

1. Raevsky O.A., Liplavskaya E.A., Yarkov A.V., Raevskaya O.E., Worth A.P.

Linear and nonlinear QSAR models of acute intravenous toxicity to mice for organic chemicals.

QSAR analysis of acute intravenous toxicity to mice for 68 monofunctional chemicals is presented. These compounds represent seven classes of organic chemicals: hydrocarbons (6 chemicals), alcohols (13), amides (22), amines (12), ethers (5), ketones (7), nitriles (3). Preliminary consideration of data for these chemicals showed that it is necessary to consider not only linear toxicity - descriptors relationships, but also nonlinear models. The linear and nonlinear QSAR models were considered for each from indicated classes of organic chemicals. Analogical models were constructed for whole subset of monofunctional chemicals. The statistical parameters and robustness of nonlinear models are essential better than statistics of linear models. Replacing a lipophilicity descriptor with molecular polarizability and H-bond ability in nonlinear models permits also to improve statistical characteristics. Clearly, if relationships between the intravenous toxicity of compounds bearing only a single functional group and lipophilicity are nonlinear, then similar relationships must be considered with compounds containing more than one functional group. To check up this idea whole set of small clusters containing structure relative compounds with few functional groups was examined from position of linear and nonlinear relationships between toxicity and lipophilicity. It was estimated in most cases advantages of nonlinear models.

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2. Lukasheva E.V., Efremova A.A., Treshalina E.M., Arinbasarova A.Ju., Medentzev A.G., Berezov T.T.

L-amino acid oxidases: properties and molecular mechanisms of action.

During previous decade L-amino acid oxidases (LAAO) attracted the steady interest of researchers due to their poly functional effects on different biological systems. The review summarizes information concerning the sources, structure, physico-chemical and catalytical properties of LAAO which exhibit antibacterial, antifungal, antiprotozoal, antiviral effects as well as the ambiguous action on platelet aggregation. Special attention is devoted to the elucidation of molecular mechanisms of LAAO action. It is proposed that the unique properties of LAAO are based on their catalytic reaction, which causes the decrease of L-amino acid levels, including the essential amino acids and formation of hydrogen peroxide. The action of liberated H₂O₂ on cells involves the synthesis of oxygen reactive species and the development of necrotic and apoptotic pathways of cell death. The presence of carbohydrate moieties in LAAO molecules promotes their attachment to cell's surface and creation of high H₂O₂ local concentrations. The wide range of LAAO biological effects is undoubtedly connected with their important functional roles in the organism. In particular, it was shown that in the mice brain the LAAO-catalyzed reaction is the single pathway of L-lysine degradation, while in the mice milk LAAO carry out the antibacterial effect and in human leucocytes LAAO take part in fulfilling their defending role. Protector action may be also attributed to the oxidases from the other numerous sources: microscopic fungi, snake venoms and sea inhabitants.

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3. Koudinova N.V., Koudinov A.R., Kezlya E.V., Kozirev K.M., Medvedev A.E., Berezov T.T.

Compensatory mechanisms to heal neuroplasticity impairment under Alzheimer's disease neurodegeneration. I: The role of amyloid beta and its precursor protein.

In-depth scholar literature analysis of Alzheimer's disease neurodegenerative features of amyloid beta protein neurochemistry modification and excessive phosphorylation of tau protein (and associated neuronal cytoskeleton rearrangements) are secondary phenomena. At early disease stage these neurobiochemical mechanisms are reversible and serve to heal an impairment of biophysical properties of neuronal membranes, neurotransmission, basic neuronal function and neuroplasticity, while preserving anatomical and functional brain fields. A β and tau could well serve to biochemically restore physico-chemical properties of neuronal membranes due to a role these proteins play in lipid metabolism. Under such scenario therapeutic block of aggregation and plaque formation of A β and inhibition of tau phosphorylation, as well as pharmaceutical modification of other secondary neurodegenerative features (such as a cascade of oxidative stress reactions) are unable to provide an effective cure of Alzheimer's disease and related pathologies of the Central and peripheral nervous systems, because they are not arraying primary pathogenetic cause. We review the role of A β in compensatory mechanisms of neuroplasticity restoration under normal physiological condition and Alzheimer's disease.

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4. Zorin N.A., Zorina V.N.

Macroglobulin signaling system.

This review will focus on the systematization of knowledge about structure of macroglobulin signaling system, which includes macroglobulin family proteins (alpha-2-macroglobulin, alpha-2-glycoprotein, pregnancy associated plasma protein A), their receptors (LRP, grp78), ligands (proteinases, cytokines, hormones, lipids, et al.) transforming and transcriptional factors for regulation of macroglobulins synthesis. After reviewing the functions of macroglobulin signaling system, and mechanisms of their realization, we discuss the complex and significant role of this system in different physiological and pathological processes.

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5. Kutyreva M.P., Mukhametzyanova A.R., Ulakhovich N.A.

Suppression of activity of *Candida albicans* proteinases by cobalt chloride.

Influence of cobalt (II) chloride on the system of *Candida albicans* proteinase (SAP *C. alb.*) (both in solution and immobilized on a surface of nitrocellulose membranes) has been investigated. In solution cobalt chloride inactivated inducible but not constitutive enzyme. In the heterogeneous system proteolytic effect of the cobalt ion on inducible proteinase was also observed.

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6. *Iskra R.Ya., Yanovych V.G.*

The influence of chromium chloride consumption on peroxidation processes and activity of antioxidant defence in rat tissues.

The supplementation of a standard vivarium food with 200 mg/kg CrCl₃·6H₂O caused an increase in chromium content and a decrease in hydroperoxide and TBARS in most tissues examined. Also in all organs and tissues of rats the activity of glutathione peroxidase, glutathione reductase and catalase increased at action of chromium increased. In brain and kidneys the level of reduced glutathione increased. Superoxide dismutase activity was significantly higher in heart and skeletal muscles of animals and equal in lungs and liver, and in other organs - brain, kidneys and spleen in animals of the studied group the enzyme activity was lower compared to animals of control group. These results demonstrate the regulatory influence of chromium on free radical process in rat tissues.

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7. *Solovyev V.G., Bychevsky A.Sh., Karpova I.A.*

The effect of estrogens and progestagens on biochemical components of hemostasis, platelets, continuous intravascular coagulation and tolerance to thrombin: correction of their effect of antioxidants.

Estrogen and progestin (ethinylestradiol and levonorgestrel, respectively) accelerate LPO in platelets, activate them, increase continuous intravascular coagulation and reduce tolerance to thrombin. Antioxidants limit these effects.

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8. *Dzugkoev S.G., Kozyrev K.M., Gumanova N.G., Dzugkoeva F.S.*

The influence of afobazole on biochemical and histo-patho-morphological parameters of endothelial function at experimental diabetes mellitus in rats.

Oxidizing stress in rats with experimental diabetes mellitus is accompanied by endothelial dysfunction develops. Its biochemical markers are the increase of concentration of blood MDA, the impairments of cell antioxidant defence and a decrease in concentration of total metabolites of NO and expression of endothelial NO-synthetase (e-NOS). Biochemical changes are considered with histopathomorphologic impairments of aortic endothelium. Treatment with afobazole suppressed free-radical oxidation, increased activity of SOD and concentration of total metabolites of NO and a level of eNOS expression and also restored of a histologic pattern of aortic endothelium due to activation of nucleocytoplasmic regenerative processes.

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9. *Shpakov A.O., Shpakova E.A.*

Development of non-hormonal regulators of adenylyl cyclase signaling system on the basis of peptides, derivatives of the third intracellular loop of somatostatin receptors.

In the majority of the serpentine type receptors the third intracellular loop (ICL-3) is responsible for interaction with heterotrimeric G-proteins and for transduction of hormonal signal to the enzymes, generators of the second messengers. It was found that the peptides corresponding to ICL-3 influence functional activity of hormonal signaling systems in the absence of the hormone and, in consequence, can be considered as prototypes for the development of selective regulators of these systems. We have originally synthesized peptides corresponding to C-terminal regions 255-269 and 240-254 of ICL-3 of type 1 and 2 rat somatostatin receptors (Som1R and Som2R). Micromolar concentrations of these peptides activated Gi-proteins and inhibited forskolin-stimulated activity of adenylyl cyclase (AC) in rat brain tissues. The peptide 255-269 of Som1R is a selective antagonist of Som1R, and the peptide 240-254 of Som2R is an agonist of Som1R. So, the peptide 255-269 of Som1R decreased the regulatory effects of somatostatin and selective Som1R-agonist CH-275 realized via the receptor homologous to them, while the peptide 240-254 of Som2R, on the contrary, increased AC inhibitory action of CH-275. Both peptides insignificantly influenced regulatory effects of the Som2R-agonist octreotide. Summing up, the peptides studied by us are selective regulators of somatostatin-sensitive AC system. Using the peptides it was shown that ICL-3 of Som1R and Som2R includes the main molecular determinants that are responsible for activation of Gi-proteins and regulation of AC system by somatostatin and its analogues.

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10. *Tanyanskiy D.A., Denisenko A.D.*

Molecular forms of adiponectin: comparative evaluation of their correlations with parameters of carbohydrate and lipid metabolism.

Interrelationship between total, multimer (MM) and oligomer (OM) adiponectin blood concentrations with some metabolic parameters has been investigated in 49 men and 49 women (mean age of 57.3±10.1 years). We have found negative correlations between total blood adiponectin and its MM form content with body mass index, waist circumference, the insulin resistance index HOMA, with blood concentrations of insulin, glucose, free fatty acids, triglycerides and also positive correlations with high density lipoprotein cholesterol content. There was a poor correlation between OM adiponectin concentration with any parameter studied. According to the regression analysis, concentration of total adiponectin but not its MM form was an independent determinant of the HOMA index in women and free fatty acid concentration in men. In the group of men with the low level of adiponectin its MM form but not total adiponectin reversely correlated with the HOMA index and was its independent determinant. Thus, correlation between blood adiponectin concentration and metabolic parameters is associated with its MM rather than OM form. Study of the role of adiponectin in development of metabolic disorders may be limited to determination of total blood adiponectin concentration except a group of male patients characterized by a low level

of this adipokine. In these patients concentrations of the MM form should be determined.

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11. Titarenko O.T., Dyakova M.E., Esmedlyaeva D.S., Pavlova M.V., Yelkin A.V., Alekseeva N.C., Bondarenko B.B.

Peculiarities of the circulating phagocytes functional activity in patients with different forms of drug-resistant pulmonary tuberculosis.

Functional activity of circulating phagocytes (macrophages - Ms and neutrophils - Ns) was studied in 30 patients with infiltrative (I) and 30 patients with fibro-cavernous (FC) pulmonary tuberculosis (PT). Difference of the functional activity of both types of cells depending on the PT form was revealed: more significant increase in the oxygen-depending activity in FCPT while bactericide potential estimated with a zymosane induced NST-test was more pronounced in IPT patients. These data correlate with the blood levels of neopterin and elastase, the markers of the M and N activity, respectively. Participation of intracellular ADA in realization of oxygen-depending processes was demonstrated. Results of the multivariant analysis of the whole complex of the studied phagocyte characteristics, reflect their different roles in their pathological process a prevailing role of Ms in the firstly diagnosed acute tuberculosis process (IPT) and Ns in the chronic progressive process (FCT).

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12. Gorudko I.V., Kostevich V.A., Sokolov A.V., Buko I.V., Konstantinova E.E., Tsapaeva N.L., Mironova E.V., Zakharova E.T., Vasilyev V.B., Cherenkevich S.N., Panasenko O.M.

Increased myeloperoxidase activity is a risk factor for ischemic heart disease in patients with diabetes mellitus.

Using previously developed spectro-photometrical method (Bioorg. Khim. 2009. V. 35. pp. 629-639), a significant increase of myeloperoxidase (MPO) activity was found in blood plasma of patients with type 2 diabetes mellitus (DM2) without of cardiovascular complications, as well as with ischemic heart disease (IHD). Plasma MPO concentration measured by an enzyme-linked immunosorbent assay was significantly higher only in blood plasma of patient with DM2 and IHD. A direct and significant correlation between MPO activity and MPO concentration was observed only in blood plasma samples from healthy donors. Increased MPO activity did not correlate with MPO concentration in blood plasma of patients with DM2 and DM2 with IHD. Taken together, these results highlight the necessity for studying of the MPO role in the development of pathological processes to determine both the amount of enzyme and its peroxidase activity in the blood. The proposed approach gives comprehensive information about the relationship between MPO activity and MPO concentration in patient blood. Since the high concentration of MPO is a diagnostically significant parameter in the prediction of endothelial dysfunction and cardiovascular disease development, the obtained results evidence the contribution of MPO-dependent reactions in cardiovascular complications associated with diabetes. MPO activity may serve as an additional diagnostic criterion for determination of risk of IHD in DM patients.

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