIH-PD has shown higher own toxicity, which negatively influenced its protective potential. This inherent toxicity apparently resulted in decrease of protection at concentrations > 300 μM. In comparison, parent chelator SIH protected the H9c2 cells already at lower concentration levels (3 μM). However, it was not able to restore viability to more than 50 % of control values due to its own toxicity.