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## ANTIOXIDANT AND ANTIAPOPTOTIC ACTIVITIES OF COPPER COMPLEXES WITH SCHIFF-BASE DERIVATIVES OF L-HISTIDINE UPON IRRADIATION

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Numerous data have demonstrated the induction of apoptosis by ionizing radiation (IR) through activation of Bax signaling pathway. It has been also shown the key role of antioxidant enzymes, namely superoxide dismutase (SOD) and catalase, in protection of cells from aberrant apoptosis stimulated by reactive oxygen species (ROS) upon IR.

The purpose of this study was to determine whether copper complexes of Schiff-base L-histidine derivatives, early shown to increase viability of the experimental animals after IR, may affect the defense capabilities of the antioxidant system and prevent the upregulated apoptosis in radiation conditions. Among targeted compounds were: Cu(II)(picolinyl-L-histidine)<sub>2</sub>, Cu(II)(nicotinyl-L-histidine)<sub>2</sub> and Cu(II)(isonicotinyl-L-histidine)<sub>2</sub>.

Experiments were performed using white male rats with the weight of 160-180 g. The animals were divided into the following groups: 1. intact animals; 2. irradiated animals (5 Gy; control); 3. animals treated subcutaneously (s/c) with radioprotectors 1 hour prior to irradiation in dose of 10 mg/kg. Blood samples were collected on days 3-28 after IR exposure. Each sample was divided into two aliquots: one was used to obtain serum for determination of Bax levels by ELISA; another was immediately used to obtain hemolyzed erythrocytes for further measurement of SOD and catalase activities by spectrophotometric assay.

Experimental data revealed that all tested compounds have SOD-mimetic effects differed from each other by duration. The detected increase in SOD activity was as much as 2-3-fold compared to the activity of this enzyme in control group, which was 2-3-fold lower than in norm. In addition, all tested compounds decreased IR-induced high BAX levels up to norm. The most pronounced effects were observed in case of Cu(II)(Isonicotinyl-L-histidine)<sub>2</sub>, which also increase the activity of catalase.

On the base of the result obtained we concluded that Cu(II)(Isonicotinyl-L-histidine)<sub>2</sub>, may be recommended as multifunctional radioprotective agent.

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Key words: Schiff-base derivatives, L-histidine, copper complexes, ionizing irradiation, superoxide dismutase, catalase, apoptosis, Bax.

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