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1. Li Jesse W.-H., Vederas J.C.

Drug discovery and natural products: end of era or an endless frontier?.

DOI: 10.18097/pbmc20115702148

2. Andrianov A.M., Anishchenko I.V.

Computer modeling of the promising inhibitors of the hiv-1 subtype a replication as a framework for the rational anti-aids drug design.

The model of the structural complex of cyclophilin B belonging to the immunophilins family with the HIV-1 subtype A V3 loop presenting the principal neutralizing determinant of the virus gp120 envelope protein as well as determinants of cell tropism and syncutium formation was generated by molecular docking methods. Basing on the conformational and energy characteristics of the built complex, computer-aided design of the polypeptide able to block effectively the functionally crucial V3 segments was implemented. From the joint analysis of the results derived with the data of literature, the generated molecule was suggested to offer a promising pharmacological substance for making a reality of the protein engineering projects aimed at developing the anti-AIDS drugs able to stop the HIV's spread.

DOI: 10.18097/pbmc20115702161

3. Zykova M.G., Ipatova O.M., Prozorovskiy V.N., Medvedeva N.V., Voskresenskaya A.A., Zakharova T.S., Torkhovskaya T.I.

Changes of doxorubicin distribution in blood and plasma after its inclusion into nanophospholipd formulation.

The drug composition based on the plant phospholipids and the antitumor drug doxorubicin (particle size <30 nm) was obtained using original technology elaborated in the Institute of Biomedical Chemistry (Russian Academy of Medical Sciences). In in vitro experiments demonstrated decreased drug association with blood cells for this nanophospholipid form as compared with free doxorubicin. This was accompanied by a with corresponding increase in its plasma level ans also by drug redistribution from plasma protein fraction to high density lipoproteins. Significance of these changes for doxorubicin biodistributon and antitumor activity is discussed.

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4. Petushok N.E., Tarasov Yu.A., Pekhovskaya T.A., Evkovich I.N., Shevalye A.A., Chumachenko S.S.

Effects of organic selenium substance, selenomethionine,in acute alcohol intoxication.

The effect of the preliminary saturation of rats with selenomethionine (50 g/kg, intragastrically, daily, 10 days) prior to acute alcohol intoxication (5 g/kg, 20% ethanol solution, intragastrically, singly on the 11th day with the exposure for 2 hours) was investigated. The activities of glutathione peroxidases (gastrointestinal mucosa, blood plasma, erythrocytes, liver), the levels of oxidized and reduced glutathione, LPO intensity and blood corticosterone level were studied.

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5. Belevich V.K., Sentchouk V.V.

Biochemical characteristics of iodperoxidase activity of human saliva.

Peroxidase-catalyzed oxidation of iodide in human saliva leads to the formation of a brown product with Î»max 287 nm and 353 nm (I3-) identified by the method of UV-spectrophotometry. I3- directly reacts with starch producing the characteristic blue complex. Salivary iodide peroxidase activity was found to be from 1.2 to 2.3 times higher then the activity of salivary peroxidases with natural substrates (SCN- and Cl-). Optimum for the iodide peroxidase activity in human saliva was found to be near Ñ€Ð• 5.8. Salivary iodide peroxidase activity progressively lowers with the rise of Ñ€Ð• value of the reaction mixture until total loss at the Ñ€Ð•>7.4 was observed. Iodide peroxidase activity in human saliva at Ñ€Ð•>7.4 is masked due to decomposition of I3- with the increase of Ñ€Ð• along with the inhibition of peroxidases and I3- reduction by low molecular weight dialyzable salivary components possibly by Cl- and NCS-. Salivary iodide peroxidase activity was completely inhibited by peroxidase inhibitors (NaN3, 2-mercaptoethanol, thiourea), while addition of the peroxidase alternative substrates (ascorbate, quercetin, thiocyanate) resulted in partial inhibition of iodide peroxidase activity. The results of the study confirm the idea, that high activity of human saliva peroxidase with iodide as a substrate may play a crucial role in the bioavailability and metabolism of biologically active iodide.

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6. Lobanok E.C., Vasilevich I.B., Vorobey A.V.

Accumulation of porphyrins in cells of system of blood induced by 5-aminolaevulinic acid.

The levels and rates of accumulation of porphyrins in lymphoid cells and bone marrow cells treated with exogenous 5-aminolaevulinic acid (ALA) were studied. The dependence of the quantity of porphyrins accumulated in cell on ALA concentrations in the medium had maximum at 0.7-1.0 mM ALA for all the cell types studied (splenocytes, thymocytes, peripheral blood lymphocytes and bone marrow cells). The rate of accumulation of uro-, copro- and protoporphyrins depended on cell types. The lowest and the highest levels were found in splenocytes and highest in bone marrow cells respectively. It is

suggested that photodynamic therapy employing ALA is potentially dangerous for blood cells.
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7. Rebrova G.A., Bykov V.A., Osipova L.A., Rebrov L.B., Vasilevsky V.K.

Modification of collagen during action light.

In work chemical modification of collagen during action visible spectrum sunlight. These changes of collagen were found to indicate a photodegradation and photooxidation processes in collagen.
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8. Aseychev A.V., Azizova O.A., Scheglovitova O.N., Sklyankina N.N., Borisenko G.G.

The influence of oxidized fibrinogen on apoptosis of endothelial cells.

Oxidative stress plays an important role in cardio-vascular diseases and atherosclerosis. Fibrinogen (FB), plasma coagulation protein, is a risk factor of atherosclerosis. Importantly, it can be readily oxidized during oxidative stress and in pathological conditions. FB can promote angiogenesis by supporting migration and proliferation of endothelial cells. On the other hand, recent reports demonstrated cytotoxicity of oxidized fibrinogen (oxFB). Endothelial dysfunction plays a critical role in the atherosclerosis development, therefore it is important to understand the effect of oxFB on human endothelial cells (hEC), and the mechanism of the cell death. Here, we studied influence of oxFB on hEC during 24 h incubation in two conditions: (1) at low serum level (0.1%) and in the absence of growth factors ("starvation"); (2) in full medium (5% FBS) with growth factor supplement. Apoptosis was evaluated using analysis of nuclear morphology, phosphatidylserine externalization on hEC surface and caspase-3 activation. In starvation, we observed significant cell death via apoptosis. FB prevented starvation-induced cell death and caspase activation. Caspase activity in the presence of oxFB was 1.5 times higher as compared to FB, yet oxFB demonstrated significant cell protection during stress. Similarly, in optimal cultivation conditions FB decreased the rate of apoptosis by three times, while oxFB supported cell viability to the lesser extent. Thus, FB can protect hEC in stress conditions (in starvation); oxidative modification of FB diminishes its antiapoptotic properties.
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9. Kolesnichenko L.S., Laletin V.S., Kulinsky V.I.

Influence of Î±-lipoic acid on liver glutathione system of healthy and ehrlich ascites carcinoma transplanted mice.

Influence of Î±-lipoic acid (LA) on liver glutathione system of Ehrlich ascites carcinoma (EAC) transplanted mice was studied. LA causes multidirectional influence on glutathione system of healthy mice. EAC transforms LA influence, strengthening prooxidative effects more expressed at introduction in early terms after inoculation of the tumor. The mechanism explaining realization of LA prooxidative effects as a result of interaction with glutathione system is suggested.
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10. Gavriliuc L.A., Corcimaru I.F., Robu M.V., Lisii L.T.

Glutathione-dependent enzymes and glucose-6-phosphate dehydrogenase of blood in patients with lymphosarcoma (non-hodgkin's disease).

Activities of glutathione-dependent enzymes and glucose-6-phosphate dehydrogenase (GPDH) were studied in blood of the patients with lymphosarcoma (LS). The activity of glutathione reductase (GR), glutathione dehydroascorbate reductase (GDAR), gamma-glutamyltranspeptidase (GGT) and G6PDH in plasma, leucocytes, lymphocytes and erythrocytes of peripheral blood in 30 patients (42-56 years) with LS and in 20 healthy have been determined with spectrophotometric methods (Humalyzer 2000 DE). Leucocytes and lymphocytes were separated from blood using Boyum method. Spearmen method used for correlative analysis. The levels of enzymes activity and results of correlative analysis showed an imbalance of antioxidative system defense and metabolic disturbances in patients with LS. The strong functional interrelation was estimated only between GR and G6PDH in the patients' lymphocytes (r=+0,716; p<0.0005). Interrelation was found between the levels of activity of antioxidative enzymes and activity (stage) of pathologic process, this may be used as the additional biochemical test for differential diagnostics of LS and estimation of the cells proliferative activity.
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11. Bonartsev A.P., Soboleva G.M., Shaytan K.V., Kirpichnikov M.P., Yakovlev S.G., Filatova E.V., Makhina T. K., Bonartseva G.A., Popov V.O.

Sustained release of the antitumor drug paclitaxel from poly(3-hydroxybutyrate)-based microspheres.

Development of systems of medicines with sustained action on the basis of biodegradable polymers is a promising trend in modern pharmacology. Polyhydroxyalkanoates (POA) attract increasing attention due to their biodegradability and high biocompatibility, which make them suitable for development of novel drug dosage forms. We obtained microspheres on the basis of poly(3-hydroxybutyrate) (PHB) loaded with the antitumor drug paclitaxel. Morphology, drug release kinetics and effect on tumor cells in vitro of microspheres were studied. The data on the kinetics of drug release, biocompatibility and biological activity of the biopolymer microspheres in vitro showed that the studied system of prolonged drug release had lower toxicity and higher efficiency compared to the traditional dosage forms of paclitaxel.
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