

# Biomeditsinskaya Khimiya

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1. Nikandrov V.N., Balashevich T.V.

## **Glycine receptors in nervous tissue and their functional role.**

The literature data on glycine metabolism in neural tissue, mitochondrial Gly-cleaving system, Gly-catching system in neural and glial cells are summarized. The peculiarities of localization and distribution of specific glycine receptors and binding-sites in nervous tissue of mammals are described. Four types of glycine-binding receptors are described: own specific glycine receptor (Gly-R), ionotropic receptor, which binds N-methyl-D-aspartate selectively (NMDA-R), and ionotropic receptors of g-aminobutyrate (GABA A -R, GABA B<sub>1</sub> -R). The features of glycine effects in neuroglial cultures are discussed

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2. Fedorova E.V., Buryakina A.V., Vorobieva N.M., Baranova N.I.

## **The vanadium compounds: chemistry, synthesys, insulinomimetic properties.**

The review considers the biological role of vanadium, its participation in various processes in humans and other mammals, and the anti-diabetic effect of its compounds. Vanadium salts have persistent hypoglycemic and antihyperlipidemic effects and reduce the probability of secondary complications in animals with experimental diabetes. The review contains a detailed description of all major synthesized vanadium complexes having antidiabetic activity. Currently, vanadium complexes with organic ligands are more effective and safer than the inorganic salts. Despite the proven efficacy of these compounds as the anti-diabetic agents in animal models, only one organic complex of vanadium is currently under the second phase of clinical trials. All of the considered data suggest that vanadium compound are a new promising class of drugs in modern pharmacotherapy of diabetes.

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3. Ksenofontova O.I.

## **Introduction of mutations in insulin molecule: positive and negative mutations.**

Introduction of mutations in an insulin molecule is one of the important approaches to drug development for treatment of diabetes mellitus. Generally, usage of mutations is aimed at activation of insulin and insulin receptor interaction. Such mutations can be considered as positive. Mutations that reduce the binding efficacy are negative. There are neutral mutations as well. This article considers both natural mutations that are typical for various members of the insulin superfamily and artificial ones which are introduced to improve the insulin pharmacological characteristics. Data presented here can be useful in developing new effective insulin analogues for treatment of diabetes mellitus.

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4. Grishin D.V., Sokolov N.N.

## **Defensins – natural peptide antibiotics of higher eucariotes.**

The goal of this review is to characterize defensins representing an evolutionary the most ancient family of antimicrobial peptides. It gives general information on functional and structural features of defensins as the main components of the first-line defense of higher eukaryote organisms against infectious agents. The review considers not only current situation in the defensin research but also perspectives of creation of recombinant antimicrobial peptides of biomedical application.

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5. Mosin O.V., Shvets V.I., Skladnev D.A., Ignatov I.

## **Microbic synthesis of deuterium labelled L-phenylalanine with different levels of isotopic enrichment by facultative methylotrophic bacterium *Brevibacterium methylicum* with RMP assimilation of carbon.**

The preparative microbial synthesis of amino acids labelled with stable isotopes, including deuterium ( $^2\text{H}$ ), suitable for biomedical applications by methylotrophic bacteria was studied using L-phenylalanine as example. This amino acid is secreted by Gram-negative aerobic facultative methylotrophic bacteria *Brevibacterium methylicum*, assimilating methanol via ribulose-5-monophosphate (RMP) cycle of assimilation of carbon. The data on adaptation of L-phenylalanine secreted by methylotrophic bacterium *B. methylicum* to the maximal concentration of deuterium in the growth medium with 98%  $^2\text{H}$  and 2% [ $^2\text{H}$ ]methanol, and biosynthesis of deuterium labelled L-phenylalanine With different levels of enrichment are presented. The strain was adapted by means of plating initial cells on firm (2% agarose) minimal growth media with an increasing gradient of  $^2\text{H}$  concentration from 0; 24.5; 49.0; 73.5 up to 98%  $^2\text{H}$  followed by subsequent selection of separate colonies stable to the action of  $^2\text{H}$ . These colonies were capable to produce L-phenylalanine. L-phenylalanine was extracted from growth medium by extraction with isopropanol with the subsequent crystallization in ethanol (output 0.65 g/l). The developed method of microbial synthesis allows to obtain deuterium labelled L-phenylalanine with different levels of isotopic enrichment, depending on concentration of  $^2\text{H}$  in growth media, from 17% (on growth medium with 24,5%  $^2\text{H}$ ) up to 75% (on growth medium with 98%  $^2\text{H}$ ) of deuterium in the molecule that is confirmed with the data of the electron impact (EI) mass- spectrometry analysis of methyl ethers of N-dimethylamino(naphthalene)-5-sulfochloride (dansyl) phenylalanine in these experimental conditions.

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6. Gorbenko M.V., Popova T.N., Shulgin K.K., Popov S.S., Agarkov A.A.

**Effect of melaxen and valdoxan on free radical processes intensity, aconitate hydratase activity and citrate content in rats tissues under hyperthyroidism.**

The influence of melaxen and valdoxan on the biochemiluminescence parameters, aconitate hydratase activity and citrate level in rats heart and liver during development of experimental hyperthyroidism has been investigated. Administration of these substances promoted a decrease of biochemiluminescence parameters, which had been increased in tissues of rats in response to the development of oxidative stress under hyperthyroidism. Aconitate hydratase activity and citrate concentration in rats liver and heart, growing at pathological conditions, changed towards control value after administration of the drugs correcting melatonin level. The results indicate the positive effect of valdoxan and melaxen on oxidative status of the organism under the development of experimental hyperthyroidism that is associated with antioxidant action of melatonin.

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7. Kosenko E.A., Beloushko E.E., Kaminsky Y.G.

**Differences between cerebellum and hippocampus in antioxidant system.**

The effect of portacaval shunting on the antioxidant status of the cerebellum and hippocampus was studied in rats using standard methods of enzymatic analysis. Endogenous ammonia levels and activities of eight antioxidant enzymes were shown to be unequal in two brain regions and to respond differently upon portal-systemic shunt surgery.

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8. Akimov M.G., Gretskeya N.M., Karnoukhova V.A., Serkov I.V., Proshin A.N., Shtratnikova V.Yu., Bezuglov V.V.

**The influence of docosahexaenoic acid moiety on cytotoxic activity of 1,2,4-thiadiazole derivatives.**

Among 3-(2-aminopropyl)-1,2,4-thiadiazole derivatives containing substitution-ready secondary amino group and exhibiting cytotoxic towards rat C 6 glioma cells three compounds with LD 50 values ranged from 6 to 48  $\mu\text{M}$  were chosen. For these compounds amides with docosahexaenoic acid were synthesised and their cytotoxic activity was studied. It was shown that, although docosahexaenoic acid itself was not toxic for C 6 glioma cells, its addition to the amino derivatives of 1,2,4-thiadiazole increased or decreased resultant cytotoxicity. The effect depended on the structure of 1,2,4-thiadiazole substituents. The obtained data show that the acylation of cytotoxic compounds with docosahexaenoic acid does not necessarily lead to the increase of their activity, but sometimes can inactivate a compound. This fact should be taken into account, especially in the case of anti-cancer drug development.

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9. Kotel'nikova O.V., Alliluev A.P., Drozhzhina E.Yu., Koroleva I.S., Sitnikova E.A., Zinchenko A.A., Gordeeva E.A., Melikhova T.D., Nokel E.A., Zhigis L.S., Zueva V.S., Razgulyaeva O.A., Serova O.V., Yagudaeva E.Yu., Rumsh L.D.

**Protective properties of recombinant IgA1 protease from meningococcus.**

The study of enzymatic and protective properties of recombinant IgA1 protease in active and mutant form showed that active form of IgA1 protease exhibited species and type-specificity for mouse and human immunoglobulins. Mutant form, which did not exhibit enzymatic activity, had protective properties against meningococcal infection, induced by meningococcus serogroup A, B and C protecting the mice from lethal infection by living virulent culture of heterologous serogroups of meningococcus. Obtained results make it possible to consider IgA1 protease as a perspective preparation at the stages of development of polyvalent vaccine for protection the people from meningococcal infection of various etiology

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10. Litus E.A., Zaitsev V.G., Verovskij V.E., Goncharova L.V., Dudchenko G.P., Ostrovskij O.V.

**Is cobalt-binding capacity of serum a new perspective diagnostic marker?**

The aim of this study was to determine the reference interval of serum cobalt-binding capacity (CoBC) and to estimate the effect of factors unrelated to oxidative modification of serum albumin on this diagnostic marker. A group of healthy volunteers (n=194), a group of patients with autoimmune diseases (n=44) and a group of patients with diabetes type 2 (n=50) participated in this study. The regional reference interval was found to be 0,462-0,744 mmol Co<sup>2+</sup>/l of serum. The study of serum CoBC in two groups of patients showed that the CoBC level strongly depends on the serum protein profile. Therefore, this diagnostic test may be used for diagnosing ischemia, but other pathologies associated with changes in a ratio of blood protein fractions can also influence the serum CoBC level.

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11. Shcherbina I.A., Lipets E.N., Abaeva A.A., Balandina A.N., Ataulakhanov F.I.

**Influence of temperature on spatial fibrin clot formation process in thrombodynamics.**

In this study we have investigated the process of spatial fibrin clot formation in non-steered platelet-free plasma at the temperatures from 20°C to 43°C using thrombodynamics the novel in vitro hemostasis assay, which imitates the process of hemostatic clot growth in vivo. During data processing the following parameters were calculated: initial ( $V_i$ ) and stationary ( $V_{st}$ ) rates of clot growth which characterize initiation and propagation phases of clotting process, and clot size on the 30 th minute. The temperature dependence of extrinsic and intrinsic tenase activities, which determine values of the initial and stationary clot growth rates, respectively, have been also measured. It was established that the temperature lowering from 37°C to 24°C extends mainly on the initiation phase of clot growth, while the stationary rate of clot growth changes insignificantly. Meanwhile none of the thrombodynamics parameters shows the dramatic change of plasma coagulation system condition at the temperature of 24°C (acute hypothermia). Using the thrombodynamics assay an assumption, that the temperature lowering does not change the state of plasma hemostasis system significantly has been confirmed.

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12. *Shevchenko V.E., Arnotskaya N.E., Ogorodnikova E.V., Davidov M.M., Ibraev M.A., Turkin I.N., Davidov M.I.*

**Search of potential gastric cancer biomarkers using low molecular weight blood plasma proteome profiling by mass spectrometry.**

Gastric cancer, one of the most widespread malignant tumors, still lacks reliable serum/plasma biomarkers of its early detection. In this study we have developed, unified, and tested a new methodology for search of gastric cancer biomarkers based on profiling of low molecular weight proteome (LMWP) (1-17 kDa). This approach included three main components: sample pre-fractionation, matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS), data analysis by a bioinformatics software package. Applicability and perspectives of the developed approach for detection of potential gastric cancer markers during LMWP analysis have been demonstrated using 69 plasma samples from patients with gastric cancer (stages I-IV) and 238 control samples. The study revealed peptides/polypeptides, which may be potentially used for detection of this pathology.

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13. *Latypova E.M., Timoshenko S.I., Kislik G.A., Vitek M.P., Schwarzman A.L., Sarantseva S.V.*

**Investigation of neuroprotective activity of apolipoprotein E peptide mimetic Cog1410 in transgenic lines of drosophila melanogaster.**

The neuroprotective activity of apolipoprotein E (apoE) peptide mimetic Cog1410, containing amino acid sequence of the receptor-binding domain apoE, has been investigated in transgenic lines of *Drosophila melanogaster* expressing human APP and beta-secretase. Expression of two transgenes caused neuropathological processes attributed to Alzheimer's disease: neurodegeneration, cognitive abnormality and amyloid deposits formation in brain. It was shown that Cog 1410 reduces neurodegeneration in brain of transgenic flies and improves cognitive functions (odor recognition). These data suggest that Cog1410 is a potential neuroprotector that can be used in AD treatment.

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