

1. Golovko A.I.

## **Amethystic agents influencing toxicodynamics of ethanol.**

The pathogenetic mechanisms of acute alcoholic intoxications are examined and is based the expediency of the search for the amethystic agents, which influence neurotransmitter systems. Promising should be considered the agents, which modulate GABA-systems (partial reverse agonists of benzodiazepine receptors), glutamate (antagonists of metabotropic receptors mGluR2/3), opioid neuropeptides (antagonists of opioid receptors), acetylcholine (reversible inhibitors of acetylcholinesterase and M-cholinoagonists), adenosine (selective antagonists of A<sub>1</sub>-receptors). The amethystic effect manifest also the substances, which modify the second messengers systems (calcium, nitrgic and cascade of arachidonic acid). The most of the means examined possesses the moderate amethystic potential, and effectiveness is manifested predominantly during the preventive application.  
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2. Fedyushkina I.V., Skvortsov V.S., Romero Reyes I.V., Levina I.S.

## **Molecular docking and 3D-QSAR on 16a,17a-cycloalkanoprogesterone analogues as progesterone receptor ligands.**

A series of 42 steroid ligands was used to predict a binding affinity to progesterone receptor. The molecules were the derivatives of 16a,17a-cycloalkanoprogesterones. Different methods of prediction were used and analyzed such as CoMFA and artificial neural networks. The best result (Q<sup>2</sup>=0.91) was obtained for a combination of molecular docking, molecular dynamics simulation and artificial neural networks. A predictive power of the model was validated by a group of 8 pentarans synthesized separately and tested in vitro (R<sup>2</sup><sub>test</sub>=0.77). This model can be used to determine the affinity level of the ligand to progesterone receptor and accurate ranking of binding compounds.  
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3. Razygraev A.V.

## **Homocysteine peroxidase activity in rat blood plasma: stoichiometry and enzymatic character of the reaction.**

Recently it was shown that the presence of rat blood plasma (as well as of erythrocyte hemolysate) in the reaction mixture containing 43 mM Tris-HCl-buffer (pH 8.5), 0.29 mM EDTA, 19.2 mM sodium azide, 1 mM DL-homocysteine (Hcy), and 198 mM hydrogen peroxide (incubation at 37°C) results in a significant acceleration of the decrease in Hcy concentration caused by addition of H<sub>2</sub>O<sub>2</sub>. In this paper, we present data indicating that the observed activity is the homocysteine:H<sub>2</sub>O<sub>2</sub>-oxidoreductase (homocysteine peroxidase) activity. It has been found that the level of H<sub>2</sub>O<sub>2</sub>-dependent Hcy decrease observed in the presence of blood plasma corresponds to homocysteine:H<sub>2</sub>O<sub>2</sub>-oxidoreductase reaction stoichiometry of 2:1 (mole ratio). The activity observed belongs to the protein fraction isolated by saturation with ammonium sulfate to 50%; the specific activity in this protein fraction is significantly higher than that in the whole plasma. The results confirm the hypothesis that the reaction between Hcy and H<sub>2</sub>O<sub>2</sub> at the presence of plasma is catalyzed by the protein component of plasma and this is the homocysteine peroxidase reaction. This activity is not associated with serum albumin, which is known to function as thiol peroxidase, and probably belongs to extracellular glutathione peroxidase (Gpx3).  
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4. Novgorodtseva T.P., Karaman Yu.K., Zhukova N.V.

## **Modification of fatty acid composition of polar and neutral lipids of blood and liver in rat in conditions of prolonged high-fat diet.**

Studied the composition of fatty acids of polar and neutral lipids of plasma, erythrocytes and liver Wistar rats under prolonged high-fat diet. It was established that during long-term (90-180 days) in rats high-fat load is blocking the cells ligand-receptor active capture polyunsaturated fatty acids (PUFAs) in the low-density lipoprotein (LDL). This is confirmed by the accumulation of blood in LDL cholesterol and lipid fractions, esterified n-3 and n-6 PUFA (triacylglycerides, sterols esters, phospholipids), while the deficit these same fatty acids in the lipids of erythrocytes. In the liver under the influence of prolonged high-fat diet increased pool monoenic (18:1 n-9) and polyunsaturated (20:5 n-3, 20:3 n-6, 22:5 n-3) fatty acids. These data suggest that prolonged exposure of rats high-fat diet contributes to compensatory de novo synthesis of fatty acids in the liver. However, due to violations of the receptor active transport of fatty acids synthesized in the liver fatty acids are not captured by cells of the peripheral organs. Identified data allow us to expand the understanding of the role of nutritional factors in the physiology and pathophysiology of the cell, modulation of lipid metabolism.  
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5. Tanygina E.S., Popova T.N., Semenikhina A.V., Matasova L.V., Krylovskiy E.D.

## **The dose-dependent influence of 3,5-dicarbomethoxyphenilbiguanide on activity of the glutathione antioxidant system in heart and blood serum of rats with the experimental myocardial infarction.**

Administration of a synthetic compound with predicted anti-ischemic and cardioprotective activity, 3,5-dicarbomethoxyphenilbiguanidDM, - to rats with experimental myocardial infarction led to a decrease in the lipid peroxidation level, glutathione peroxidase activity, the level of reduced glutathione, activity of NADP-isocitrate dehydrogenase in the heart and blood serum, and also activity of glucoso-6-phosphate dehydrogenase in heart in comparison with their levels in untreated animals with myocardial infarction. This may be attributed to a decrease of free radical processes and reduction of antioxidant system loading. At the same time the increase glutathione reductase activity observed under these conditions in the heart and and blood serum probably associated with specific influence of 3,5-dicarbomethoxyphenilbiguanidDM on this enzyme.

6. *Marchenko M.M., Ketsa O.V.*

**Functional activity of NADH-dependent reductase system in liver and Guerinâ€™s carcinoma microsomal fraction in rats exposed to preliminary irradiation.**

The activity of liver and Guerinâ€™s carcinoma microsomal NADH-dependent reductase system has been investigated in tumor-bearing rats exposed to preliminary irradiation. Preliminary irradiation of rats (before transplantation of Guerinâ€™s carcinoma) resulted in the decrease of NADH-cytochrome b reductase activity and contents of cytochrome b in the Guerinâ€™s carcinoma microsomal fraction in the logarithmic phases of oncogenesis compared with the non-irradiated tumor-bearing rats. The effect of irradiation preceding transplantation of the tumor to rats results in the increase of enzymatic activities of liver microsomal NADH-cytochrome b reductase in the latent and logarithmic phases of tumor growth as compared with non-irradiated tumor-bearing rats. At the same time the contents of cytochrome b decreases. During longer periods after irradiation the investigated parameters approached to those in the group of non-irradiated tumor-bearing animals.

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7. *Kislin M.S., Stroev S.A., Gluschenko T.S., Tulkova E.I., Pelto-Huikko M., Samoilov M.O.*

**Hypoxic preconditioning modifies the activity of prond antioxidant systems in rat hippocampus.**

The effects of repetitive mild hypobaric hypoxic preconditioning upon pro- and antioxidant systems in rat hippocampus were studied. It was found that three-trial preconditioning by mild hypobaric hypoxia (360 mm Hg, 2 h) induced moderate oxidative stress immediately after the last preconditioning trial. In addition, it down-regulated the levels of peptide antioxidants (Trx-1, Trx-2, Cu,Zn-SOD) and several lipid peroxidation products 24 h later.

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8. *Babich O.O., Prosekov A.Y.*

**Optimization of L-phenylalanine-ammonia-lyase liophilization.**

The influence of freezing-thawing on the activity of recombinant L-phenylalanine-ammonia-lyase has been investigated. Conditions of liophilization of recombinant L-phenylalanine-ammonia-lyase at which enzyme loses about 10% of activity in a single freeze-thaw cycle are chosen. Dependence of cryoscopic temperature of enzyme from concentration of protein in a preparation is studied. The optimum temperature of freezing of enzymatic preparation L-phenylalanine-ammonia-lyase for sublimatic drying is chosen.

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9. *Raetska Ya.B., Ischuk T.V., Ostapchenko L.I.*

**Dynamics of rat blood serum biochemical parameters under malignant growth in condition of the antioxidant substance â€™greenization GREEN Râ€™ introduction.**

Under malignant growth, the alterations of blood serum biochemical parameters including activity of studied enzymes were observed. The drug â€™Grinization GRIN Râ€™ was shown to stabilize the tumor growth of Guerinâ€™s carcinoma as well as biochemical parameters in the range close to normal values. The changes of protein metabolism parameters appeared to be significant. Also the considerable changes of AST and ALT activities were demonstrated. In the case, there was significant difference between the groups studied ( $\bar{N} \leq 0.05$ ). Administration of rats with drug â€™Grinization Grin Râ€™ in different doses led to decreasing of average tumor volume in dynamics. Increasing and normalization of total protein level in rats with Guerinâ€™s carcinoma was established under â€™Grinization GRINâ€™ administration in doses 115 mg/kg and 270 mg/kg. The meaning of albumin concentration approached to physiological normal value under â€™Grinization GRINâ€™ administration in dose 270 mg/kg. Meanwhile AST and ALT activities were approaching to normal values in rats with Guerinâ€™s carcinoma under â€™Grinization GRINâ€™ administration in dose 270 mg/kg. Such effects were observed mainly at the 18th and 23th days after tumor inoculation in comparison with tumor control (Guerinâ€™s carcinoma) values.

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10. *Orlov Y.P., Lukach V.N., Dolgih V.T., Soboleva E.L., Ivanov A.V., Ivanova A.M., Boltruchenko A.S., Boronenko V.V., Kozhevnikova E.F., Pozharov S.V.*

**Critical conditions as a logical and appropriate chain of iron methabolism disorders (the summary of experimental studies).**

It is revealed that in all models of critical conditions will activate the free-radical oxidation, decreasing the total antioxidant activity, the concentration of transferrin decreases in the serum of the blood, increase of the concentration of ferritin, the rheological properties of the blood are violated and the signs of endothelial dysfunction are identified. Pre-entered deferoxamine in the dose of 80 mg/kg reduced the intensity of free-radical oxidation processes, restoring the antioxidant potential, concentration of the transferrin, and a lower level of ferritin, contributed to the normalization of blood rheological properties and a reduction of the extent endothelium destruction as a result of the reduction Fe<sup>2+</sup> concentration in blood serum.

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11. *Scherbinina S.P., Levina A.A., Lisovskaya I.L., Ataullakhanov F.I.*

**The effect of exogenous antioxidants on the antioxiidant status of erythrocytes and hepcidin content in blood of patients with disorders of iron metabolism regulation.**

In many diseases associated with impairments in iron metabolism, erythrocytes exhibit an increased sensitivity to oxidative stress induced in vitro. In this study, we have examined the antioxidant status of erythrocytes from healthy donors and from 12 patients with disorders of iron homeostasis by measuring the extent of t-BHP-induced hemolysis in vitro. The extent of hemolysis observed with patient erythrocytes was significantly higher than that observed in experiment with normal cells. After therapeutic infusions of the antioxidants mexidol or emoxypin, oxidative hemolysis in patients was

restored to normal values and blood hepcidin content increased significantly. A significant correlation was observed between hepcidin concentration after treatment and t-BHP-induced hemolysis before treatment. These data suggest that antioxidants may exert a favorable effect under pathological conditions associated with iron overload disease.

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