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ABSTRACT BOOK

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New approaches to prevent toxic effects of chemotherapy

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Introduction: Due to the attempts to modify the chemical structure of anthracyclines, the adverse effects of this group of chemotherapy drugs have been somewhat reduced. However, the problem of pharmacotherapeutic prevention, primarily of specific myocardial damage, remains unresolved [1].

Materials and methods: Adult Wistar rats (weight: 180-220 g); doxorubicin-KMP (5,0 mg/kg once a week IM 5 weeks); coordination compounds of germanium with nicotinic acid (5,0; 10,0; 30,0 mg/kg IP 35 days) in comparison with niacin in same dosage. In the myocardial and liver homogenates were investigated products of lipid (conjugated dienes, TBA – active compounds and Schiff bases) and protein peroxidation (total, protein-bound and non-protein SH-groups), energy metabolism by ATP-ADP-AMP level and the activity of superoxide dismutase and catalase. Statistical processing of results was performed using t-test or Mann-Whitney test. Quantum-chemical characteristics of molecules were calculated by the "HyperChem rel.7".

Results: The coordination compounds of germanium with nicotinic acid in the presence of intoxication with the doxorubicin reduces the degree of oxidative stress, as evidenced by an increase in the activity of the antioxidant system enzymes, inhibition of lipid and protein peroxidation and normalization in the level of ATP of myocardial and liver tissues ($P<0.05$). Niacin had less pharmacological effect, than as the bioligand with metal. The increased pharmacological activity of coordination compounds of germanium with nicotinic acid versus free nicotinic acid is confirmed by the quantum chemical analysis result.

Conclusions: The results provide a rationale for further studies of coordination compounds of germanium as a potential cytoprotector in chemotherapy with anthracycline antibiotics. Based on the established "structure-action" relationship, the targeted synthesis and the study of new substances of this line with the specified action become promising.

References

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