ABSTRACT

Recent evidence suggests that oxidative stress plays a crucial role in the pathogenesis of many serious cardiovascular diseases. Hydroxyl radicals, which are formed by catalytic effect of free cellular iron, belong among the most reactive and toxic forms of reactive oxygen species (ROS). Iron chelation could therefore effectively prevent the ROS formation. This study deals with toxicity (reduction cell viability as determined by neutral red uptake assessment) of hydrogen peroxide (H_2O_2) and *tert*-butyl hydroperoxide (t-BHP) on H9c2 rat cardiomyoblast cell line and with capability of the iron chelator salicylaldehyde isonicotinoyl hydrazone (SIH) to prevent this damage.

24-hour incubation with H_2O_2 (IC_{50}= 81.5 μM) or t-BHP (IC_{50}= 66.4 μM) dose-dependently resulted in pronounced change of cellular morphology, mitochondrial depolarization and cell death. Co-incubation with SIH dose-dependently reduced or abolished cell damage and morphological changes (EC_{50}= 1.2 μM for toxicity of 100μM H_2O_2, EC_{50}= 5.7 μM for 200μM H_2O_2 and EC_{50}= 2.9 μM for 100μM t-BHP, EC_{50}= 8.8 μM for 200μM t-BHP, respectively). 100μM SIH was able to completely protect cells exposed to as high as 300μM H_2O_2 or t-BHP concentrations. Own toxicity of SIH tested by 24-hour incubation (10 - 600 μM) was very low and did not reach the IC_{50} value, the 72-hour SIH incubation showed IC_{50}= 447.1 μM.

This study confirms key role of free cellular iron in peroxidative cell damage and points to significant protective ability of iron chelation with SIH against Fenton type of oxidative stress induced by both H_2O_2 and t-BHP.