

**Radioprotection by Cu(II) Chelates of Nicotinyl-L-Aminoacidates**

M. Malakyan, S. Bajinyan, A. Boyajyan, D. Yeghiazaryan, V. Matosyan and V. Tonoyan

*Scientific Center of Radiation Medicine and Burns, Davidashen, P.O. Box 25., 0048, Yerevan, Armenia*

*labbio@web.am*

Essential metalloelement chelates presents a promising class of compounds for search and development of novel anti-radiation agents, study of which offers a new approach to overcome the pathological effects of ionizing radiation. In this study Cu(II) chelates of Nicotinyl-L-Tyrosinate and Nicotinyl-L-Tryptophanate Schiff Bases were synthesized and investigated as radioprotectors in animal experiments against injuries caused by ionizing irradiation. Based on the assessment of average life-span indices and 30-day animal survival after radiation exposure at LD50/30 (4.8 Gy) or LD100/30 (8.7 Gy) the radioprotective effects of 0 mg/kg (Vehicle), 10 mg/kg, 20 mg/kg, or 40 mg/kg Cu(II)(Nicotinyl-L-Tyrosinate)<sub>2</sub> or Cu(II)(Nicotinyl-L-Tryptophanate)<sub>2</sub> as well as their parents Schiff Bases were studied in case of single subcutaneous and oral administration to rats 1, 3, 6 and 24 hours prior to X-ray irradiation. The mixture of 4% propylene glycol and 1.4% polyvinyl alcohol in saline was used as a Vehicle for the administration of compounds to animal organism. According to the results obtained, administration of the metallochelates to the rat organism prior to X-ray irradiation provided strong radioprotective effects expressed upon application of all considered dose, mode and time treatment schedules: in groups of animals treated with Cu(II) chelates there was an remarkable increase in the indices of survival and average life-span in a 30-day period post exposure compared to the control Vehicle treated - irradiated rats. The appropriate parents Schiff Bases Nicotinyl-L-Tyrosinate and Nicotinyl-L-Tryptophanate also exerted the radioprotective action. However, these compounds were active as effective radioprotectors only in case X-ray irradiation at a dose level equal to or less than LD50/30. Data of analyses indicated that Cu(II) chelates as well as their initial amino acid Schiff Bases did not avert the development of disturbances of hematological indices of animals exposed at LD50/30. However, the findings of immunological studies have demonstrated the inhibiting effects of these compounds on circulating immune complexes (CICs) in blood plasma, which are the major mediators of immune response and are considered as indicators of the autoimmune and inflammatory components of radiation-induced up-regulated immune response. Unlike to Nicotinyl-L-Aminoacidate Schiff Bases their corresponding Cu(II) chelates diminished the harmful effects of radiation-induced CICs formation not only in case of irradiation at LD50/30, but also at much higher radiation dose levels. Thus, the single administration of Cu(II)(Nicotinyl-L-Tyrosinate)<sub>2</sub> and Cu(II)(Nicotinyl-L-Tryptophanate)<sub>2</sub> at non-toxic doses provides effective radiation protection and high level of survival of exposed animals. Research is performed in the frames of ISTC A-1321 Project.