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resulted in 25% increase in survival and 1.5-fold increase in catalase activity in brain homogenates compared to free substances. Using the model of endothelial dysfunction in rats induced by L-NAME it was shown, that RES markedly attenuated the inhibition effect of L-NAME on NO synthesis. RES in phospholipid nanoparticles had the same action at a dose 10 times lower compared to free RES. Load test with resistance (clamping of the ascending aorta for 30 sec) showed that phospholipid formulation of RES possessed more pronounced protective effect due to the stimulation of endothelial NO-synthase.
DOI: 10.18097/PBMC20156105598

6. Sirotkina O.V., Laskovets A.B., Goldobin V.V., Topanova A.A., Karelov D.V., Vavilova T.V.

The molecular mechanisms of platelets activation in patients with cerebrovascular disease.

Cerebrovascular disease is a main cause of mortality and one of the big medical problems. After the vascular wallâ€™s damage the endothelial cells secrete the von Willebrand factor which then connects with its plateletâ€™s receptor GP Ib-V-IX. There are two polymorphisms Thr145Met and T(-5)C of the GP Iba gene associated with arterial thrombosis development. Also the difference in plateletsâ€™ genes expressions was shown in patients with various clinical course of ischemic heart disease. The aim of this study was to investigate the role of plateletâ€™s receptor for von Willebrand factor in plateletsâ€™ activation in patients with cerebrovascular disease. 123 patients with cerebrovascular disease and 97 healthy donors were included into the study. We analyzed the level of receptor for von Willebrand factor on plateletâ€™s membrane by flow cytometry, Thr145Met and T(-5)C GP Iba polymorphiams by PCR-RFLP, the GP Iba gene expression by RT-PCR and ADP-induced platelet aggregation by Born method. We have shown: 1) the 145Met GP Iba allele prevalence in patients with atherotrombotic stroke development due to macroangiopathy; 2) the pre-mRNA transform into the mature mRNA in activated platelets and this process may be stopped by the antiplatelet therapy by acetylsalicylic acid.
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7. Ulanova T.S., Gileva O.V., Stenno E.V., Veikhman G.A., Nedochitova A.V.

Determination of strontium content in whole blood and urine by ICP-MS.

Parameters of strontium determination in the whole blood and urine of children living near ore deposits containing up to 20% strontium sulfate have been determined. The average strontium content in the whole blood of two children groups of 109.52Â±11.07 mg/L and 131.62Â±12.95 mg/L, significantly exceeded the level in the comparison group 44.2Â±4.24 mg/L. The average strontium contents of two groups of children in urine were 1252.3Â±332.2 mg/L and 1341.5Â±241.8 mg/L, these values were 4.2 and 4.5 times higher than in the comparison group 296.4Â±61.5 mg/L. The conditions for blood and urine sample preparation were optimized to reduce measure errors and to determine strontium at the reference concentration level. The accuracy of the results has been confirmed by analysis of the standard samples SeronormTM Whole Blood L1, L2, L3 and SeronormTM Urine.
DOI: 10.18097/PBMC20156105613

8. Trofimenko A.S., Gontar I.P., Paramonova O.V., Simakova E.S., Zborovskaya I.A.

Experimental modeling of nucleoprotein disposal disorders in systemic lupus erythematosus.

The objective of this research was to adapt the experimental model simulating the nucleoprotein disposal disorders in systemic lupus erythematosus (SLE) for further study of its extracorporeal correction, as well as to assess validity of the model by short-term experiment. Twenty to female Wistar rats were intraperitoneally injected with the chromatin-containing extract from bovine liver followed by intravenous administration of anti-DNA antibodies derived from SLE patients. After these procedures plasma concentrations of anti-dsDNA, circulating immune complexes and DNA became sharply increased, together with distinct elevation of leukocytes. On the contrary, changes in erythrocytes, platelets, total protein concentration, creatinine, asparagine and alanine aminotransferase activities, as well as blood coagulation time were changed insignificantly. Using direct immunofluorescence of cryosections, we detected human IgG deposition in rat kidneys treated in accordance with the simulation protocol. Thus, our model reproduces essential DNA disposal disorders in SLE without any animal death or the life-threatening changes in examined markers during short-term experiment.
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9. Trofimenko A.S., Gontar I.P., Paramonova O.V., Simakova E.S., Zborovskaya I.A.

Extracorporeal treatment of nucleoprotein disposal disorders using the systemic lupus erythematosus model: evaluation of efficacy and safety in a short-term simulated experiment.

Efficacy and safety of the extracorporeal blood perfusion through DNase I- and C1q-containing magnetic beads have been evaluated using the experimental model simulating the nucleoprotein disposal disorders in systemic lupus erythematosus (SLE). The study was performed using 20 rats in which the essential impairments of nucleoprotein catabolism typical for SLE were modeled. The animals were randomized into the experimental group and the placebo perfusion control group. Rats of the experimental group were characterized by the statistically significant reduction of increased levels of circulating immune complexes and plasma DNA as well as diminished levels of plasma creatinine and kidney IgG deposition as compared with placebo controls. During short-term experiment there were neither animal deaths nor substantial blood cell destruction and hepatotoxicity signs.
DOI: 10.18097/PBMC20156105622

10. Narezhnaya E., Krukier I., Avrutskaya V., Degtyareva A., Igumnova E.A.

Determination of glutamic acid in biological material by capillary electrophoresis.

The conditions for the identification and determination of Glutamic acid by capillary zone electrophoresis without their preliminary derivatization have been optimized. The effect of concentration of buffer electrolyte and pH on determination of Glutamic acid has been investigated. It is shown that the 5 Mm borate buffer concentration and a pH 9.15 are optimal. Quantitative determination of glutamic acid has been carried out using a linear dependence between the concentration of the analyte and the area of the peak. The accuracy and reproducibility of the determination are confirmed by the method â€œintroduced - foundâ€•. Glutamic acid has been determined in the placenta homogenate. The duration of analysis doesnâ€™t exceed 30 minutes. The results showed a decrease in the level of glutamic acid in cases of pregnancy complicated by placental insufficiency compared with the

physiological, and this fact allows to consider the level of glutamic acid as a possible marker of complicated pregnancy.
DOI: 10.18097/PBMC20156105628

11. Ivanov A.S., Medvedev A.E., Buneeva O.A., Gnedenko O.V., Ershov P.V., Mezencev Y.V., Yablokov E.O., Kaluzhsky L.A., Florinskaya A.V., Moskaleva N.E., Zgoda V.G.

Influence of gravity discharge on the content of isatin-binding proteins in mice: results of ground-based and space research under the program Bion-M â„–1.

Isatin-binding activity of mice liver proteins has been investigated in the samples from the control and flight groups by using the methods of biosensor and proteomic analysis. It was found the higher isatin-binding activity in mice of flight group. The content of a number of individual isatin-binding proteins in the samples of the flight groups differ slightly from the ground control. However, in samples from animals which have weekly post-flight adaptation, the level of certain proteins was significantly increased. The latter allows us to assume that the main events in the proteome of mice (at least in subproteome of isatin-binding proteins), occurs in early post-flight period.
DOI: 10.18097/PBMC20156105632

12. Spasov A.A., Smirnova L.A., Grechko O.U., Raschenko A.I., Shtareva D.M., Anisimova V.A.

Pharmacokinetic and analgesic properties of the injectable dosage form of a new imidazobenzimidazole derivative RU-1205 with kappa agonist activity.

Pharmacokinetic properties of imidazobenzimidazole derivative compound RU-1205 were investigated after subcutaneous administration to rabbits as a substance and a dosage form (lyophilisates for injection) at a dose of 25 mg/kg. The lyophilisate was characterized by high values of the relative bioavailability. In tests, the â€œhot plateâ€• and â€œvinegar crampsâ€• the dosage form and the substance exhibited the same analgesic effect.
DOI: 10.18097/PBMC20156105636

13. Verevkin A.N., Popova T.N., Agarkov A.A., Semenikhina A.V.

Effect of melaxen on free radical processes intensity and some antioxidant enzymes activity in rats liver and blood serum under type 2 diabetes mellitus.

The effect of melaxen on free radical processes and activity of superoxide dismutase and catalase in rats with type 2 diabetes mellitus (T2DM) has been investigated. It was established that melaxen administration to diabetic rats caused a decrease of the intensity of free radical processes as evidenced a decrease of the lipid peroxidation primary products content and biochemiluminescence parameters. The activity of the antioxidant enzymes changed towards normal values. These effects were probably induced by the correction of the melatonin level at the result of the melaxen action.
DOI: 10.18097/PBMC20156104640

14. Eldarov M.A., Sklyarenko A.V., Dumina M.V., Medvedeva N.V., Jgoun A.A., Satarova J.E., Sidorenko A.I., Emperian A.S., Yarotsky S.V.

Recombinant cephalosporin-acid synthesase: optimisation of expression in E.coli cells, immobilisation and application for biocatalytic cefazolin synthesis.

Cephalosporin acid synthetase (CASA) is responsible for specific to synthesis of cephalosporin-acids, its expression in Escherichia coli cells is accompanied by accumulation of unprocessed insoluble precursor. In order to optimize conditions of recombinant CASA production we have studied the effects of several parameters of strain cultivation, including growth media composition, temperature, and inoculation dose. Also plasmids for production of CASA variants with the signal sequence of Erwinia carotovora L-asparaginase (ansCASA) and â€œleaderlessâ€• CASA were created in search of more efficient expression constructs. Removal of the N-terminal secretion signal sequence reduced the production of functionally active CASA more than 10-fold and inhibited strain growth. Insertion of the L-asparaginase signal sequence increased the specific enzyme activity in the resultant recombinant strain. The ansCASA producing strain was used to develop the method of immobilization of the recombinant enzyme on an epoxy-activated macroporous acrylic support. The resultant biocatalyst performed effective synthesis of cefazolin from 3-[(5-methyl-1,3,4-thiadiazol-2-il)-thiomethyl]-7-aminocephalosporanic acid (MMTD-7-ACA) and methyl ester of 1(H)-tetrazolilacetic acid (ÐœETzAA), under mild conditions a transformation level of MMTD-7-ACA to cefazolin of 95% is reached.
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15. Lebedev L.R., Danilenko E.D., Telegina Yu.V., Zaitsev B.N.

An antitumor osteotropic agent based on tumor necrosis factor.

A novel drug for treatment of bone metastases based on human recombinant tumor necrosis factor (TNF-alpha) has been designed. The drug is a molecular structure containing yeast double-stranded ribonucleic acid (dsRNA) covered by the conjugate of polyanion dextran with TNF-alpha and bisphosphonate, alendronic acid. The structure is characterized by the combination of substances possessing antitumor activity (TNF-alpha, dsRNA) and a vector molecule (bisphosphonate) providing tropism to hydroxyapatite, the main mineral component of the bone tissue matrix. The conjugation conditions were optimized and the conjugates of TNF-alpha and alendronic acid with dextran were synthesized. Molecular structures were obtained by self-assembly, and the resulting complexes were separated by gel filtration on Sepharose CL-6B. The electrophoretic analysis method revealed decreased mobility of dsRNA in the complex with the conjugate as compared to the mobility of the original dsRNA. This confirms formation of the designed structures. Transmission electron microscopy confirmed the presence of particles with sizes of 30-40 nm in the drug. Evaluation by the sorption/desorption method showed a higher affinity of TNF-alpha conjugates to hydroxyapatite as compared to the original TNF-alpha molecules (from 1.0 to 1.8 mol/L vs. 0.3 mol/L of potassium phosphate buffer for desorption, respectively).
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16. Kruchinina A.D., Gengin M.T.

Effect of reboxetine on activity of carboxypeptidase E in the nerve tissue of rats.

Depression is one of the most common mental disorders, but its etiology is not completely understood. It is assumed that peptidergic system components are involved in the formation of this pathology. Neuropeptides play an important role in the regulation of mental and emotional states. Ð¡arboxypeptidase E is a key enzyme of peptide processing; it regulates neuropeptide levels in the various structures of the nervous system. We have studied effects of a single dose of reboxetine on the activity of carboxypeptidase E in various brain regions and the adrenal glands of rats. The reboxetine injection decreased carboxypeptidase E activity in the pituitary gland (12 h after injection), in the pituitary gland, the quadrigeminal bodies, the medulla oblongata, the hypothalamus, the hippocampus and the amygdala (24 h after injection), in the pituitary gland and striatum (72 h after injection). The enzyme activity in adrenal glands remained basically unchanged. Apparently, the decrease of carboxypeptidase E activity may influence the level of regulatory peptides involved in the pathogenesis of depression.

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