Biomeditsinskaya Khimiya

ISSN 2310-6905 (online), ISSN 2310-6972 (print)

2011 volume 57 issue 3

1. Buneeva O.A., Medvedev A.E.

Mitochondrial disfunction in Parkinson's disease.

Mitochondrial structural and functional abnormalities in Parkinson's disease and experimental animal models of this pathology are described. Special attention is paid to the inactivation of mitochondrial enzymes, mutations in mitochondrial and nuclear DNA, and genomic and proteomic research of mitochondrial proteins in Parkinson's disease and experimental parkinsonism of animals.

DOI: 10.18097/pbmc20115703246

2. Kugaevskaya E.V., Elisseeva Yu.E.

Ace inhibitors - activators of kinin receptors.

Angiotensin converting enzyme (ACE) inhibitors are widely used for treatment of cardiovascular diseases. The effects of ACE inhibitors on the human bradykinin receptors were investigated. The mode of action of ACE inhibitors is considered. There is evidence that ACE inhibitors exert effects on the vascular system that cannot be attributed simply to the inhibition of ACE activity and accumulation of locally produced bradykinin. ACE inhibitors augment bradykinin effects on receptors indirectly by inducing cross-talk between ACE and the B2 receptor when enzyme and receptor molecules are sterically close, possibly forming a heterodimer. ACE inhibitors activate B1 receptors directly and independently of ACE via the zink-binding consensus sequence HEXXH, which is present in B1, but not in B2 receptor. Particular structure of B2 and B1 are represented, as well as receptor amino acids coupled with the G-proteins. Activation of kinin receptors by ACE inhibitors leads to clinically beneficial effects of ACE inhibitors.

DOI: 10.18097/pbmc20115703282

3. Severina I.S., Schegolev A.Yu., Ponomarev G.V., Medvedev A.E.

Inhibition of NO-dependent soluble human platelet guanylate cyclase by isatin.

Isatin (indole-dione-2,3) is an endogenous indole that exhibits a wide spectrum of biological and pharmacological activities. Physiologically relevant concentrations of isatin (ranged from 1 nM to 10 M) did not influence basal activity of soluble human platelet guanylate cyclase (sGC), but caused a bell-shaped inhibition of the NO-activated enzyme. Inhibition of the NO-dependent activation by isatin did not depend on a chemical nature of the NO donors. The inhibitory effects of ODC (a heme-dependent inhibitor of sGC) and isatin were non-additive suggesting that the inhibitory effect of isatin may involve the heme binding domain (possibly heme iron) and experiments with hemin revealed some isatin-dependent changes in its spectrum. Isatin also inhibited sGC activation by the allosteric activator YC-1. It is suggested that the bell shaped inhibition of the NO-dependent activation of sGC by isatin may be attributed to complex interaction of isatin with the heme binding domain and the allosteric YC-1-binding site of sGC.

DOI: 10.18097/pbmc20115703300

4. Polyakov L.M., Sumenkova D.V., Knyazev R.A., Panin L.E.

The analysis of interaction between lipoproteins and steroid hormones.

Using the methods of ultracentrifugation, gel-filtration and fluorescence quenching, we demonstrated, that plasma lipoproteins bind steroid hormones and can therefore play a role of their active transport form in an organism. High density lipoproteins have revealed the highest affinity to steroids for. It has been found, that protein component of lipoproteins takes part in the formation of lipoprotein-steroid complex. The apolipoprotein A-I, the main protein component of high density lipoproteins, is responsible for binding of steroid hormones. The calculated constants formation of the complexes of lipoproteins with steroid hormones testifies to specificity of linkage. The results obtained allow to considering real opportunity of transfer of steroid hormones into cell by a receptor-mediated endocytosis in structure of lipoproteins complexes.

DOI: 10.18097/pbmc20115703308

5. Tsybulsky A.V., Popov A.M., Artyukov A.A., Kostetsky E.Y., Krivoshapko O.N., Maseyka A.N., Kozlovskaya E.P.

The comparative study of the medical action of lyuteolin, rosmarinic acid and echinochrom A at experimental stress-induced cardiopathology.

The method of the physical load in condition of the coronary circulation of the blood disturbance, caused mesaton injection, induced development rat cardiopathology, bring about of the heart function decompensation and 40% death of experimenthal animals. Under electronic-microscopic study of rat cardiomyocytes are discovered signs to disorganizations of mitochondrial apparatus of these cells. Administration to therapeutic mode of luteolin and echinochrome A preparations has provided to 100% animal probability of survival. At the same time, mitochondrial apparatus of cardiomyocytes was characterized by the normal parameter i.e. given preparations have provided of defensive adative effect at cardiomyocytes level. Similar activities for rosmarinic acid have not shown. Study some metabolic parameter and endocrine status animal has also allowed revealing of therapeutic effect of luteolin and echinochrome A.Findings be evidence of that echinochrome Ð• and luteolin capable to play the important positive role in metabolism of cardiomyocytes by stimulating of mitochondrial biogenesis and by changing of adaptative mechanisms of the organism cardiovascular system protection.

DOI: 10.18097/pbmc20115703314

6. Rotskaya U.N., Ovchinnikova L.P., Vasunina E.A., Sinitsina O.I., Kandalintseva N.V., Prosenko E.A., Nevinsky G.A.

Evaluation of cytotocicity and efficiency of antioxidant protection of hydrophilic derivatives of 2,4,6-trialkylphenols in Escherichia coli cells.

The effects of five new derivatives of 2,6-dialkyl-4-propylphenole containing in para-radical different ionogenic groups (-SO3Na, -S-SO3Na, -S-(NH2)2Cl) in the presence and in the absence of hydrogen peroxide on the survival of E. coli AB1157 cells and its isogenic strain defective in repair enzyme genes were studied. Cell survival treated with hydrogen peroxide was remarkably increased in the presence of (3-(3,5-dimethyl-4-hydroxyphenyl)propyl)-1-sulphonate of sodium (Đ¡1). Replacement of methyl Đ¾rtho-radicals in the structure of Đ¡1 for tret-buthyl or cyclohexyl groups led to a decrease of the compounds ability to protect the cells from exogenic hydrogen peroxide. Between derivatives of 2,6-di-tret-buthylphenol the compound with thiosulphonate group demonstrated properties comparable with those for its sulphonate analog, then a chloride of isotiurone at concentration 3 mM completely suppressed the growth of cells in presence and in the absence of Đ•2Đž2. Compound C1 may be considered as most perspective for detail analysis as antioxidant.

DOI: 10.18097/pbmc20115703326

7. Kosenko E.A., Suslikov A.V., Venediktova N.I., Kaminsky Y.G.

Antioxidant enzymes in erythrocytes from hypertension patients receiving lisinopril monotherapy or combined lisinopril plus simvastatin therapy.

Statins and angiotensin-converting enzyme (ACE) inhibitors have beneficial impact on the serum cholesterol and blood pressure. It is supposed that statins and ACE inhibitors may modify the antioxidative status of erythrocytes. The study objective was to compare the effects of two treatments, lisinopril alone vs lisinopril plus simvastatin, on erythrocyte antioxidant enzyme activities. The study involved 32 patients with arterial hypertension, the initial serum total cholesterol, LDL-cholesterol and triglycerides within the normal range. Patients of two groups, each of 16 subjects, were treated with lisinopril (10 mg/day) or with lisinopril (10 mg/day) plus simvastatin (20 mg/day). Before and after 3 and 6 months of follow-up therapy, activities of superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), glutathione reductase (GLR) in purified erythrocytes were determined. In all patients, significantly higher catalase activity (by 79.3-106.5%, p<0.0001) and significantly lower GPx activity (by 20.7-30.6%, p<0.001) were observed after therapy as compared to the baselines. Just the same results were obtained in both groups (lisinopril and lisinopril + simvastatin), after both periods (3 and 6 month) of treatments. SOD activity was increased only in the lisinopril group and only after 6 months (p=0.0345). No changes of GLR reductase activity were seen under all conditions indicated. Thus, the lisinopril monotherapy and combined lisinopril plus simvastatin therapy exhibit specific, pronounced and equipotent effects on antioxidant enzymes in human erythrocytes. Administration of lisinopril or lisinopril plus simvastatin may protect erythrocytes and other tissues from oxidative damage.

DOI: 10.18097/pbmc20115703335

8. Shumyantseva V.V., Shich E.V., Machova A.A., Bulko T.V., Kukes V.G., Sizova O.S., Ramenskaya G.V., Usanov S.A., Archakov A.I.

The influence of vitamin B group on monooxygenase activity of cytochrome P450 3A4: pharmacokinetics and electro analysis of catalytic properties.

It was shown that vitamin B group permit to shorten the longitude of diclofenak therapy and to reduce the daytime dose of this drug. All three schemes of diclofenac treatment - only diclofenac, diclofenac plus 2 tablets of Gitagamp (mixture of vitamin B group), and diclofenac plus 4 tablets of Gitagamp - gave maximum value of diclofenal in blood through 1 hour after treatment. In the case of diclofenak treatment without vitamins Cmax corresponds to 1137.2Â±82.4 ng/ml, with 2 tablets of Gitagamp - Cmax 1326.7Â±122.5 ng/ml, and with 4 tablets - Cmax 2200.4Â±111.3 ng/ml. Positive influence of vitamin B group on the decrease of pain syndrome was shown. Pharmacodynamics and pharmacokinetics data were confirmed in electrochemical experiments with cytochrome P450 3A4. For enzyme immobilization screen printed graphite electrodes modified with gold nanoparticles and synthetic membrane-like compound didodecyldimethylammonium bromide (DDAB/Au) were used. Electrochemical analysis reviled the influence of vitamin B group on metabolism of non steroid anti inflammation drug diclofenac catalyzed by cytochrome P450 3A4. Riboflavin was the most effective inhibitor of diclofenac hydroxylation by cytochrome P450 3A4 as was compared at 300 M concentration of vitamin B group (B1, B2, B6). These data confirmed the opportunity of pharmacokinetic parameters regulation and the level of pharmacodynamic effects by the influence of vitamin B group on the catalytic activity of cytochrome P450 3A4.

DOI: 10.18097/pbmc20115703343