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5. Vakhrusheva T.V., Sokolov A.V., Kostevich V.A., Vasilyev V.B., Panasenko O.M.

Enzymatic and bactericidal activity of monomeric and dimeric forms of myeloperoxidase.

This study was carried out to compare the enzymatic and bactericidal activity of mature, dimeric myeloperoxidase (MPO) and its monomeric form. Dimeric MPO was isolated from HL-60 cells. Hemi-MPO obtained from dimeric MPO by reductive cleavage of a disulfide bond between protomeric subunits was used as the monomeric form. Both peroxidase and halogenating (chlorinating) activities of MPO were assayed, each of them by two methods. Bactericidal activity of the MPO/Đ•2Đž2/Cl- system was tested using the Escherichia coli laboratory strain DH5a. No difference in the enzymatic and bactericidal activity between dimeric MPO and hemi-MPO was found. Both forms of the enzyme also did not differ in the resistance to HOCl, the main product of MPO. HOCl caused a dose-dependent decrease in peroxidase and chlorinating activity, and the pattern of this decrease was identical for dimeric MPO and hemi-MPO. At equal heme concentration, a somewhat higher bactericidal effect was observed for the hemi-MPO/Đ•2Đž2/Cl- system compared with the dimeric MPO/Đ•2Đž2/Cl- system. However, this is most likely not related to some specific property of hemi-MPO and can be accounted for by the higher probability of contacting between bacterial surface and hemi-MPO molecules due to their two-fold greater number relative to that of dimeric MPO molecules at the same heme concentration. By using Western-blotting with antibodies to MPO, we showed, for the first time, that the dimeric molecule of MPO could be cleaved into two monomeric subunits by HOCl, most probably due to oxidation of the disulfide bond between these subunits. This finding suggests that appearance in blood of MPO corresponding in mass to its monomer may result from the damage of dimeric MPO by reactive halogen species, especially upon their overproduction underlying oxidative/halogenative stress in inflammatory diseases.

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6. Yakimovskii A.F., Shantyr I.I., Vlasenko M.A., Yakovleva M.V., Kryzanovskaia S.Yu.

The influence of acizolum to bioelements content in rat's blood plasma, parenchimal organs and brain.

Zinc content in blood plasma and brain tissue of rats was studied by analytic mass-spectrometry with inductively coupled plasma. In control (saline-treated animal) zinc content in plasma was 3.6Â±1.4 mg/ml, in the liver â€“ 12.5Â±2.5 mg/mg, in the spleen â€“ 10.9Â±4.1 mg/mg, in the brain â€“ 8.7Â±3.0 mg/mg. After a single intraperitoneal injection of zinc donator acizolum (24 mg/kg) zinc content decreased in all examined tissues, especially in brain. After a course of sequential acizolum injections (seven administrations during two weeks) essential elevation of zinc content in blood plasma and tissues investigated was detected. The maximal increase zinc concentration in blood plasma and liver was detected in 15 h after the last acizolum injections. Selen, calcium, copper and iron contents demonstrated a more complex behaviour. The obtained data suggest that prolonged acizolum administration has a significant impact on the bioelements content, and this should be taken into consideration when this zinc donator is used as a drug.

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7. Kalatanova A.V., Makarov V.G., Faustova N.M., Gushchin Ya.I., Makarova M.N.

Evaluation of the cardioprotective effect of ubiquinol on the model of reperfusion injury of rat myocardium.

The cardioprotective effect of ubiquinol on the model of myocardium reperfusion injury in rats was investigated. The study was carried out using mature males of outbred rats. Myocardial ischemia-reperfusion injury was performed after 30-minute ligation of the left coronary artery followed by reperfusion. The main criteria for assessing the development of pathology included the results of electrocardiography, biochemical analysis of blood plasma, histological and histochemical study of the myocardium. Development of the reperfusion damage of the myocardium caused specific changes in non-treated animals. The best therapeutic effect on biochemical indices was provided by a drug with the known cardioprotective activity â€“ MexidolÃ¢ and the tested object ubiquinol at doses of 2-6 mg/kg. Evaluation of the results of electrocardiography allowed to confirm the development of ischemic myocardial damage in all groups. The results of histochemical and histological examination of the myocardium suggest a high cardioprotective activity of ubiquinol at a dose of 3 mg/kg and a potential cardioprotective effect of ubiquinol in doses closest to the therapeutic doses of 2 and 6 mg/kg. Ubiquinol is a dose 9 mg/kg showed signs of prooxidant activity, manifested in the form of aggravation of reperfusion injury of the myocardium. The most effective in the conditions of experimental pathology is 1% solution of ubiquinol, at a dose of 3 mg/kg, whose cardioprotective effect is comparable or higher than that for the reference drug MexidolÃ¢ at the therapeutic dose. In doses that are greater than therapeutic ubiquinol is able to act as a pro-oxidant.

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8. Usynin I.F., Poteryaeva O.N., Russkikh G.S., Zubova A.V., Boiko K.Yu., Polyakov L.M.

Apolipoprotein A-I stimulates secretion of insulin and matrix metalloproteinases by islets of Langerhans.

The development of type 2 diabetes mellitus (DM2) is accompanied by disturbances in lipid metabolism. These include the increase in serum levels of atherogenic fractions of very low-density (VLDL) and low-density lipoproteins (LDL), total cholesterol, triglycerides and apo B. In contrast, the level of antiatherogenic high density lipoproteins (HDL) and the content of apolipoprotein A-I (apoA-I) decreased. To study the effect of the observed metabolic changes on insulin secretion in vitro, we used the islets of Langerhans isolated from the rat pancreas. It has been found that incubation of the islets in the presence of serum of the obese patients and patients with decompensated DM2 leads to a decrease in insulin secretion by 2.4 and 5.0 times, respectively. On the contrary, the addition of HDL to the incubation medium increased the insulin secretion by 3.4 times. A similar effect was observed in the presence of apoA-I, the main protein component of HDL. In the presence of apoA-I, the extracellular activity of matrix metalloproteinases (MMPs) demonstrated a 10-fold increase. The addition of LDL and VLDL to the islets did not change the secretion of insulin and activity of MMP. Our results testify to the important role of HDL and apoA-I in regulation of the insulin secretion by b-cells and the activity of MMPs in the islets of Langerhans.

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9. Taraskina A.E., Zabotina A.M., Nasyrova R.F., Sosin D.N., Sosina K.A., Ershov E.E., Grunina M.N., Krupitsky E.M.

The effect of antipsychotic drug on monoamine receptors in peripheral blood mononuclear cells: affinity linked mechanism.

Schizophrenia is one of the most serious and common mental disorders, which is characterized by high levels of pathogenic heterogeneity as well as neuroimmune abnormalities, which require treatment with antipsychotic drugs. Monoamines are one of the key neurotransmitters which play an important role in neuroimmune interactions of the human organism. We suggest that the quantity of the monoamine receptors on mononuclear cells of the peripheral blood (PBMCs) can be associated with the cytokine profile of patients. With this quantity being a key component of the mental status correction mechanism in antipsychotic therapy. In this study we measured cytokine levels (IL-6, IL-1b and TGF-b) in blood serum, the protein expression status of the serotonin receptor 5HTR2A and the dopamine receptors D1 (DRD1), DRD2, DRD3 in PBMCs of drug-naive, first episode schizophrenia patients before and after the treatment with olanzapine and haloperidol. This study has shown for the first time that the antipsychotic therapy leads to a decrease in protein levels of monoamine receptors in PBMCs associated with the affinity of the drug used. Blood cytokine levels were significantly higher in serum from studied patients as compared with the reference values. The antipsychotic-linked change of the TGF-b production caused by the therapy is probably associated with the reduction of various monoamine receptors. The relationship between the psychopathological status and the protein level of 5THR2A suggests that the amount of 5HTR2A may serve as a potential biomarker for the personalized appointment of the antipsychotic therapy.
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10. Skuratovskaia D.A., Vulf M.A., Kirienkova E.V., Mironyuk N.I., Zatolokin P.A., Litvinova L.S.

The role of single nucleotide polymorphisms in GIPR gene in the changes of secretion in hormones and adipokines in patients with obesity with type 2 diabetes.

The relationship between the rs2302382, rs8111428 and Glu354Gln (rs1800437) polymorphisms in GIPR (glucosedependent insulinotropic polypeptide receptor) gene and plasma levels of mediators involved in the regulation of carbohydrate metabolism in obese patients with type 2 diabetes (before and after a test breakfast) was investigated. The contribution of polymorphic variants of rs2302382, rs8111428 in GIPR gene in the predisposition to type 2 diabetes in individuals belonging to the Slavic population of Russia was found. Polymorphisms rs2302382 and rs8111428 in the GIPR gene were characterized by the nonequilibrium cohesion. The decrease in the level of expression of the GIPR gene in adipose tissue of the small intestine mesentery in the carriers of the CC genotype rs2302382 and AA rs8111428 was associated with the increase in the plasma leptin level, whereas during normal expression, the plasma content of insulin, and GIP (in persons with the genotype of the polymorphism rs2302382 and AG polymorphism rs8111428), resistin and ghrelin (in individuals with the genotype of the polymorphism rs2302382) increased. We propose the stimulating effect of GIP on the secretion of resistin, leptin and ghrelin, with an increase in insulin production in obese patients with type 2 diabetes.
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