

1. Klimov A.N., Parfenova N.S., Golikov Y.P.

One century of the cholesterol model of atherosclerosis.

2012 sees the centennial of the development of the cholesterol model of atherosclerosis by N.N. Anitchkov and S.S. Khalatov. Its appearance became an important stage in the development of atherosclerosis pathogenesis and determined the further directions by Anitchkov's investigations direction as well as others Russian and world researchers. The Anitchkov biography and the history of experimental cholesterol atherosclerosis model creation described in details. This article considers the history of the development of the cholesterol model, some modern concepts on the nature of hypercholesterolemia (Watanabe's genetic model), demonstrating importance of the cell receptors in the homeostasis maintenance.

DOI: 10.18097/pbmc20125801005

2. Buzanovskii V.A.

Electrochemical sensors based on carbon nanotubes and their use in biomedical research.

Electrochemical sensors based on carbon nanotubes are widely used in biomedical studies. According to design the sensors can be divided into three groups: (i) sensors based on a carbon nanotube array; (ii) sensors manufactured by means of composites containing carbon nanotubes; (iii) sensors, which are electrodes with working surface containing carbon nanotubes. The development directions of sensors of the first and the second group, and also sensors of the third group which are manufactured by abrasive immobilization of carbon nanotubes on an electrode surface and by solvent dispersion and casting immobilization of carbon nanotubes on an electrode surface by means of N,N-dimethylformamide, surfactants, and Nafion are analyzed. The general information on manufacturing techniques of these sensors is given. The opportunities of these sensors for biomedical researches are demonstrated.

DOI: 10.18097/pbmc20125801012

3. Pyatakova N.V., Severina I.S.

Soluble guanylate cyclase in the molecular mechanism underlying the therapeutic action of drugs.

The influence of ambroxol - a mucolytic drug - on the activity of human platelet soluble guanylate cyclase and rat lung soluble guanylate cyclase and activation of both enzymes by NO-donors (sodium nitroprusside and Sin-1) were investigated. Ambroxol in the concentration range from 0.1 to 10 μ M had no effect on the basal activity of both enzymes. Ambroxol inhibited in a concentration-dependent manner the sodium nitroprusside-induced human platelet soluble guanylate cyclase and rat lung soluble guanylate cyclase with the IC₅₀ values 3.9 and 2.1 μ M, respectively. Ambroxol did not influence the stimulation of both enzymes by protoporphyrin IX. The influence of artemisinin - an antimalarial drug - on human platelet soluble guanylate cyclase activity and the enzyme activation by NO-donors were investigated. Artemisinin (0.1-100 μ M) had no effect on the basal activity of the enzyme. Artemisinin inhibited in a concentration-dependent manner the sodium nitroprusside-induced activation of human platelet guanylate cyclase with an IC₅₀ value 5.6 μ M. Artemisinin (10 μ M) also inhibited (by 71 \pm 4.0%) the activation of the enzyme by thiol-dependent NO-donor the derivative of furoxan, 3,4-dicyano-1,2,5-oxadiazolo-2-oxide (10 μ M), but did not influence the stimulation of soluble guanylate cyclase by protoporphyrin IX. It was concluded that the signalling system NO-soluble guanylate cyclase-cGMP is involved in the molecular mechanism of the therapeutic action of ambroxol and artemisinin.

DOI: 10.18097/pbmc20125801032

4. Ershov P.V., Gnedenko O.V., Molnar A.A., Lisitsa A.V., Ivanov A.S., Archakov A.I.

Kinetic and Thermodynamic Analysis of Dimerization Inhibitors Binding to HIV Protease Monomers by Surface Plasmon Resonance.

Here, we describe the analysis of kinetic and thermodynamic parameters for binding of peptide and nonpeptide dimerization inhibitors to immobilized HIV protease (HIVp) monomers by using surface plasmon resonance. Molecular interactions were investigated at different inhibitors concentrations (0-80 μ M) and temperatures (15-35 ^\circ C). The kinetic, equilibrium and thermodynamic parameters have been determined. It was found that both inhibitors were characterized by similar interaction parameters. The complex formation is entropically driven process for both inhibitors. The entropic term ($-\Delta\Delta^\ddagger S$) had the value about -20 kcal/mol while the enthalpic term ($\Delta^\ddagger H$) had the positive value about 14 kcal/mol and counteracted the complex formation.

DOI: 10.18097/pbmc20125801043

5. Mezentsev Yu.V., Molnar A.A., Sokolov N.N., Lisitsina V.B., Ivanov A.S., Archakov A.I., Archakov M.A.

Specificity of molecular recognition in oligomerization of bacterial L-asparaginases.

Bacterial L-asparaginases, which are widely used in the antitumor therapy, act only as homotetramers, because their active sites are located at the interface between the subunits of the enzyme. Since salt bridges substantially stabilize L-asparaginase tetramers, we have supposed that oligomerization of bacterial L-asparaginase is a high-avidity process. This assumption was proved by bioinformatic and biosensoric methods. It was shown, that a stable tetrameric complex can be formed only by the subunits of the same L-asparaginase. Using two mutants of L-asparaginase *Helicobacter pylori* it was shown that specificity of molecular recognition is significantly reduced even by single point mutation at the interface of high-homologous closely-related subunits.

6. Baskova I.P., Alekseeva A.Yu., Kostyuk S.V., Neverova M.E., Smirnova T.D., Veiko N.N.

Use of the most recent reagent (CuF) for stimulation of NO synthesis by the medicinal leech salivary cell secretion in the cultures of human endothelium cells (HUVEC) and in rat cardiomyocytes.

The medicinal leech salivary cell secretion (SCS) may stimulate NO-production in cultures of human endothelium cells (HUVEC) and rat cardiomyocytes (RCM). This effect was detected using a NO specific reagent, - the complex Cu²⁺ with a fluorescein derivative (Cu-FI). NO had also been detected in the cells by fluorescent electronic microscopy and determined quantitatively in the cells and in culture fluid by the fluorescence method. SCS stimulated NO synthesis in HUVEC cells (but not in RCM) is accompanied by NO release into intercellular space. Localization of NO synthesis centers is presented and it is shown that the increase in NO levels during the SCS action on HUVEC and RCM is associated with the increase in the activity of eNOS/nNOS, but not iNOS. In endothelial cells SCS activates nitrosylation processes, assessed by the increase of nitrite-ions in the culture medium. It is therefore important to use Cu-FI, other than Griss-reagent, during the first hour of analysis of NO synthesis. The NO-dependent mechanism of SCS action on endothelial cells might be a factor in providing of its positive action in hirudotherapy.

DOI: 10.18097/pbmc20125801065

7. Sirota T.V.

A new approach to studying the autoxidation of adrenaline: possibility of the determination of superoxide dismutase activity and the antioxidant properties of various preparations by polarography.

The reaction of adrenaline autoxidation in an alkaline buffer with the formation of superoxide radicals and the product of its oxidation, adrenochrome, which models the quinoid pathway of adrenaline conversion in the body, is accompanied by oxygen consumption. This reaction is applicable for polarographic determination of the activity of superoxide dismutase and the antioxidant properties of biological and chemical compounds, it is based on evaluation of the latent period and the rate of oxygen consumption, which are measured in the presence of the compounds examined. It was assumed that the neuro- and cardiotoxicity of quinone products of adrenaline oxidation is related not only to their own properties and reactive oxygen species formed but also the hypoxia of those regions of the cell and tissue where the quinoid oxidation of adrenaline occurs.

DOI: 10.18097/pbmc20125801077

8. Li K., Nu L.Z., Khe K.L., Song K.H.

Determination of phenobarbital in human urine and serum using flow injection chemiluminescence.

A sensitive chemiluminescence method, based on the enhance effect of phenobarbital on the chemiluminescence reaction between luminol and dissolved oxygen in a flow injection system, was proposed for the determination of phenobarbital. The chemiluminescence intensity responded to the concentration of phenobarbital linearly ranging from 0.05 to 10 ng·ml⁻¹ with the detection limit of 0.02 ng·ml⁻¹ (3 σ). At a flow rate of 2.0 ml·min⁻¹, a complete determination of phenobarbital, including sampling and washing, could be accomplished in 0.5 min, offering the sampling efficiency of 120 h⁻¹ accordingly. The method was applied successfully in an assay of PB for pharmaceutical preparations, human urine and serum without any pretreatment with recovery from 95.7 to 106.7% and RSDs of less than 3.0%.

DOI: 10.18097/pbmc20125801088

9. Mityanina V.A., Kuptzov V.N., Saveliev S.V., Shvets V.I., Selishcheva A.A.

Erythrocyte lipid composition at different stages of type 1 diabetes in children.

Complete profiles of phospholipid and ceramide molecular species from erythrocyte lipid extracts of children without carbohydrate metabolism disorders, and children with type 1 diabetes were compared by means of high performance liquid chromatography/mass spectrometry. For the first time a statistically significant increase ($p < 0.05$) of lysophosphatidylcholine content in two groups of diabetic children with different duration of the disease (less than one year and more than one year) was found. Statistically significant changes in other lipid classes were not observed. The dependence of the content of phosphatidylcholine and phosphatidylethanolamine molecular species containing arachidonic acid residue (20:4) on the duration of the disease was found. The observed shift in lipid metabolism suggests of phospholipase A2 and chronic inflammatory process at different stages of diabetes mellitus, in cells (erythrocytes), which are not involved in the immune response.

DOI: 10.18097/pbmc20125801095

10. Popov S.S., Shulgina K.K., Pashkov A.N., Zoloyedov V.I., Shvedov G.I., Rakhmanova T.I.

Peculiar properties of glutathione system and nadph-generated enzymes functioning in blood of patients with drug-induced hepatitis under combined treatment with epifamin.

Activity of the glutathione antioxidant system has been studied in patients with drug-induced hepatitis treated with standard base therapy and combined with epifamin therapy. In blood serum of patients before treatment the decrease of reduced glutathione (GSH) level and the increase of glutathione peroxidase (GP) and glutathione reductase (GR) activities versus control were observed. Combined treatment with epifamin changed GSH level to the normal values. Treatment with epifamin was accompanied by pronounced increase in GP and GR activities compared with standard therapy. Activities of the NADPH-generated enzymes, glucose-6-phosphate dehydrogenase and NADP-isocitrate dehydrogenase, which decreased at this pathology, also demonstrated a more significant increase than standard treatment.

DOI: 10.18097/pbmc20125801104

11. Alexeev Y.V., Likhacheva E.V., Tereshkin D.V., Ponomarev G.V., Mazur E.M.

Effective photosensibilizer selection for e.n.t.-organ diseases treatment, based on their accumulation in pathologically changed tissues.

Accumulation of photosensibilisators - derivatives of E6 chlorines ("Radachlorine", "Photoditazine", "Zelevsky's balsam".) in the mucous membrane and selection of most effective sources of emission have been investigated in 30 patients with rhinosinusitis and 10 with tonsillitis. As a source of emission we used light emitting diode (LED) matrix device "ACT" (wavelength approximately 405 nm (Sore band)) and a laser device LAHTA-"MILON"-ML500-SP (wavelength - 662 nm). Drug accumulation in the mucous membrane and changes of their concentrations after emission were evaluated by changes of fluorescence, measured with a LESA-01-BIOSPEC spectrometer. The percent of fluorescence decrease ranged from 50% to 92.7%. This suggests intensive disintegration of photosensibilisators, and consequently, high therapeutic activity of this method. Effectiveness of this method is also confirmed by clinical results.

DOI: 10.18097/pbmc20125801112