

P25. Bioactive coordination compounds action on the intensity of the oxidative stress and antioxidant system activity in animals under physiological

Olga Tagadiuc^{1*}, Olga Stirba¹, Lilia Andronache¹, Olga Garbuz², Veaceslav Popa¹

¹*State University of Medicine and Pharmacy Nicolae Testemitanu,*

²*State University of Moldova, Chisinau, Republic of Moldova*

Background: Non-platinum metal coordination compounds (CC) with halogensemi-carbazides based chelation and macrolydic ligands exhibit strong antiproliferative and cytotoxic properties, exceeding tens and hundreds of times antitumor activity of e.g. doxorubicin [Gulea A., et al., 2007, 2009], but their action on normal tissues is insufficient studied. Based on these considerations, the **aim** of research was to study the peculiarities of the influence of the new non-platinum metal CC with chelation and macrolydic ligands – CMD-4, CMD-8, CMJ-23, CMJ-33 și CMT-67, on the intensity of the oxidative stress and antioxidant system activity in the liver of the experimental animals under physiological conditions.

Methods: Biological activity of the CC, was evaluated in experiments on a group of 46 male rats Wistar line, randomly divided into 8 groups. The first group – control (sham), were inject i/m saline solution daily for 30 days. The experimental animals from groups 2-12 were administered subcutaneously the studied CC twice weekly for 30 days: group 2 – CMD-4 (100 nM/kg), group 3 – CMD-4 (1000 nM/kg), group 4 – CMD-8 (100 nM/kg), group 5 – CMJ-23 (100 nM/kg), group 6 – CMJ-33 (100 nM/kg), group 7 – CMJ-33 (1000 nM/kg), group 8 – CMT-67 (100 nM/kg). The amount of the oxidative stress markers – malonic dialdehyde (MDA), nitric oxide (NO), advanced glycation end products (AGE), the ischemia-modified protein (IMP), advanced oxidation protein products (AOPP) and the content of S-nitrosothiols, was determined. Changes the antioxidant protection were assessed by evaluating the activity of superoxide dismutase (SOD), catalase, histidine dipeptide's content and total antioxidant activity levels (AAT).

Results: The study revealed that the level of the MDA, decreases statistically significant by 14%-40% in the liver under the influence of most of the studied CC, except CMD-8 (100 nM/kg) and CMJ-33 (100 nM/kg) that induced just a discrete decrease tendency. The tested CC did not influenced conclusive the levels of NO, except CMD-8 (100 nM/kg), that produced a 40% increase of the NO content compared with the control. The results of our studies show the ability of the tested CC to induce a tendency to decrease the intensity of AGE products formation in the liver. CMD-4 and CMJ-33 (1,000 nM/kg) diminished the amount of the S-nitrosothiols by 16%-20% ($p < 0.05$) compared with the control group. The study reveals that SOD activity decreased statistically conclusive by 24% ($p < 0.05$) after the administration of CMD-4 (1000 nM/kg), while CMD-4 (100 nm/kg) and CMT-67 (100 nM/kg) diminished by 23% ($p < 0.05$) the activity of catalase.

Conclusions: The influence of the tested CC on the studied markers of the oxidative stress and AOS is selective. This selectivity can be the foundation of their particular strong antiproliferative and cytotoxic selective action upon the tumor cells, but not on the healthy one.

* Corresponding author, tel. +373 022 205 136, e-mail address: olga.tagadiuc@usmf.md