

1. *Ramenskaya G.V., Shohin I.E., Savchenko A.Y., Volkova E.A.*

The dissolution test in biorelevant media as a prognostic tool for modeling of drug behavior in vivo.

The review deals with the modern tool for modeling of drug behavior in vivo, - the dissolution test in biorelevant media, imitating gastrointestinal fluids. The formulations and preparation methods of fasted state simulation intestinal fluid, FaSSIF and fed state simulation intestinal fluid, FeSSIF, are defined. In addition, the dissolution characteristics of APIs from different BCS classes in biorelevant media are described. Possible applications of biorelevant media in regulatory practice and science are also shown.

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2. *Sokolovska J., Rumaks J., Karajeva N., Grinvalde D., Sharipova J., Klusha V., Kalvinsh I., Sjakste N.*

The influence of mildronate on peripheral neuropathy and some characteristics of glucose and lipid metabolism in rat streptozotocin-induced diabetes mellitus model.

Streptozotocin (STZ) was used to induce the diabetic rat model. STZ rats were treated with mildronate (100 mg/kg daily, per os or intraperitoneally for 6 weeks). Body weight, blood glucose, triglyceride, ketone body concentrations, glycosylated hemoglobin percent (HbA1c%), glucose tolerance, and the development of neuropathic pain were monitored throughout the experiment. In the STZ + mildronate group, mildronate treatment caused a significant decrease in mean blood glucose (on week 4) and triglyceride concentrations (on weeks 3-6), significantly slowed the increase in HbA1c% (on week 6) and improved glucose tolerance 120 minutes after glucose ingestion during oral glucose tolerance test versus the STZ group. Mildronate completely protected development of STZ-induced neuropathic pain from the first administration week up to end of the experiment. The obtained data indicate clinical usefulness of the drug for the treatment of diabetes mellitus and its complications.

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3. *Kovalenko N.A., Zhdanov D.D., Bibikova M.V., Gotovtseva V.Y.*

The influence of compound itel1296 on telomerase activity and the growth of cancer cells.

Telomerase is a ribonucleoprotein that synthesizes telomeric repeats and identified as a promising target for anticancer therapy. Here we describe a new compound aITEL1296 as a potent telomerase inhibitor. Its inhibitory activity was a bit higher (IC50 = 0,19±0,02 ng/ml) than that of BIBR1532, one of the most potent telomerase inhibitors known to date. Besides telomerase inhibition aITEL1296 activated apoptotic mechanisms and effectively suppressed proliferation of tumor cell lines (GI50 = 5,0±0,2 ng/ml for most sensitive cell line LnCap) but not normal fibroblast cell line.

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4. *Baskova I.P., Kharitonova O.V., Zavalova L.L.*

Lysozyme activity of the salivary gland secretion of the medicinal leech *h. verbana*, *h. medicinalis* and *h. orientalis*.

Salivary gland secretions of three species of the medicinal leech differ in the level of lysozyme peptidoglycan-lysing activity. Using the synthetic fluorogenic substrate, 4-methyl-umbelliferyl tetra N-acetyl- β -chitotetraosid, the glycosidase activity (as one of peptidoglycan-lysing activities) of salivary gland secretion of three species of the medicinal leech was quantitatively evaluated in comparison with egg lysozyme. It is supposed, that lysozyme activity of the leech secretions is determined not only by 5 isoforms of destabilase-lysozyme, but by some other enzymes which can utilize this substrate. These may be lysozymes other than i- (invertebrate) lysozymes (such as destabilase-lysozyme, or related enzymes).

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5. *Sukhoveeva O.V., Popova T.N., Makeeva A.V., Iskusnykh I.Yu.*

The influence of n-[imino(1-piperidinyl)methyl]guanidine and n-[imino(4-morpholinyl)methyl]guanidine on citrate content, aconitase and citrate synthase activities at ischemia-reperfusion of rats brain.

The influence of some guanidine derivatives on the level of brain citrate, brain activities of aconitase and citrate synthase has been investigated in rats subjected to ischemia-reperfusion. Administration of N-[imino(1-piperidinyl)methyl]guanidine and N-[imino(4-morpholinyl)methyl]guanidine resulted in changes of specific activities of aconitase and citrate synthase towards control values. Under these conditions the citrate level considerably decreased versus rats with untreated ischemia-reperfusion. Treatment with these compounds also decreased the degree of DNA fragmentation markedly increased in rats with ischemia-reperfusion.

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6. *Pogosian L.H., Nersesova L.S., Gazariants M.G., Mkrtchian Z.S., Akopian J.I.*

Some inhibitors of purine nucleoside phosphorylase.

Purine nucleoside phosphorylase (PNP) catalyzes reversible phosphorolysis of purine deoxy- and ribonucleosides with formation (d)Rib-1-P and corresponding bases. PNP plays a leading role in the cell metabolism of nucleosides and nucleotides, as well as in maintaining the immune status of an organism. The major aim of the majority of studies on the PNP is the detection of highly effective inhibitors of this enzyme, derivatives of purine

nucleosides used in medicine as immunosuppressors, which are essential for creating selective T-cell immunodeficiency in a human body for organ and tissue transplantation. The present work is devoted to the study of the effects of some synthetic derivatives of purine nucleosides on activity of highly purified PNP from rabbit spleen and also from human healthy and tumor tissues of lung and kidneys. Purine nucleoside analogues modified at various positions of both the heterocyclic base and carbohydrate residues have been investigated. Several compounds, including 8-mercapto-acyclovir, 8-bromo-9-(3,4-hydroxy-butyl)guanine, which demonstrated potent PNP inhibition, could be offered for subsequent study as immunosuppressors during organ and tissue transplantation.

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7. *Dolgikh M.S., Livak D.N., Krashennikov M.E., Onishchenko N.A.*

The cultivation of bone marrow cells and cell lines on polymeric films.

The cultivation of multipotent mesenchymal stromal bone marrow cells and cells of A-431, MDCK, Vero, 3T3 and Hep-G2 was performed on polymeric films (PVA) with different hydrophobic fatty acid residues. The cells of different types grew on these films with different intensity, but in the most cases comparable with the cultivation control on usual plastic. The examined films were nontoxic to cells and sufficiently adhesive. They did not change pH of cultural media, were optically transparent under microscope and comfortable in the experimental work. These films can be used as a model for the artificial organ construction. The covalent binding of different fatty acids to PVA shows possibility of the adaptable changes of films properties (hydrophobicity and adhesiveness), and therefore possibility of the creation of optimal conditions for different cell types attachment and growth.

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8. *Rogozhina T.V., Rogozhin V.V.*

Phenothiazines are slowly oxidizable substrates of horseradish peroxidase.

Reactions of peroxidase oxidation of triftazine and thioproperazine have been investigated in the presence of horseradish peroxidase using steady state kinetic methods. It has been shown that phenothiazines are slowly oxidizable substrates for horseradish peroxidase. k_{cat} and K_m values have been determined in the range of pH from 4.5 to 7.5. The study of co-oxidation of phenothiazines and o-dianisidine (ODN) revealed that in the presence of aminazine and ODN in the reaction medium both substances follow sequential oxidation. ODN oxidation was not observed until full conversion of aminazine. At pH 4.5-5.5 thioproperazine bound to the enzyme-substrate complex and caused a noncompetitive inhibition of peroxidase. At pH > 5.5 sequential substrate oxidation with preferential thioproperazine conversion occurred. In the range of pH from 4.5 to 7.5 triftazine did not influence ODN oxidation.

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9. *Andreeva I.P., Vorobyeva N.T., Vinnitsky L.I., Bogush S.S., Gavrilova E.M., Egorov A.M.*

Enzyme-linked immunosorbent assay for determination of cyclosporin a in whole blood.

A test-system based on enzyme-linked immunosorbent assay (ELISA) for quantitative determination of cyclosporin A (CSA) in human whole blood has been developed. The detection limit of the method was 25 ng/ml, the linearity of the method in the concentration range 60-1400 ng/ml varied from 94 to 105%, the variation coefficient did not exceed 8%. The novel method exhibited good correlation with radio-immunoassay and polarization fluoroimmunoassay methods; the linear regression coefficients were 0.965 and 0.983, respectively. The developed test system is stable for at least 9 months when stored at 4°C and can be used in clinical practice.

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10. *Gorina A.S., Kolesnichenko L.S., Mikhnovich V.I.*

Catecholamines and their metabolites in children with asperger and kanner syndromes.

Children with Asperger and Kanner syndromes in the stable state demonstrate similar decrease in plasma norepinephrine. In the aggravated state, these changes become more expressed and are characterized by a decrease in plasma tyrosine, norepinephrine, normetanephrine and by an increase in dopamine and homovanilic acid and a decrease in excretion of norepinephrine and an increase in excretion of homovanilic acid, epinephrine and MHPG. Only in children with Kanner syndrome in the aggravated state plasma MHPG increases, excretion of tyrosine decreases and excretion of normetanephrine increases. The observed imbalance in dopamine and epinephrine/norepinephrine systems justifies combined analysis of changes in catecholamines and their metabolites levels as the most informative approach in the study of the effect of autistic disorders.

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11. *Shilina N.M., Komarova O.N., Medvedev F.A., Kon I.Ya.*

Changes in the fatty acid composition of blood cell membranes in children with inflammatory diseases.

Fatty acid composition of erythrocyte and leukocyte membranes has been studied in children (with normal body mass and obesity) with inflammatory diseases of the gastrointestinal tract and children with bronchial asthma in comparison with basically healthy children. Fifty seven children aged from 7 to 14 years were examined: 13 with inflammatory diseases of the gastrointestinal tract (IDGIT) (eosophagitis, gastroduodenitis, stomach ulcer), 25 with obesity stages (I-III) complicated by IDGIT, 9 with bronchial asthma and 10 basically healthy children. The study revealed that both IDGIT and bronchial asthma caused significant and similar changes in fatty acid composition of cell membranes. These included accumulation of ω -3-eicosapentaenoic acid (EPA) and the decrease of docosahexaenoic acid (DHA); this phenomenon observed in both erythrocyte and leukocyte membranes suggests a common feature of the detected changes in fatty acid composition of cell membranes in inflammation. There was a significant decrease in the level of membrane ω -6 polyunsaturated fatty acids (PUFA), first of all arachidonic acid and total ω -6 PUFA. Consequently, EPA accumulation in membranes may be a compensatory response to low dietary arachidonic acid supply and/or its increased synthesis of pro-inflammatory eicosanoids (prostaglandins, leukotriens, thromboxans) during inflammatory process.

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