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Application of natural polyhydroxynaphthoquinone echinochrome A for treatment and prevention of atherosclerosis

Key words: sea urchin, polyhydroxynaphthoquinone, atherosclerosis

In conditions of clinical trial, the effect of low doses of natural polyhydroxynaphthoquinone pigment of sea urchin *Scaphechinus mirabilis* (sand dollar) – echinochrome A was studied as part of Histochrome® medicinal preparation and Thymarin biologically active food additive (dietary supplement), on lipid metabolism, antioxidant status and condition of immune system including cytokine profile, in patients with cardiovascular system diseases. The results of clinical studies on the effects of low doses (0.4 – 2.5 mg/day) of polyhydroxylated 1,4-naphthoquinones on patients with cardiovascular pathology demonstrate correction of lipid and carbohydrate metabolism disorders, as well as functional changes in the immune system in these patients. After treatment with Histochrome, as can be seen from the investigation /experimential data, there is a transition of the immune system to quite different level of functioning, wherein energy supply of the with ATP is normalized through activation of peroxisomal-mitochondrial biogenesis and increase in the number of mitochondria in the cells The increase in HLA-DR expression reflects the strengthening of the capability of immune cells of intercellular cooperation and increases the efficiency of antigen processing and presentation, and the decrease in the expression level of a marker of apoptosis CD95+ is a testament to the completion of the processes of cell renewal in the body.

EchA producing hydrogen peroxide in the body increases the expression of PGC-1α co-activator of the receptors of PPARS family (H_2O_2 is the cause of over expression of PGC-1α [1]), which functioning increases the number of peroxisomes in the cells. The increase in the number of peroxisomes leads to the increase in the content of catalase in these organelles. The decrease in the level of H_2O_2 in the cells exposed to catalase expressed in peroxisomes is the cause of lowering the values of CD95+ after therapy of patients with Histochrome preparation. Hydrogen peroxide is capable of inducing the expression of Fas-ligand (CD178+) in predominantly activated cells of the immune system such as Th1 and natural killers (NK) [3]. The simultaneous increase in the levels of CD95+ and CD178+, apparently contributes to apoptosis of the cells in the body that is confirmed in our study by increased levels of creatine kinase MB – intracellular marker of the decay of cardiomyocytes in the blood of patients after treatment with EchA.

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The observed changes in cytokine profile in patients after their treatment with Histochrome preparation indicate directed action of EchA to normalize the population of macrophages, shifting their differentiation to phase M2, thereby reducing the development of atherosclerotic inflammation. Anti-atherosclerotic effect of Histochrome is most likely associated with the activation by EchA of receptors-activators of peroxisome proliferation and nuclear factor Nrf2, the functioning of which is aimed at the urgent expression of enzymes detoxifying compounds of quinonoid nature, such as DT-diaphorase. In addition to detoxifying functions, this enzyme plays an important protective role in cardiovascular diseases [2]. EchA is the agonist of receptors of PPARs family and, in addition to inhibiting of LDL oxidation and transferring of the immune system to a higher level of functioning and normalizing OXPHOS in it, it eliminates a great numbers of atherosclerotic inflammation.

The data obtained allow recommending Histochrome and Thymarin dietary supplements as a means of complementary therapy for patients with cardiovascular diseases to correct disorders of metabolic processes, as well as for preventive monotherapy among these patients during remission to prolong and stabilize it.

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