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on induced aggregation of platelets in the presence of hydrogen peroxide. Antioxidant activity of SOD-CHS-CAT appeared at much lower doses than for other CAT derivatives. We detected the antiaggregation effect of SOD-CHS-CAT for platelet aggregation induced by ADP, serotonin, TRAP (with their different mechanism of action). Novel properties of SOD-CHS-CAT confirmed with its action agains spread-eagle platelets on glass surface. The new characteristics of SOD-CHS-CAT conjugate underline the prospects of its biopharmaceutical development for antioxidant therapy.
DOI: 10.18097/pbmc20125803300

7. Chanyshev M.D., Pustylnyak V.O., Gulyaeva L.F.

Tissue-specific expression of hormonal carcinogenesis target genes in rats treated with polycyclic aromatic hydrocarbons.

We have investigated the effect of polycyclic aromatic hydrocarbons (PAHs) on estrogen- metabolizing genes CYP1A1, CYP1B1, CYP19 and ERÎ± and cyclin D1 genes, which control of cell division in estrogen-depended tissues. Treatment of rats with benzo(a)pyren (BP) or 3-methylcholantrene (MC) significantly up-regulated CYP1A1, CYP1B1 gene expression in liver, uterus and ovary, whereas alfa-naphthoflavone (Î±-NF) did not have any effect. The high level of aromatase gene (CYP19) expression was detected in ovary only. Treatment of rats with BP or MC significantly down-regulated expression of this gene (15- and 5,5-fold, respectively), whereas Î±-NF did not have any effect. BP produced an increase in ERÎ± and cyclin D1 gene expression in rat liver. This effect was not seen with MC and Î±-NF. ERÎ± and cyclin D1 mRNA levels were unchanged in uterus of rats after PAHs treatment. On the other hand, BP treatment caused an increase of the ERÎ± and cyclin D1 mRNA levels (3,5- and 2,5-fold, respectively) in ovary, whereas MC and Î±-NF did not have any effects. Thus, our results give evidence for tissue-specific effects of PAHs on expression of genes, which participate in hormonal carcinogenesis. Moreover, the fact that BP and MC treatment affects the expression of estrogen-metabolizing genes and genes, which control of cell division, supports the view that PAHs may be one of the causes of endocrine disorder and consequent hormonal carcinogenesis.
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8. Makarenkova I.D., Logunov D.Y., Tukhvatulin A.I., Semenova I.B., Zvyagintseva T.N., Gorbach V.I., Ermakova S.P., Besednova N.N.

Sulfated polysaccharides of brown seaweeds - ligands of toll-like receptors.

The interaction of sulfated polysaccharides - fucoidans from brown seaweeds Laminaria japonica, Laminaria cichorioides and Fucus evanescens with Toll-like receptors (TLRs) expressed on membranes of embryonic human kidney epithelial cells (HEK293-null, HEK293-TLR2/CD14, HEK293-hTLR4/CD14-MD2 and HEK293-hTLR2/6) was investigated. In vitro fucoidans specifically interacted with Ð¢LR-2, Ð¢LR-4, and the heterodimer Ð¢LR-2/6 resultated in activation of transcription nuclear factor NF-ÎºB. Analysis of composition the hydrolyzed fucoidan from F. evanescens was carried out by gas-liquid chromatography and chromatography-mass spectrometry. Results indicated the absence of 3-3-hydroxytetradecanoic acid (3-OHC14), the basic component of lipopolysaccharides in the preparation. Thus, the obtained results suggested that fucoidans from brown seaweeds possessing immunotropic activity are independent ligands for TLRs, and are able to induce genetically determined biochemical processes of protection organisms against pathogenic microorganisms.
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9. Moiseeva E.V., Kuznetsova N.R., Svirshchevskaya E.V., Bovin N.V., Sitnikov N.S., Shavyrin A.S., Beletskaya I.P., Combes S., Fedorov A.Yu., Vodovozova E.L.

Liposome formulations of combretastatin a4 and 4-arylcoumarin analog prodrugs: antitumor effect in the mouse model of breast cancer.

The antimitotic agent combretastatin A4 (Ð¡Ð•-4) has been suggested as an antivascular agent for anticancer therapy relatively recently. To reduce systemic toxicity by means of administration in liposome formulations, in this study new lipophilic prodrugs, oleic derivatives of Ð¡Ð•-4 and its 4-arylcoumarin analog (Ð¡Ð•4-Ole and ArC-Ole, respectively), have been synthesized: Liposomes of 100 nm mean diameter prepared on the basis of egg phosphatidylcholine and phosphatidylinositol from bakers yeast have been shown to include completely up to 10 mol. % of Ð¡Ð•4-Ole, or 7 mol. % of ArC-Ole. Also, prodrug bearing liposomes decorated with tetrasaccharide selectin ligand Sialyl Lewis X (SiaLeX) have been constructed to achieve targeting to endothelium under neovascularization. The antitumor activity in vivo was studied in the model of slowly growing mouse breast cancer. Under the used dose (22 mg/kg) as well as the regimen of treatment (four injections, one per a week, starting from the appearance of palpable tumors) cytostatic CA-4 did not reveal any anticancer effect, and oppositely even stimulated tumor growth. Liposome formulations of CA4-Ole did not show such stimulation. However, to achieve pronounced antitumor effect, number of injections of liposomes should be apparently elevated. New antimitotic agent ArC revealed cytotoxic activity of only one tenth value obtained for CA-4 in vitro in the culture of human breast carcinoma cells. Nevertheless, in vivo in the mouse model of breast cancer this compound showed antitumor effect under double Ð¡Ð•-4 equivalent dose. The results demonstrate availability of SiaLeX-liposomes loaded with ArC-Ole: this preparation began to inhibit tumor growth already after the second injection. It is necessary further to choose doses and regimens of administration both for ArC and liposome formulations bearing ArC-Ole.
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10. Lankin V.Z., Konovalova G.G., Tikhaze A.K., Nedosugova L.V.

The influence of glucose on the free radical peroxidation of low density lipoproteins in vitro and in vivo.

It was shown that glucose in concentration 12.5-100 mM stimulated of Cu2+-mediated free radical peroxidation of low density lipoproteins (LDL) from human blood plasma. On the base investigation of kinetic parameters of LDL peroxidation it was stated that intensification of this process in the conditions of our experiments is caused by formation of free radical intermediates of glucose autoxidation during active oxygen species generation in the presence of metal ions with variable valence. It was found that glucose level normalization in the blood of patients with type 2 diabetes during therapy accompanied by significant decreasing of LDL oxidizing. During therapy with sugar-lowering drug metformin which utilizate methylglyoxal the LDL peroxidation from blood diabetes mellitus in vivo inhibited in more higher degree probably in consequence of decreasing of methylglyoxal-dependent generation of superoxide anion radicals as was shown by us early [Biochemistry (Moscow), 2007, 72: 1081-1090; Biochemistry (Moscow), 2009, 74: 461-466].
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